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International Journal Devoted to Inflammatory Bowel Diseases

Official Journal of the European Crohn's and Colitis Organisation

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Aims and Scope

The Journal of Crohn's and Colitis is the official journal of the European Crohn's and Colitis Organisation (ECCO) and is concerned with the dissemination of knowledge on clinical, basic science and innovative methods related to Inflammatory Bowel Diseases. The journal publishes original articles, review papers, editorials, leading articles, ECCO Guidelines viewpoints, short reports and letters to the editor. All submitted material is subject to a peer-review process.

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Oral presentations

Oral presentations

OP001
Transmissive Crohn's disease-like ileitis is caused by functional dysbiosis in the intestinal microbiota independent of inflammation-driven Paneth cell failure

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Background: Dysbiosis of the intestinal microbiota is associated with Crohn´s disease (CD). Functional evidence for a causal role of bacteria in the development of small intestinal inflammation is still lacking. Similar to human pathology, TNFdeltaARE/+ (ARE) mice develop a CD-like transmural inflammation with predominant ileal involvement.
Methods: Mice (C57BL6/N-heterozygous ARE and respective WT littermates) were housed under conventional (CONV), specific-pathogen-free (SPF) or germfree (GF) conditions. CONV-ARE mice were treated with vancomycin and metronidazole and disease activity was monitored at the age of 12 to 18 weeks. GF mice were colonized with Escherichia coli LF82 or caecal content from ARE mice. Pathology was assessed by microscopic evaluation of ileal and colonic tissue sections. Granulocyte infiltration and Paneth cell function was quantified by immunofluorescence analysis. Microbial communities were analyzed by high-throughput 16S rRNA gene sequencing (V3/V4 regions). Metaproteomes were measured using LC-MS analysis.
Results: GF-ARE mice were completely free of intestinal inflammation and antibiotic treatment of CONV-ARE mice induced remission of ileitis but not colitis, demonstrating that disease severity and location are microbiota dependent. SPF-ARE mice were free of colitis but developed three different ileitis phenotypes associated with changes in histopathology, granulocyte infiltration, TNF and IL-17 expression and loss of Paneth cell function. 16S rRNA gene sequencing and metaproteomic analysis identified compositional and functional divergence of gut bacterial communities according to the three disease phenotypes. Members of the Clostridiales and specific bacterial enzymes involved in nucleotide and carbohydrate metabolism were associated with inflammation. Transfer of microbiota from SPF-ARE into GF-ARE recipient mice caused CD-like inflammation only with dysbiotic communities from inflamed SPF donors, while recipients of non-inflamed ARE microbiota showed no signs of intestinal inflammation. Loss of Paneth cell function was associated with aberrant lysozyme and UEA-1 expression pattern in the crypt base showing a concomitant but not preceding failure of Paneth cell function in the development of inflammation-driven ileal pathology. Monoassociation with CD-associated E. coli strain LF 82 did not induce inflammation, suggesting that complex bacterial communities are required for disease initiation.
Conclusions: The transfer of a functionally dysbiotic microbiota from inflamed ARE mice induced ileal inflammation in GF mice independent of disease preceding Paneth cell failure, supporting a causal role of bacteria for the development of CD-like pathologies in the susceptible host.

OP002
UK IBD twin and multiplex registry: Concordance and environmental risk factors of twins with IBD

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Background: The UK IBD Twin and Mutliplex Registry is a research database established in October 2013; this study reviews concordance and environmental risk factors of twins recruited. Previous twin studies show concordance in monozygotic (MZ) twins with CD and UC to be 20-55% and 6.3-17%. Dizygotic (DZ) concordance is 0-3.6% (CD) and 0-6.3% (UC) [1] .
Methods: Subjects were recruited via IBD charities, retracing members of a dormant database and clinician referral. Adult twin pairs discordant and concordant for IBD were recruited. Participants completed a questionnaire regarding disease history and environmental exposure. Medical records were reviewed when available.
Results: Demographics, Concordance and Zygosity: 100 twin pairs were recruited. Mean age 57 years 5 months, range 21-83 years. 31 MZ:69 DZ. Ratio CD:UC = 48:52. Concordance of twin pairs classified by zygosity and disease type is outlined in table 1.
Early Environment: Higher rates of exclusive breastfeeding were reported in concordant pairs (27.3% n=22 pairs vs 16.7% n=78 pairs). Self reports of perceived childhood illness did not show any difference between IBD and healthy twins of discordant pairs (16.7%, 13/78 vs 19.2%, 15/78). However, the IBD twin more often recalled frequent gastrointestinal infection (10.3%, 8/78 vs 3.8%, 3/78).
Diet: IBD twins of discordant pairs had higher rates of consuming "ready made" meals at least weekly before disease onset (12.8%, 10/78 vs 5.1%, 4/78).
Smoking: On review of discordant twin pairs (n=72), there was no significant difference in numbers of current, ex and non smokers

Concordance of twin pairs classified by zygosity and disease type.

	Crohn's Disease	Ulcerative Colitis
Monozygotic	53.3%	25%
Dizygotic	10%	19.4%

between subjects with UC (n=41), CD (n=32) and their healthy twin at time of symptom onset.

Medication and Stress: On review of all IBD sufferers, 7.1% (8/112) and 13.4% (15/112) used NSAIDS and antibiotics within 3 months preceding onset. 48.2% (54/112) reported significant stress within the year before diagnosis.

Time of onset in concordant pairs: The mean lag between diagnosis of concordant pairs was 7 years 5 months.

Conclusions: Concordance of twin pairs with CD is in keeping with the literature. UC concordance is greater than previously quoted. However DZ and MZ concordance of UC twins is similar inferring low heritability. DZ UC pair concordance is 4 fold expected non twin sibling concordance [2], suggesting early environment to be important. This study supports an associaton between diet, stress and gastrointestinal infection with IBD onset. The lack of associatoin with smoking at incidence may reflect sample size.

References:

[1] Brant S, (2012), Update on the heritability of IBD: The importance of Twin Studies. , IBD

[2] Bodger et al, (2010), Concordance for IBD among twins compared to ordinary siblings - a Nowegian population based study., JCC

OP003
Faecal microbiota transplantation in Ulcerative Colitis: A randomised controlled trial

N. Rossen*[1], S. Fuentes[2], M. van der Spek[1], J. Tijssen[3], J. Hartman[2], A. Duflou[1], L. Mathus-Vliegen[1], W. de Vos[2], E. Zoetendal[2], G. D'haens[1], C. Ponsioen[1]

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Background: An aberrant microbiota has been implicated in the pathophysiology of ulcerative colitis (UC) and several case series reported favorable effects of faecal microbiota transplantation (FMT). We aimed to assess the efficacy FMT in active UC patients in a randomized parallel group study.

Methods: Patients with mild-moderate UC (Simple Clinical Colitis Activity Index [SCCAI] score of 4-11 and a Mayo endoscopic score of at least 1) were randomly assigned (1:1) to FMT derived from faeces from a healthy donor: FMT-D or their own faeces used as a placebo: FMT-P. FMT was administered via a naso-duodenal tube at week 0 and 3. Patients, physicians and endoscopists were blinded, with exception of the nurse who performed randomisation and prepared the faeces filtered with normal saline. The composite primary endpoint was clinical remission (SCCAI score 2 or lower) and endoscopic response (at least 1 point decrement on the Mayo endoscopic score) at week 12. Main secondary endpoints were microbiota composition in faecal samples and safety.

Results: Of 50 patients who were screened, 48 were randomised (23 to FMT-D and 25 to FMT-P. In the ITT analysis, seven out of 23 patients (30.4%) in the donor arm versus five out of 25 patients in the placebo arm (20.0%) achieved the primary endpoint, P= .51. In the per protocol analysis 37 patients completed endoscopic follow-up; seven out of 17 patients in the donor arm (41.2%) versus five out of 20 (25.0%) in the placebo arm achieved the primary endpoint, P= .29. The majority of patients experienced mild adverse events with spontaneous recovery. Serious adverse events occurred in four patients and were considered not related to FMT. The trial was terminated after 50 inclusions due to futility. Redundancy analysis showed that at 12 weeks faecal microbiota of responders in the FMT-D group overlapped with healthy donors, which was associated with occurrence of Clostridium cluster XIVa. This was not seen in responders from the FMT-P group.

Conclusions: FMT with faeces of a healthy donor did not result in statistically higher clinical and endoscopic remission rates as compared to placebo in moderately active unselected UC patients. However, both FMT(donor) and FMT(placebo) are associated with signature changes in responders. Future studies should focus on mode of administration, matching of for selected patients, as well as the observed shifts in microbiota composition in responders. ClinicalTrials.gov number NCT01650038.

OP004
Adalimumab and infliximab levels in neonates (ERA study)

M. Julsgaard*[1, 2], L.A. Christensen[1], P.R. Gibson[3], R. Gearry[4], J. Fallingborg[5], J. Kjeldsen[6], S. Wildt[7], L. Svenningsen[8], W. Connell[2], C.L. Hvas[1], M.P. Sparrow[3], A. Walsh[9], S.J. Connor[10], G. Radford-Smith[11], I. Lawrence[12], J.M. Andrews[13], K. Ellard[14], O. Rosella[3], A. Grosen[1], J. Santamaria[15], S.J. Bell[2]

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Background: Limited data on anti TNF alpha therapy (ATNF) during pregnancy exist. We examined drug levels of ATNF in cord blood of newborns exposed in pregnancy and correlated these with maternal levels, duration of ATNF and time to drug clearance.

Methods: Pregnant IBD women exposed to Remicade (IFX) or Humira (ADA) were included during 2012-14 at 14 sites in Denmark, Australia and New Zealand. Drug levels were measured by ELISA at delivery (Matriks Biotek). If positive at birth, infants were tested 3 monthly

until negative. Demographics, disease activity, medication, and pregnancy outcomes were prospectively collected. Multivariate and logistic regression analysis determined factors correlated with drug levels at birth in mothers and newborns and time to clearance in newborns.

Results: Of 89 women recruited, 5 (5.6%) miscarried, 4 failed blood collection, leaving 80 mother-baby pairs (44 IFX, 36 ADA). 49% were on thiopurines. There were 3 (4%) preterm births, 3 (4%) small for gestational age and 2 (2.5%) congenital malformations. Development was normal in all babies using routine infant checks. There was an inverse correlation between duration since last dose and both cord drug levels (IFX: r = -0.58; ADA: r = -0.41, both p <0.0001) and maternal levels (IFX: r = -0.63; ADA: r = -0.64, both p <0.0001). Cord blood and maternal drug levels also correlated (IFX: r = 0.67; ADA: r = 0.64, both p < 0.0001). Last ATNF dose was at median gestational week (GW) 30 in IFX, (8-37) and 35 in ADA (14-41) treated mothers. Drug was ceased prior to GW 30 in 31% of mothers. Cessation prior to GW30 did not increase the risk of disease activity in the 3rd trimester or postpartum. Median maternal and cord drug levels were 2 (0-22.2mcg/ml) and 5.9 (0.12-28.7mcg/ml) for IFX and 1.5 (0-10mcg/ml) and 2 (0-12.1mcg/ml) for ADA. Levels were significantly lower when drug was stopped prior to GW30.

Conclusions: No increased risk of adverse pregnancy or developmental outcomes. Maternal and cord ATNF levels inversely correlated with duration since last exposure. Cord blood levels correlated with maternal level at delivery. Maternal cessation of ATNF prior to week 30 significantly reduced fetal exposure without disease exacerbation. However, clearance took up to 12 months. Therefore, live vaccinations should be avoided prior to 1 year unless drug clearance is documented.

44 (55%) babies have cleared drug, 36 are still in testing. Median time to clearance was 6 months (0-12) for both drugs. Drug type and weeks since last dose predicted clearance by 3 months (AUROC 0.81, p=0.002).

OP005
Infliximab trough level thresholds vary depending on the efficacy criterion chosen in IBD patients

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Background: Several studies and meta-analyses have shown a correlation between infliximab trough levels (TLI) and clinical remission. Isolated cut-off points vary according to the techniques used. No study has been carried out to determine whether the variations in this therapeutic cut-off depend on the analysis criterion. The aim of our study was to compare whether there were similarities in this threshold for clinical remission (CR) or biomarkers assessment in IBD.

Methods: we included in a monocentric observational study including all consecutive IBD patients treated with IFX between 2010 and 2013. The TLI measurements (ELISA technique, Theradiag) were performed immediately prior to an infusion of IFX (5mg/kg) simultaneously with the CRP (mg/L) and faecal calprotectin (µg/g of stools). The CDAI or partial Mayo scores were reported for all the patients. Exclusion criteria were primary non-responders to IFX, patients previously treated with another anti-TNF agent, patients optimized at a dose other than 5 mg/kg/8W and exclusive anoperineal CD. Clinical remission was defined for CD by a CDAI score of < 150 and for UC by a partial Mayo score of < 3. Normal CRP was defined as CRP < 5 mg/L in patients having a high CRP level at the start of treatment. Faecal calprotectin was defined as normal for a level below 250 µg/g of stools. The TLI cut-off was investigated using a ROC curve analysis to isolate a threshold associated with CR, and normal CRP and calprotectin levels.

Results: 213 patients (131 with CD; mean age: 38 years; M:F sex ratio: 0.8; mean duration of IFX: 14.9 months) were included. 145 patients were in CR. Mean TLI were significantly higher during CR (2.6 vs. 1.2 µg/ml; p<0.01). The optimal cut-off associated with CR was 2.1µg/ml (sensitivity: 78%; specificity: 76%). Of the 140 patients who had high CRP levels at the start of treatment, 85 showed normal CRP and clinical remission. The mean TLI were significantly higher when normal CPR levels associated with CR observed (3.5 vs. 1.6 µg/ml; p<0.01). The optimal cut-off associated with normal CRP associated with CR was 2.9 µg/ml (sensitivity: 69%; specificity: 66%). 121 patients showed normal faecal calprotectin associated with clinical remission. The mean TLI were significantly higher in presence of normal faecal calprotectin levels associated with clinical remission (4.9 vs. 1.7 µg/ml; p<0.001). The optimal cut-off associated with normal faecal calprotectin was 3.9 µg/ml (sensitivity: 74%; specificity: 80%).

Conclusions: The TLI to target varies depending on the treatment objective chosen in IBD patients. The therapeutic level required for obtaining deep remission defined by clinical and biomarker remission, is higher than the level required to achieve clinical remission only.

OP006
Disease burden outweighs the impact of drug concentrations and antibodies to infliximab in primary non-response to infliximab in Crohn's disease patients

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Background: The mechanisms behind primary non-response (PNR) to infliximab (IFX) in IBD are still incompletely understood. The role

Median (range) drugs levels at birth according to time of cessation of anti-TNF3.

	IFX level (mcg/ml)			ADA level (mcg/ml)		
	Last infusion prior to GW 30	Last infusion at or after GW 30	P value	Last injection prior to GW 30	Last injection at or after GW 30	P value
	N=17	N=24		N=6	N=28	
Mother	0.6 (0.0–3.3)	4.0 (0.0–22.2)	< 0.001	0.3 (0.0–0.7)	2.0 (0.0–10.0)	< 0.004
Cord Blood	1.9 (0.1–8.9)	9.6 (1.9–28.7)	0.0001	0.5 (0.0–1.2)	2.4 (0.0–12.1)	< 0.02

of IFX trough levels (TL) and early antibody formation (ATI) during the induction phase (0-2-6 weeks) are contradicting. Furthermore, the evolution of serum TNF during IFX induction has been sparsely studied. We investigated if serum markers of inflammation or drug exposure help in understanding what is driving PNR.

Methods: We studied a cohort of 201 anti-TNF naïve Crohn's disease (CD) patients who received IFX induction and had serum samples drawn at weeks 0, 2, 6 and 14. In all samples CRP, albumin, TNF, ATI (homogeneous mobility shift assay, Prometheus Laboratories Inc.) and TL (in-house-developed ELISA) were assessed. PNR was defined as complete absence of clinical improvement at week 14 (physician global assessment).

Results: The incidence of PNR was 8% (n=16). In univariate analysis, low albumin at w6 was associated with PNR (P=0.01, Mann Whitney test). We observed a significant increase of serum TNF after each IFX infusion (see figure 1) with medians at w0 and w14 of 1.6 pg/ml (IQR 0.9-2.7) and 7.7 pg/ml (IQR 4.5-11.5) respectively (P<0.0001, Kruskal-Wallis test).

In patients with PNR, this rise in TNF (w14-w0) was significantly lower than in responders (P=0.03, Mann Whitney test). In an attempt to classify inflammation driven by TNF relative to the overall inflammation, we compared TNF/CRP ratio between both groups. A stepwise multiple logistic regression model identified albumin at w6 and TNF/CRP at w0 to be independent significant predictors (P<0.01) of PNR to infliximab at w14, with OR (95% CI) of 0.08 (0.02–0.37) and 3.10 (1.54–6.25) respectively.

Conclusions: A high disease burden (represented by low albumin, high CRP and serum TNF) and not IFX TL or ATI (detectable in 21% of patients at w14) are the most important factors driving PNR to IFX. TNF and CRP separately did not predict primary response but a higher TNF/CRP ratio before start of IFX was predictive for PNR, contradicting the theorem that PNR might be due to 'non-TNF-driven' disease. Although the median TL at w14 between both groups did not differ significantly (P=0.48), this ratio indicates that the contribution of TNF in inflammation might even be higher in PNR before IFX start, and possibly demanding a higher loading dose. We further observed an increase of serum TNF after IFX and this was less in PNR. The mechanism behind this increase remains unclear. These results warrant further investigation for the role of disease burden in PNR to IFX.

OP007

Deep remission in Crohn´s disease does not prevent disease relapse after withdrawal of anti-TNFa therapy

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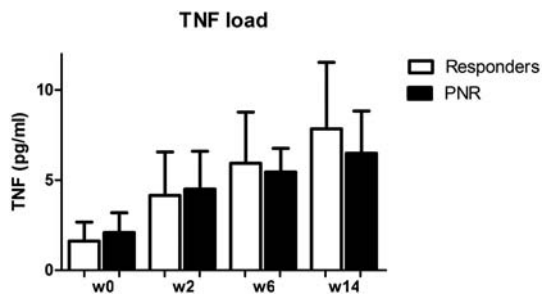

"Figure 1: Evolution of median TNF concentrations (with IQR) for every time point"

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Background: There is an ongoing debate whether cessation of anti- TNFa therapy in Crohn´s disease (CD) patients who are in remission is plausible from the long-term perspective. The aim of our study was to assess the proportion of CD patients who relapse after cessation of biological treatment at the time of endoscopic remission, to identify potential risk factors of disease relapse and to evaluate the risk of development of complicated disease behaviour.

Methods: Consecutive patients with CD followed at our centre who discontinued anti- TNFa therapy from 2010 to 2013 were included. At the time of therapy withdrawal all patients had to be in steroid-free clinical remission and all but one were also in endoscopic remission defined as absence of any ulceration. Patients were followed-up prospectively according to predefined protocol. Follow-up visits were scheduled every 2 months during the 1st 6 months and every 3 months thereafter. Relapse was defined as clinical worsening of the disease confirmed by endoscopy and/or imaging procedure or new onset of perianal abscess both leading to change of the medical therapy or surgery.

Results: Sixty one patients were included and followed-up for a median of 28 months (range 7-47). After withdrawal of anti-TNFa therapy (44 infliximab and 17 adalimumab) 47 (77%) patients continued thiopurines. 32 (52.5%) patients relapsed until the end of follow-up with a median time to relapse of 8 months (range 1-25). The cumulative probability of maintaining remission was 82% at 6 months, 59% at 1 year and 51% at 2 years. Analysis of 28 patients who were in deep remission (endoscopic healing; faecal calprotectin <150mg/kg; CRP <5mg/l) revealed no better survival (82%, 64% and 40% at 6 months, 1 and 2 years, respectively). Four (8%) of relapsing CD patients required surgery 5 to 19 months after anti-TNFa cessation (2 for new stricture development, 1 for medically refractory flare and 1 for high grade dysplasia). In multivariate model only disease localization was risk factor of disease relapse (colonic vs. ileal/ileocolonic: OR 0.16, 95%CI: 0.03-0.72; p=0.02). Type of anti- TNFa preparation, smoking, disease behaviour, corticosteroid or thiopurine therapy, biological markers and anti-TNFa trough levels did not impact disease relapse.

Conclusions: Approximately half of CD patients relapsed within 2 years after anti- TNFa discontinuation despite being in endoscopic remission when anti-TNFa was stopped. The highest relapse rate was observed during the 1st year. Ileal disease increased the risk of disease flare, while no other risk factor was identified.

Acknowledgement: This study was supported by IBD-COMFORT foundation.

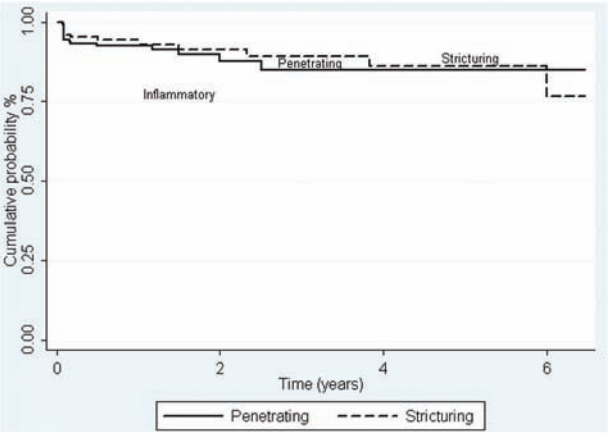
OP008

The first prospective Australian population-based study of newly diagnosed IBD identifies frequent use of immunomodulators, low surgery rates and high cost from medications and investigations.

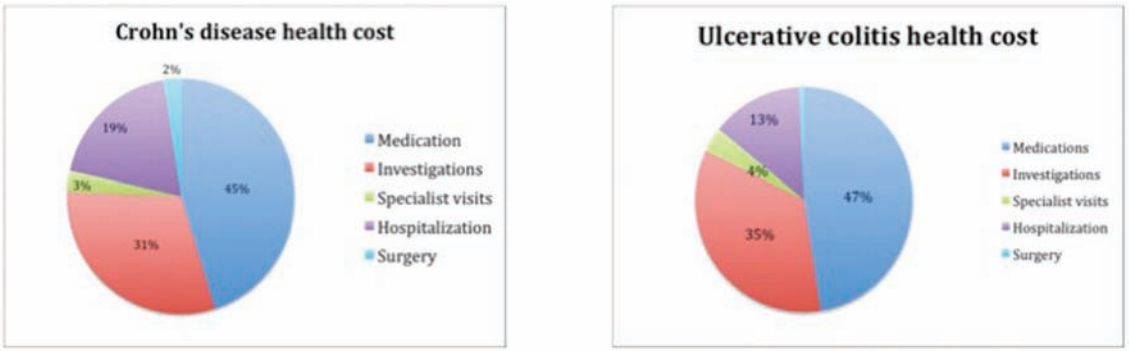
O. Niewiadomski*[1], C. Studd[1], C. Hair[2], J. Wilson[1], J. Ding[1], N. Heerasing[2], A. Ting[2], K. Ross[2], J. Santamaria[3], E. Prewett[2], P. Dabkowski[2], S. Alexander[2], D. Dowling[2], B. Allen[2], B. Popp[4],

Patient demographics.

		Crohn's disease (n=146)	Ulcerative Colitis (n=96)
Phenotype	Ileal	46 (32%)	Proctitis 31 (32%)
	Colonic	44 (30%)	Left sided 30 (31%)
	Ileacolonic	56 (38%) + 17 (12%)upper GI + 17 (12%) perianal	Pancolitis 35 (36%)
Hospitalization		53 (36%)	23 (24%)
Exposure to treatment steps	5ASA	77 (53%)	86 (90%)
	Steroids	99 (68%)	48 (50%)
	Immunomodulator	83 (57%)	11 (11%)
	Biologica therapy	18 (12%)	2 (2%)
	Surgery (resective)	19 (13%)	6 (6%)



"Disease behaviour in CD over 5 years"



"Total expenditure for a) CD and b) UC patients in the first 12 months."

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Background: We have previously shown that in Barwon, Victoria (pop. 283,000) the incidence of IBD was 29 & 25 per 100,000 during the periods 2007-8 and 2010-2011, respectively. A prospective registry was established to investigate the natural history of disease and health resource utilization after diagnosis.

Methods: Incidence cases of IBD were identified from 2007-2008 and 2010-2013. Details about disease state after diagnosis were prospectively assessed by 6 monthly review of case notes. Severity was assessed by need for hospitalization, surgery and biological use.

Results: 252 of 276 incidence cases (91%, 146 Crohn's disease, CD, and 96 Ulcerative colitis, UC) were followed for a median of 18 months (range 1-5 years), including 38 paediatric cases,
. 53 CD patients (36%) required hospitalisation, 41 (77%) in the first year. Ileocolonic disease (HR 3.2, p=0.005) and penetrating disease (HR 2.6, p=0.013) at diagnosis were risk factors for hospitalization. 23 UC patients (24%) were hospitalized, most (70%) in the first 12 months. An elevated CRP at diagnosis predicted hospitalization in UC (HR4.4, p=0.006). Intestinal resection rates in CD were 13% at 1 year, and 23% at 5 years. Risk factors include penetrating or stricturing disease (p<0.001), and ileal involvement (p<0.05) at diagnosis. Colectomy rates in UC were 2% at 1 year, and 13% at 5 years. An elevated CRP predicted need for colectomy (HR 11, p=0.04). IM use was high (57% CD and 19% UC); as were adverse events due to IM (25% in all patients). Biological therapy was used in 13% of CD patients. The cost in the first year in CD was a median $4855/patient (AUS$1571- $57,845); whilst in UC the median was $4608 ($1488- $26,093). Most of the expense was due to medications and investigations

Conclusions: This first Australian population based study found a high rate of inflammatory disease and immunosuppression in CD and low rate of surgery in both CD and UC. Penetrating, structuring and ileal disease are risk factors for severe disease in CD; high CRP in UC predicts severe disease. Medication use and investigative procedures account for most cost in the first year.

OP009
Unchanged surgery and hospitalization rates in an East-West European inception cohort despite differences in use of biologicals - 3-year follow-up of the ECCO-EpiCom cohort

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Background: The EpiCom-cohort is a European prospective population-based cohort of unselected, uniformly diagnosed patients with inflammatory bowel disease (IBD) diagnosed in 2010 in centres from Western and Eastern European countries [1] [2] . The cohort aims at describing differences in occurrence, treatment strategies, disease course and prognosis within Europe.

Methods: Patients were followed from diagnosis and each 3rd month for the first year of follow-up and then according to the treating physician for the 2nd and 3rd year of follow-up. Clinical data on surgery, biological treatment, hospitalization and medical treatment were captured prospectively throughout the follow-up period and entered in a validated, web-based database, www.epicom-ecco.eu. The aim of the study was to investigate differences in disease outcome and the use of biologics between Eastern and Western Europe.

Results: A total of 923 patients aged 15 years or older from 19 centres (13 Western, 6 Eastern European) were eligible for follow-up of whom 482 (52%) had ulcerative colitis (UC), 340 (37%) had Crohn's disease (CD), and 101 (11%) had IBD unclassified (IBDU). At 3-years follow up 86 patients had undergone 1st surgery (resections or colectomy) (16 from Eastern Europe, 70 from Western Europe), 136 had received biological therapy (13 from Eastern Europe, 123 from Western Europe) and 191 were hospitalized (32 from Eastern Europe, 159 from Western Europe). Crude annual rates for surgery, biological treatment and hospitalization are shown in Table 1. Significantly more patients in Western Europe received biological therapy ($p<0.05$), while surgery and hospitalization rates did not differ between the regions at both 1 and 3-year follow-up. The risks of surgery and treatment with biological agents were higher for CD than UC patients ($p<0.01$). Cox regression analysis revealed that stricturing or penetrating disease carried the highest risk for surgery, hospitalization and receiving biological therapy for CD, and extensive disease carried the highest risk for hospitalization in UC.

Conclusions: In an era of early and aggressive immunological therapy, surgery and hospitalization rates for CD and UC patients were similar in Eastern and Western Europe and comparable to population-based cohorts from the past decade and pre-biological era. This similar disease course was in spite of more early and aggressive treatment with biologics, with significantly more CD and UC patients in Western Europe receiving biologics.

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OP010
Medication-induced microscopic colitis: do recency and duration of use matter?

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Background: Microscopic colitis (MC) is a colonic disorder characterised by chronic watery diarrhoea. There is increasing evidence

Crude rates for surgery, biological therapy and hospitalization after 1 and 3 years follow-up in the EpiCom-cohort.

		Biological treatment		Surgery		Hospitalization	
		1 year	3 years	1 year	3 years	1 year	3 years
Crohn's disease	Eastern Europe	5 (6%)	8 (10%)	10 (13%)	14 (18%)	15 (19%)	19 (24%)
Crohn's disease	Western Europe	52 (20%)	72 (27%)	28 (11%)	43 (16%)	48 (18%)	66 (25%)
Ulcerative colitis	Eastern Europe	1 (1%)	5 (5%)	1 (1%)	2 (2%)	6 (6%)	13 (13%)
Ulcerative colitis	Western Europe	22 (6%)	40 (11%)	11 (3%)	21 (6%)	51 (13%)	76 (20%)

that exposure to commonly prescribed drugs like non-steroidal anti-inflammatory drugs (NSAIDs), proton pump inhibitors (PPIs), selective serotonin reuptake inhibitors (SSRIs), and statins is associated with an increased risk of MC. However, the attributive risk of recent or longer use and the effect of higher dosages has never been investigated, although this information would give more insight in the possible mechanism of medication-induced MC.

Methods: A case-control study was conducted using the British Clinical Practice Research Datalink. Cases were diagnosed with microscopic, lymphocytic (LC) or collagenous (CC) colitis between 1992-2013. For each case, up to 5 randomly selected controls without MC were matched by year of birth, gender, and practice. The index date of the case defined that of the controls. Prescriptions within 60 days prior to index date were excluded to take into account a latency (lag) time and to minimize reverse causality. Exposure status was classified as current (61-90 days), recent (91-150 days), and past use (>150 days) according to the time since most recent prescription prior to index date. In current users, duration of continuous use and average daily dose was assessed. Conditional logistic regression analysis was applied to quantify the strength of the associations and to correct for confounders.

Results: In total, 1.211 cases with MC (394 CC, 292 LC, 525 undefined MC) and 6.041 controls were identified. Current use of NSAIDs (OR 1.79, 95% CI 1.36-2.36), PPIs (OR 3.93, 95% CI 2.25-4.74), and SSRIs (OR 2.27, 95% CI 1.79-2.89) was associated with an increased risk of MC compared to never and past use. Especially a 4-12 months continuous use of NSAIDs, PPIs, and SSRIs increased the risk of MC. Long-term use (>24 months) attenuated this risk. Exposure to more than 1.25 standardised daily dosages was associated with an elevated risk of MC in PPI (OR 6.90, 95% CI 3.82-12.49) and SSRI users (OR 4.15, 95% CI 2.47-6.97). Analysis per MC subtype showed a positive association between current use of NSAIDs (OR 2.28, 95% CI 1.46-3.54) and PPIs (OR 6.15, 95% CI 4.41-8.58) in CC and current use of PPIs (OR 2.40, 95% CI 1.60-3.59) and SSRIs (OR 2.65, 95% CI 1.69-4.15) in LC.

Statin use was not associated with MC. A sensitivity analysis with a lag time of 90 days showed conclusions consistent with the primary analysis.

Conclusions: Use of NSAIDs, PPIs, and SSRIs is associated with an increased risk of MC. Especially in current users with a continuous exposure duration of 4 to 12 months, drug exposure as cause for MC should be considered.

OP011
Budesonide MMX® 9 mg for Inducing Remission in Patients with Mild-to-Moderate Ulcerative Colitis Not Adequately Controlled with Oral 5-ASAs

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Background: Budesonide MMX® (B-MMX) is a once-daily, extended release oral formulation designed to provide targeted delivery of budesonide throughout the colon. Here we present data from a prospectively designed, randomised, double-blind, placebo-controlled trial to evaluate the efficacy and safety of B-MMX in patients experiencing an active UC flare despite treatment with an oral 5-ASA.

Methods: Patients with mildly to moderately active UC (UCDAI ≥4 and ≤10) inadequately controlled with oral 5-ASAs were randomised 1:1 to add once-daily B-MMX 9 mg or placebo (PBO) for 8 weeks to their existing 5-ASA. Patients were required to be on a stable, therapeutic dose of an oral 5-ASA (e.g., mesalamine ≥2.4 g/day or equivalent dose of another 5-ASA) throughout the study. Patients who increased their 5-ASA dose or administered other UC therapies were considered non-responders. The primary efficacy endpoint was combined clinical and endoscopic remission at Week 8, as defined by a UCDAI score of ≤1, with subscores of 0 for rectal bleeding, stool frequency and mucosal appearance. Secondary and exploratory endpoints assessed clinical remission (rectal bleeding and stool frequency subscores = 0), endoscopic remission (mucosal appearance subscore = 0) and histological healing (histological activity grade = 0, as assessed via central reading). Patients with missing data were considered non-responders.

Results: Of 510 patients enrolled, 458 (230 B-MMX, 228 PBO) were included in the intent-to-treat population (46% female, mean age: 44.5), which excluded patients with normal baseline mucosal histology or infectious colitis. Combined clinical and endoscopic remission was achieved in a greater percentage of B-MMX-treated patients than PBO-treated patients (13% vs. 7.5%, p=0.0488). This treatment effect was driven primarily by the mucosal appearance subscore. On this measure, a greater percentage of B-MMX-treated patients than PBO-treated patients achieved a score of 0 (20% vs. 12.3%, p=0.0248), indicative of endoscopic remission. B-MMX also induced histological healing in a greater percentage of patients than placebo (27% vs. 17.5%, p=0.0155). Overall, 31.8% and 27.1% of patients treated with B-MMX or placebo reported an AE, and the majority were mild or moderate in severity. Study discontinuation due to AEs occurred in 4.7% and 3.5% of the B-MMX and placebo groups, respectively.

Conclusions: In patients experiencing an active flare of UC despite baseline oral 5-ASA therapy, adding B-MMX 9 mg was significantly more effective than placebo at inducing combined clinical and endoscopic remission as well as histological healing. B-MMX was generally well-tolerated when given in combination with an oral 5-ASA.

ClinicalTrials.gov identifier: NCT01532648

OP012
Information needs and concerns of patients with Inflammatory Bowel Disease: What can we learn from participants of a national clinical cohort?

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Background: Patients suffering from Inflammatory Bowel Disease (IBD) are confronted with needs and concerns related to the

specificity and uncertainty of their illness condition. This study aims to explore information expectations of patients in a national IBD cohort in Switzerland (SIBDC) and to assess their association with clinical, socio-demographic and psychosocial characteristics.

Methods: A semi-narrative questionnaire survey was conducted to investigate information-seeking behaviour among 1506 patients from the SIBDC, in 4 different stages of their disease: 1) when experiencing the first symptoms, 2) at the time of diagnosis, 3) in active phases, and 4) during remission. Two focus group discussions based on vignette cases describing clinical situations were then conducted with 14 IBD patients to explore and assess the relevance of the survey's findings. Narrative answers and discussions were fully transcribed; content analysis was undertaken, and interactional dynamics were compared for the two discussions. Data collected within the framework of the SIBDC was used to characterize responders to the survey.

Results: 728 patients (51%) replied to the survey (responders); half of them were males (N=346), 56% were diagnosed with CD (N=407). Responders had a median duration of disease of 8 years, 90% were secondary/tertiary level educated, and 62% had a full/part-time working activity. Almost half of patients sought for information, regardless of the stage of the disease. Importantly, 27% of them were dissatisfied with information at the time of first symptoms. The main reasons for dissatisfaction were: misdiagnosis, symptoms not taken into consideration, insufficient knowledge on disease from other specialists, and unclear information. During flares, 43% were concerned about drugs and therapies (overall information on drugs and side effects, alternative medicines, surgery), as compared to 11% at diagnosis and 30% in remission. Concerns on research and new developments were those of 57% in remission (5% at diagnosis, 24% during flares). Needs for information related to daily disease management were expressed by 28% of patients with active or quiescent disease. The focus groups confirmed a perceived lack of information about general functioning and course of the disease, treatments and their risks, and extra-intestinal symptoms and manifestations.

Conclusions: This study shows that information remains insufficient for patients with IBD, and their relatives. A lack of information in specific domains can cause stress or anxiety and hinder detection of symptoms, or clinical outcomes. Better information giving should be considered as a decisive mean step to potentially improve outcomes, e.g., patients' adherence to treatment and quality of life.

OP013
Patient-relevant Endpoints in Inflammatory Bowel Diseases - Have Changes Occurred in Germany over the Past Twelve Years?

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Background: Inflammatory bowel diseases are gaining increasing medical as well as economic significance. Improving medical treatment options can have a positive effect on patient-relevant endpoints such as, for example, the number of hospitalized patients, necessary operations, or the inability to work.

Methods: To understand patient-relevant endpoints in patients with IBD, the 2000 to 2012 data on IBD patients published by the Federal Statistical Office and the 2012 data according to Article 21 of the Hospital Reimbursement Act were assessed. In addition, data records on the medication of IBD patients of a large public health insurance company (Barmer-GEK) were evaluated.

Results: During the period evaluated, the number of inpatients that suffer from IBD (ICD 10 K50, K51) rose from 38,533 to 43,452 (+12.7%). The largest increase was found in patients younger than fifteen years of age. The necessity of surgical intervention (ileocecal or partial colon resection, proctocolectomies) increased during the period under review. The number of people unable to work ("inability-to-work cases" from 2002-2008) developed differently for Crohn's disease (CD) and ulcerative colitis (UC). CD shows an increase of 2.1%, and UC shows a decrease in inability-to-work cases of 9.5%. Entry of persons into the statutory pension insurance system did not significantly decline from 2000 to 2012. The number of potential years of life lost (PYLL) in patients that suffer from IBD also remained constant during the period under review (2000-2002: 2017 PYLL vs. 2011 PYLL (2010-2012)). From 2009 to 2013 the percentage of patients treated with an anti-TNF-antibodies rose (2009: CD: 4.3%; UC: 1.4%; 2013: CD: 8.4%; UC: 3.2%). However, even the 2013 rate is significantly lower than what could be expected from a consistent implementation of the treatment guidelines.

Conclusions: For the patient-relevant endpoints "hospitalizations", "number of necessary operations", "frequency of the inability to work", and "potential years of life lost," a positive development was not observed between 2000 and 2012 in patients that suffer from IBD in Germany. Improvements can only be achieved through structured and overlapping treatment concepts involving all health care providers.

OP014
Use of anti-TNF-α agents in relation to first-time surgery for ulcerative colitis and Crohn's disease during childhood

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Background: Following the introduction of anti-tumour necrosis factor-alpha (anti-TNF-α) agents in the medical treatment of inflammatory bowel disease (IBD) it is now debated whether anti-TNF-α agents delay or prevent the need for surgery in childhood and adolescent IBD. It has not earlier been described how the use of anti-TNF-α has been implemented in the actual treatment in relation to surgery based on an unselected nationwide cohort of children with IBD. Based on Danish data from the latest 14 years on patients with ulcerative colitis (UC) and Crohn's disease (CD), we thus aimed to describe the use of anti-TNF-α agents in relation to first time bowel surgery during childhood and adolescence.

Methods: The availability of nationwide Danish registries makes it possible to access data on patients (age ≤21 years) with a diagnosis of CD and UC, the use of anti-TNF-α agents and surgical interventions. We included all Danish children and adolescents having a first

time discharge diagnosis of CD or UC during the period from 1 July 2000 through 30 June 2012, with two years of follow up.

The results are reported using descriptive statistics to illustrate the changes in treatment strategy and first time surgical interventions within strata of three years calendar periods.

Results: Overall, 1,609 children and adolescents were diagnosed with CD during the study period. Of these, 344 (21.4%) were at some time treated with anti-TNF-α agents within two years after CD diagnosis, and 36 (2.2%) had a first time surgery within a period of two years from first CD diagnosis. 1,976 children and adolescents were diagnosed with UC. Of these, 228 (11.5%) were treated with anti-TNF-α agents within two years after UC diagnosis, and 169 (8.6%) had a first time surgery within a period of two years from first UC diagnosis.

The anti-TNF-α agents were introduced mid-2003 and hereafter the number of patients treated with anti-TNF-α agents within two years after being diagnosed increased to 173 patients with CD and 126 patients with UC (strata of 2010-2012).

During the study period the number of CD patients, who had a first time surgery was (10, 10, 6, 10 in strata periods of three years) and for UC (44, 47, 42, 36).

The time until first time surgery for CD patients was (median: 6, 27.5, 52.5, 46 weeks in strata periods of three years). The time until first time surgery for UC patients was (median: 23.5, 37, 37.5, 36 weeks).

Conclusions: Following the introduction of anti-TNF-α agents in IBD children and adolescents the number of first time surgeries within two years after diagnosis were at the same level, and the time to surgery seemed to be the same for UC, whereas we observed a tendency that the time to surgery was postponed for patients with CD.

OP015
Multicentre clinical trial with topical administration of the Toll-Like receptor 9 agonist DIMS0150 shows evidence for efficacy in moderate to severe Ulcerative Colitis

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Background: The Toll like receptor 9 agonist DIMS0150 was evaluated for its efficacy and safety as add-on therapy in patients with moderate to severe ulcerative colitis, refractory to conventional therapy.

Methods: The efficacy of DIMS0150 (orphan drug designation in Europe) was evaluated in a randomized, double blind, placebo-controlled, multicentre phase III trial in 131 patients with moderate to severe active ulcerative colitis who at enrolment were on concomitant corticosteroid medication. Patients were randomly assigned to receive two single doses of DIMS0150 (30 mg) or placebo (in a 2:1 ratio) administered topically through endoscopy to the inflamed mucosa at baseline and after 4 weeks. The primary endpoint was clinical remission at week 12, defined as a Clinical Activity Index (CAI)≤4. Secondary efficacy endpoints were clinical remission at week 4, clinical remission with mucosal healing (CAI)≤4 and endoscopic Mayo score of 0 or 1) at week 4, mucosal healing at week 4 and symptomatic remission (absence of blood in stool and number of weekly stools < 35) at week 4 and 8. The patients were followed for one year after administration of the first dose to evaluate long-term efficacy and safety.

Results: In the intention-to-treat population, 44.4% (36/81) of DIMS0150 treated patients vs 46.5% (20/44) for placebo treated patients (p=0.91) achieved clinical remission at week 12 (primary endpoint). At week 4 28.4% (per protocol (PP): 26.5%) of DIMS0150 treated patients achieved clinical remission vs. 20.9% (PP: 12.9%) for placebo (p=0.28 [PP: p=0.10]). The proportion of patients in clinical remission with mucosal healing at week 4 was 21.0% in the DIMS0150 group vs 4.7% in the placebo group (p=0.02). The rate of mucosal healing at week 4 was 34.6% for DIMS0150 and 18.6% for placebo (p=0.09). Significantly more patients treated with DIMS0150 achieved symptomatic remission than recipients of placebo at week 4 (32.1% vs 14.0%, p = 0.02) and week 8 (44.4% vs. 27.9%, p = 0.06 [PP: 45.6% vs 22.6%, p=0.03]). A total of 13.8% SAEs were reported across both treatment groups with 18.6% of patients in the placebo group and 11.5% patients in the Kappaproct group reporting serious AEs, supporting the previously observed safety profile of DIMS0150.

Conclusions: Despite not meeting the primary endpoint, the results of this phase III trial suggest that topical administration of the TLR-9 agonist DIMS0150 is able to induce remission in ulcerative colitis patients, as judged by objective clinical and endoscopic measures. Therefore, the concept of TLR-9 activation is a promising and well-tolerated novel therapeutic option for refractory ulcerative colitis patients, warranting further clinical trials.

OP016
Treatment strategy during the first year after diagnosis in patients with inflammatory bowel diseases from the 2011 ECCO-EpiCom inception cohort

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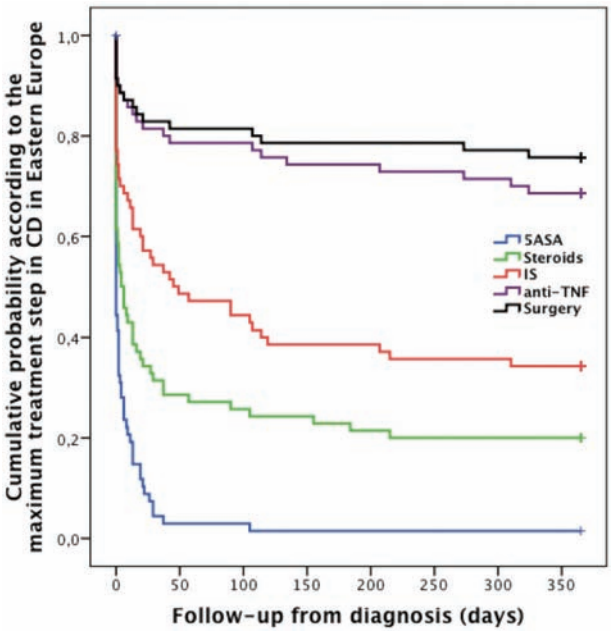
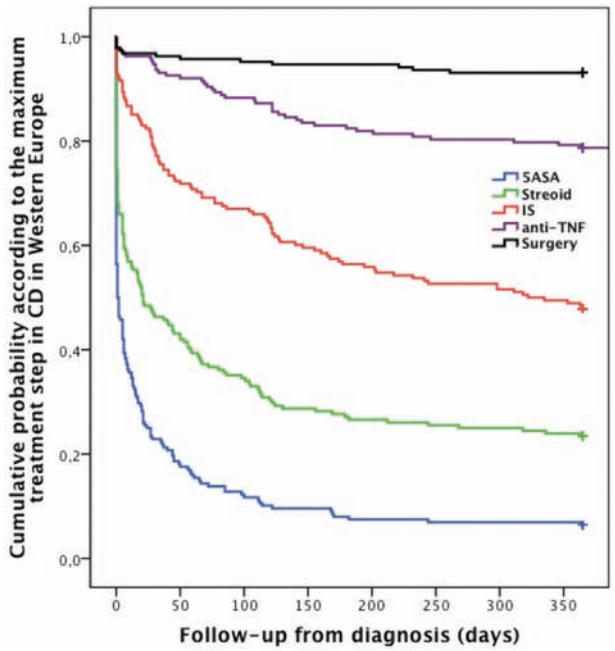


"Figure 1. Cumulative probability of the highest treatment steps in CD in Eastern Europe"



"Figure 2. Cumulative probability of the highest treatment steps in CD in Western Europe/Australia"

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Background: The ECCO-EpiCom study investigates the differences in the incidence, disease characteristics and therapeutical management of inflammatory bowel diseases (IBD) between Eastern and Western Europe. The aim of this study was to analyze the differences in the therapeutical strategy in the 2011 ECCO-EpiCom inception cohort within the first year after diagnosis.

Methods: Fourteen European (9 Western and 5 Eastern European centers) and one Australian center with 258 CD, 380 UC and 71 IBDU patients (65% from Western, 25% from Eastern Europe, 10% from Australia; female/male: 326/383; mean age at diagnosis: 40.9 years, SD: 17.3 years) participated in the one-year follow-up. Patients' data regarding disease characteristics and medical therapy were registered and entered in the web-based ECCO-EpiCom database every third month during the first 12 months after diagnosis.

Results: Both in CD and UC, a significant difference was found in the probability of highest treatment steps reached within one year after diagnosis between Eastern and Western Europe and Australia (Figure 1. and 2.).

Overall, the disease behavior (B2 and B3) was the driver for immunosuppressive (IS) therapy (pLogRank<0.001). In Eastern Europe, total 5ASA use was higher in patients with L1(ileal) and B1(non stricturing-non-penetrating) disease (pLogRank=0.001), and in L3(ileocolonic) location received earlier and more IS (pLogRank=0.037). In Western Europe/Australia significantly more CD patients were treated with biological therapy (p=0.04). Overall, penetrating disease behavior was the driver for biological therapy (pLogRank=0.035). In UC, patients in Western Europe/Australia received more steroids (43% vs. 26%, p=0.03, pLogRank=0.01), however disease extent was not different. In contrast, time to 5ASA, IS, biological therapy and colectomy was not different between Eastern and Western Europe/Australia. Time to 5ASA and steroid treatment was dependent on the extent (pLogRank5ASA=0.007 and pLogRanksteroid< 0.001).

Conclusions: We found a significant difference in the maximum treatment step in both CD and UC during the first year after the diagnosis between Eastern and Western Europe/Australia, with higher exposure to biologicals and lower exposure to 5ASA in CD patients in Western Europe/Australia, while only steroid exposure was different in UC.

OP017

Long-term outcomes in a cohort of patients with acute severe ulcerative colitis refractory to intravenous steroids treated with cyclosporine or infliximab

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Background: Cyclosporine (Cys) and infliximab (IFX) are the two second-line drugs for acute severe ulcerative colitis (ASUC) refractory to intravenous steroids. In the CYSIF trial, Cys was not more effective than IFX to achieve short-term remission and to avoid emergent colectomy (Laharie et al. Lancet 2012). However, few long-term data comparing both drugs are available so far. The aim of the present study was to assess long-term follow-up of patients randomized in the CYSIF trial.

Methods: From June 2007 to August 2010, 115 patients with steroid-refractory ASUC defined by a Lichtiger score>10 after at least 5 days of intravenous methyl-prednisolone more than 0.8mg/kg/d have been randomized in 23 GETAID and 6 ECCO centres, to receive Cys (2mg/kg/d for one week, then switched orally during 98 days) or IFX (5mg/kg at weeks 0-2-6). Azathioprine was started at a dose of 2.5mg/kg/d in all patients with clinical response at day 7. The randomized phase ended at day 98. Patients were then followed until death or last news alive up to October 2014. According to treatment allocated at randomization, outcomes were colectomy-free survival and survival without UC relapse leading to systemic therapeutic change (steroids, immunosuppressant or new biologic agent) or colectomy. Time-to-event curves from randomization were derived through Kaplan-Meier method and compared according to randomized treatment through logrank test.

Results: The median follow-up of the entire cohort of the 115 patients (58 assigned to Cys and 57 to IFX) was 5.0 years (IQR: 4.2 - 5.9). Three (3%) patients have died since randomization: a 66-year-old man (Cys) from a myocardial infarction after 4.3 months, a 55-year-old man (Cys secondary treated with IFX) from a pancreatic adenocarcinoma after 21.2 months and a 69-year-old women (Cys) from unknown origin after 28.6 months. Colectomy-free survival rates ± SE (# patients at risk) at 1, 2 and 5 years were respectively 70±6% (39), 65±6% (34) and 61±7% (17) in patients randomized to Cys and 70±6% (39), 68±6% (38) and 65±7% (19) in those randomized to IFX (p=0.86).

Conclusions: In this multicenter long-term follow up cohort of steroid-refractory ASUC patients randomized to Cys or IFX, colectomy-free survival did not depend on initial treatment. These long-term results are confirming good efficacy and safety profiles of these two agents and do not favour one drug over the other.

OP018

Prolonged Deep Remission of Ileocolonic Crohn's Disease following Autologous Haemopoetic Stem Cell Transplantation, presented on behalf of all the ASTIC Trialists

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Background: The ECCO-EBMT ASTIC trial showed autologous Haemopoietic stem cell transplantation (HSCT) to cause mucosal healing in severe refractory Crohn's disease. Here we report prolonged endoscopic regression of ileocolonic disease over 2 years.

Methods: Patients with impaired quality of life from active Crohn's disease not amenable to surgery, despite treatment with ≥3 immunosuppressive agents, all underwent cyclophosphamide-based stem cell mobilisation before randomisation to immunoablation, followed by unselected cyclophosphamide-based conditioning and HSCT after 1 month (Early HSCT) or 1 year (Delayed HSCT). They were assessed using the Crohns Disease Activity Index (CDAI), Simple Endoscopic Score (SES-CD), Inflammatory Bowel Disease Questionnaire (IBDQ) and EuroQoL Visual Analogue Scale (VAS).

Results: Forty four patients with ileocolonic involvement underwent stem cell mobilisation before randomisation to Early (n=23, all treated) or Delayed (n=21) HSCT. One Early HSCT patient died 14 days after HSCT. One randomised to Delayed HSCT withdrew immediately, 4 did not proceed because they required surgery (n=3) or were too well after 1 year (n=1). Sixteen patients underwent delayed HSCT. The CDAI fell from 321 (median, IQR 242-433) to 162 (76-294) one year after active treatment compared to 353 (300-462) to 310 (236-403) over year 1 prior to Delayed HSCT. At year 2 the CDAI was maintained at 161 (59-232) in Early HSCT patients and had fallen to 165 (88-298) in Delayed HSCT patients. The SES-CD was 13 (8.5-24.5) at baseline, 3 (1-10) after one year and 3 (0-9) at two years in early HSCT t patients compared to 13 (6.5-18), 7 (4-20) and 2 (0-7) in delayed HSCT patients. Ten patients (baseline SES-CD score of 7 [5-13.5]) became free of endoscopic evidence of active or inactive Crohn's disease (SES-CD = 0) one year after HSCT compared to none following control treatment. Three of 4 remained disease free and 4 more became free of endoscopic disease in year two after HSCT. The CDAI was <150 in 16 patients one year after HSCT vs one of 21 following control treatment. IBDQ scores at baseline, 1 and 2 years were 129 (103-142), 153 (121-203) and 173 (126-211) in the early HSCT group compared to 109 (83-137), 124 (87-154) and 148 (113-195) in the delayed HSCT group. Comparable values for the EuroQuol VAS score were 61 (40-66), 80 (62-88) and 85 (63-90) in the early HSCT group vs 43 (31-63), 50 (35-70) and 80 (70-85) in the late HSCT group.

Conclusions: Improvements gained one year after HSCT are maintained into a second year. HSCT delayed by one year appears to be effective. There is a progressive improvement in quality of life. If improvements remain durable, the risks of HSCT might become acceptable for a wider group of patients.

OP019
Forty-Year Analysis of Colonoscopic Surveillance for Ulcerative Colitis Reveals Decreasing Risk of Interval and Advanced Cancer and Reducing Colectomy Rate for Dysplasia

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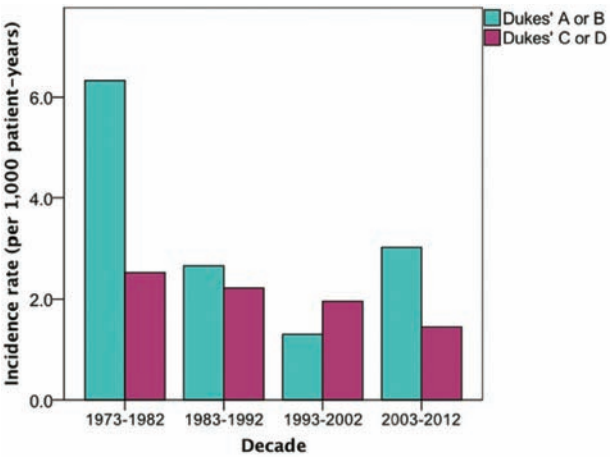
Background: While many aspects of colonoscopic surveillance program for colorectal cancer (CRC) in patients with ulcerative colitis (UC) have evolved, it is unknown how the risk of CRC changed over time. We report data from one of the largest and longest-running UC surveillance programs in the world, revealing an important recent trend in CRC risk.

Methods: A retrospective review of histologically confirmed extensive UC patients enrolled in long-term surveillance was performed. The primary end point was defined as death, colectomy, withdrawal from surveillance, or the census date (January 1, 2013). We compared per-decade CRC incidence rate over the last forty years. Cancer detected in symptom-driven investigations or surgery prior to the next scheduled surveillance was defined as interval CRC.

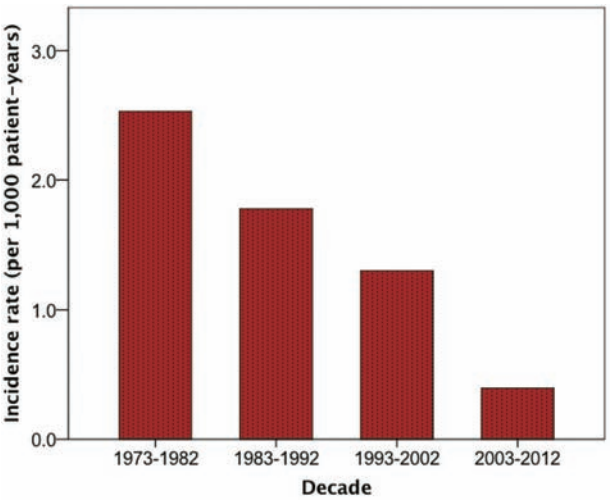
Results: A total of 1,375 patients underwent 8,650 colonoscopies (median, 5 per patient; interquartile range (IQR), 3 - 8 per patient) during 15,234 patient-years of follow-up (median, 11 years; IQR, 7 - 17 years). Cancer was detected in 72 patients (5% of study population), of which 15 were interval CRC (20.8%). While the overall CRC incidence rate had decreased over the first three decades, there was a non-significant increase in the fourth decade (4.9 per 1,000 patient-years (PY)) compared with the third decade (3.7 per 1,000 PY; Chi-squared, P=0.30), which was attributable to a significant increase in Dukes' A or B cancer incidence rate in the fourth decade (3.2 per 1,000 PY) compared with the third decade (1.3 per 1,000 PY; P=0.045; figure 1). Likewise, there was an increase in incidence rate of UC-associated dysplasia (17.7 versus 11.7 per 1,000 PY; P=0.01). The incidence rate of Dukes' C or disseminated cancer showed a linear decreasing trend over the last four decade (2.5 to 1.4 per 1,000 PY in the first decade to last decade; Pearson's correlation, -0.99; P=0.01; figure 1).

Furthermore, despite the decrease in colectomy rate for dysplasia (linear regression, R= -0.43; P=0.007), incidence rate of interval CRC showed significant reduction over time (2.5 to 0.4 per 1,000 PY in the first decade to last decade; Pearson's correlation, -0.99; P=0.007; figure 2).

Conclusions: The colonoscopic surveillance is increasingly becoming effective in detection of cancer at an earlier stage and for reducing the interval cancer risk.



"Figure 1: Per-decade incidence rate of CRC by Dukes' stage"



"Figure 2: Per-decade incidence rate of interval CRC"

OP020
Patients with Inflammatory Bowel Disease and a history of cancer: The risk of cancer following exposure to immunosuppression

J. Axelrad*[1], O. Bernheim[2], J.-F. Colombel[2], S. Malerba[3], A. Ananthakrishnan[4], V. Yajnik[4], G. Hoffman[5], M. Agrawal[6], D. Lukin[7], A. Desai[8], E. Mceachern[9], B. Bosworth[8], E. Scherl[8], A. Reyes[10], H. Zaidi[11], P. Mudireddy[12], D. DiCaprio[13], K. Sultan[11], B. Korelitz[12], E. Wang[14], R. Williams[14], L. Chen[15], S. Katz[15], S. Itzkowitz[2]

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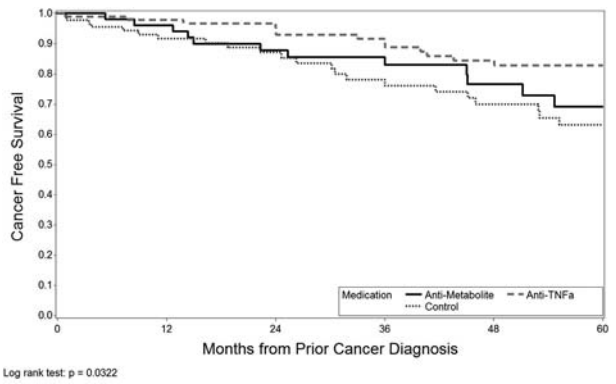
York, United States, [9]Weill Cornell Medical College, Medicine, New York, United States, [10]North Shore- Long Island Jewish University Hospital, Medicine, Manhasset, United States, [11]North Shore- Long Island Jewish University Hospital, Division of Gastroenterology, Manhasset, United States, [12]North Shore- Long Island Jewish Lenox Hill Hospital, Division of Gastroenterology, New York, United States, [13]North Shore- Long Island Jewish Lenox Hill Hospital, Medicine, New York, United States, [14]NYU Langone Medical Center, Medicine, New York, United States, [15]NYU Langone Medical Center, Division of Gastroenterology, New York, United States

Background: Most of our knowledge about the rates and types of malignancy associated with the use of antimetabolites and biologic agents in patients with inflammatory bowel disease (IBD) comes from studies of individuals who had no prior history of cancer. In patients with IBD and a history of cancer, little is known about their risk of new or recurrent cancer. The aim of this study was to investigate whether IBD patients with a history of cancer subsequently exposed to immunosuppression are at an increased risk of developing new or recurrent cancer.

Methods: Patients from 7 academic medical centers were identified based on a diagnosis of IBD and cancer with subsequent exposure to anti-TNF ("anti-TNF arm"), thiopurines or methotrexate ("antimetabolite arm"), or without subsequent immunosuppression exposure ("control arm"). Charts were reviewed for the primary outcome of incident cancer: new or recurrent. Baseline characteristics were compared with chi-square, anova, and t-test where appropriate. Time to incident cancer was compared between study arms using the log-rank test.

Results: Of patients with IBD and a history of cancer, 255 met inclusion criteria. Prior cancers included 121 solid, 62 gastrointestinal, 55 dermatologic, and 17 hematologic malignancies. Patients in the control group were more likely to have later stage primary cancers compared to the other study arms (p = 0.0003). During the follow-up period, 75 (29.4%) patients developed subsequent cancer: 36 (14.1%) a new cancer, 33 (12.9%) a recurrent cancer, and 6 (2.4%) a new and recurrent cancer. Incident cancer rate per 100 person-years for patients exposed to anti-TNF was 2.6 with 795 person-years of follow up, 14.8 with 122 person-years of follow up for patients in the antimetabolite arm, and 8.52 with 422 person-years of follow up for controls. There was a significant difference in time to subsequent cancer between groups (Figure, Log-rank p = 0.0322), with patients exposed to anti-TNF being less likely to develop a new or recurrent cancer compared to controls (p= 0.0110). There were no significant differences in type of subsequent cancer between groups.

Conclusions: In this series of IBD patients with a history of cancer, exposure to either anti-TNF or an antimetabolite following a cancer diagnosis was not associated with an increased risk of an incident cancer compared to patients who did not receive these agents. Prospective data is needed to confirm these findings, but our study supports growing evidence for the safety of anti-TNF in IBD patients with a history of cancer.



"Figure. Time to incident cancer, new or recurrent, between study groups."

OP021
TURANDOT: a randomized, multicenter double-blind, placebo-controlled study of the safety and efficacy of Anti-MAdCAM Antibody PF-00547659 (PF) in patients with moderate to severe Ulcerative Colitis (UC)

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Background: Inhibiting WBC trafficking from capillary into gut mucosa is a new approach to treating UC. Until now, all agents have acted on integrins found on circulating WBC. PF, a fully human monoclonal antibody, acts directly on MAdCAM, a cell adhesion molecule expressed mainly by intestinal venules. The TURANDOT study was designed to identify the preferred dose of PF to induce remission in subjects with moderate to severe UC.

Methods: Adults 18-65y with ≥3m history of documented UC that extended >15cm beyond the rectum, a total Mayo Score ***6 and endoscopic subscor ≥ 2, who had failed at least 1 approved therapy were eligible. Anti-TNF therapy was stopped ≥ 6 weeks before treatment and other drugs had to be stable. Prednisone doses >20mg/d (or equivalent) were prohibited. Immunosuppressant agents were stopped by week 12. Randomized treatment groups were placebo, 7.5mg, 22.5mg, 75mg or 225mg PF every 4 weeks for 3 doses. The primary end point was week 12 remission, defined as total Mayo score ≤2 with no subscore >1. Secondary end points were week 12 response (Mayo score decrease ≥3 and ≥30% decrease from baseline) and mucosal healing (Mayo endoscopy subscore ≤1).

Results: 357 subjects were enrolled and 7 patients remain in safety follow-up. Treatment arms were generally comparable in age (mean 40.2 years) and gender distribution (58% male). 43% of subjects were anti-TNF naïve and the baseline Mayo score ranged from 8.1 (1.6) to 8.7 (1.7).

Remission and mucosal healing were significantly greater in the 22.5mg and 75mg dose groups vs placebo, while response was significantly greater for 22.5mg and 225mg groups vs placebo.

Conclusions: The primary endpoint of the study was met, with the strongest signal derived from every 4-weeks doses of 22.5-75 mg. PF appears to be well-tolerated and not associated with increased rate of infection.

Effect size (active - placebo) of remission, response and mucosal healing

Dose	7.5mg	22.5mg	75mg	225mg
Remission	8%*	13%*	12%*	3%
Response	9%	25%*	16%*	21%*
Mucosal Healing	8%	19%*	16%*	7%

*p<0.05

OP022
Anti-MAdCAM-1 Antibody (PF-00547659) for Active Refractory Crohn's Disease: Results of the OPERA study

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Background: Inhibition of white blood cell (WBC) translocation from the bloodstream to the intestine is a promising new approach to the management of Inflammatory Bowel Disease. PF-00547659 (PF) is a fully human monoclonal antibody targeting MAdCAM on endothelial cells instead of its integrin ligand. OPERA is a randomized, multicenter double-blind, placebo-controlled study of safety and efficacy of PF in subjects with Crohn's disease (CD)
Methods: Adults ages 18-75, with active moderate to severe CD (CDAI 220-450) and a history of failure or intolerance to anti-TNF and/or immunosuppressant drugs were eligible if they had hsCRP >3.0 mg/L and ulcers on colonoscopy. Subjects were randomized to placebo, 22.5 mg, 75 mg or 225 mg arms. The primary end point was CDAI-70 response at week 8 or 12. Secondary end points were remission and CDAI-100 response and safety. Disease biomarkers studied were blood β 7+ CD4+ central memory T-cell level (frequency and β 7 expression) by FACS, CRP, and soluble MAdCAM
Results: 267 subjects were enrolled, and 2 patients remain in safety follow-up. CDAI-70 response showed a nominal difference between PF-00547659 and placebo without reaching statistical significance. However, remission at week 12 appeared to be substantially higher in the subjects with above median baseline CRP levels (CRP >18). Soluble MAdCAM in treated, but not in placebo subjects decreased significantly at week 2 compared with baseline, in a dose-related manner, and remained low during the study. Circulating β 7+ CD4+ central memory T-lymphocytes increased at weeks 8 and 12, in PF treated subjects in a dose-dependent manner.
Baseline characteristics and selected outcomes are presented in Table 1 and efficacy results in Table 2.
Conclusions: While the primary endpoint was not met because of a high placebo response, PF was pharmacologically active as shown by a dose-related increase in circulating β 7+ T lymphocytes and a sustained dose-related decrease in MAdCAM. Higher baseline CRP levels appear to differentiate responders to PF versus placebo. No safety signal was observed in this study

Table 1 Patient charecteristics.

Value	Placebo	22.5mg	75mg	225mg
N	63	67	64	68
Age, yrs (mean sd)	34.4 (11.1)	37.0 (13.1)	34.7 (10.6)	35.9 (1.0)
CD Duration years (median, range)	10.5 (0.8-51.8)	11.5 (1.9-38.1)	8.2 (0-36.5)	12.4 (0-30.5)
Baseline CDAI (mean, sd)	313 (61)	308 (71)	324 (65)	316 (64)

Analysis using a generalized linear mixed model and reporting proportions for subset analysis

Table 2 Efficacy results at Week 12.

	Placebo	22.5mg	75mg	225mg
Response 70 week 12	59% (9.0%)	62% (9.0%)	65% (9.0%)	58% (8.9%)
Remission week 12 (se)	23% (8.3%)	27% (9.1%)	28% (9.7%)	29% (9.3%)
Remission week 12 with baseline CRP>18 (se)	14% (7.6%)	37% (11%)	24% (9.2%)	39% (10.2%)

OP023
Methotrexate for corticosteroid-dependent ulcerative colitis: results of a placebo randomized controlled trial.

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Background: There is no controlled trial of parenteral methotrexate (MTX) in ulcerative colitis (UC). We conducted a prospective, controlled, randomized, double-blind trial of intra-muscular or subcutaneous MTX at a dose of 25mg/week vs placebo in patients with steroid-dependent UC.

Methods: Eligible patients had active or inactive UC and were on prednisone at a daily dose of 10 to 40 mg at inclusion. Exclusion criteria were resistance to oral steroids, need for colectomy, alcohol consumption, pulmonary, renal or liver disease, obesity or diabetes mellitus, pregnant or breast-feeding female subjects, infection with HIV, HBV, HCV, a past history of malignant condition, use of other immunosuppressants within 1 month prior to inclusion or anti-TNF treatment within 2 months prior to inclusion. The primary endpoint was success at week 16 as defined by a Mayo score < or = 2 with no item >1, complete steroid withdrawal with a forced tapering regimen, and no need for other IS, anti TNF or colectomy. Secondary endpoints were success at week 24, success at week 16 and 24, mucosal healing (Mayo endoscopic subscore = 0 or 1), clinical remission (Mayo clinical subscore < or =χ2 with no item>1) without steroids and no need for other IS, anti TNF or colectomy at week 16 and/or 24. Endpoints were compared using chi square tests. The analysis was performed on an intent-to-treat basis. We expected a success rate of 45% with methotrexate and 20% with placebo. One hundred and ten patients were deemed sufficient to show a statistically significant difference with a 80% power and an alpha risk of 5% (bilateral test).

Results: One hundred and eleven patients (59 male, median age 42) were included in 26 European centers: 60 were randomized to the MTX arm and 51 to the placebo arm. Median dose of prednisone was 25 mg/d at inclusion. Rates of success at week 16 were 32% of patients among patients given MTX vs 20% among patients given placebo (difference 12.1% [CI 95%: -4.0%; +28.1%]; p=0.15). Clinical remission without steroids and no need for other IS, anti TNF or colectomy at week 16 was observed in 42% of patients given MTX vs 23.5% of patients given placebo (difference 18.1% [IC 95%: 1.1%; 35.2%]; p=0.04). The other secondary endpoints were not significant. Mucosal healing was observed in 35% of patients given MTX vs 25.5% of patients given placebo (difference 9.5% [CI 95%: -7.5% ; + 26.5]; p= 0.28). Rates of serious adverse events were 10% in the MTX group and 6% in the placebo group (p =0.5).

Conclusions: Treatment with parenteral MTX was not significantly superior to placebo for the primary endpoint. However it induced clinical remission without steroids in a significantly larger percentage of patients with steroid dependent UC than placebo.

OP024
A randomized, double-blind, placebo-controlled induction trial of an oral S1P receptor modulator (RPC1063) in moderate to severe Ulcerative Colitis: Results of the TOUCHSTONE study

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Background: RPC1063 is an oral, selective sphingosine 1-phosphate (S1P) 1 and 5 receptor modulator in clinical development for the treatment of ulcerative colitis (UC) and relapsing multiple sclerosis. The objective of this study was to evaluate the efficacy of 0.5 mg (low dose, LD) and 1.0 mg (high dose, HD) RPC1063 in comparison to placebo (PBO), and characterize the safety of RPC1063 in patients with moderate to severe UC.

Methods: This was an international, 8-week induction trial in UC, with a continuing maintenance period for responders. 197 patients were randomized (1:1:1) and treated once daily with PBO (n=65), LD (n=65) or HD (n=67). The primary endpoint was the proportion of subjects in remission (Mayo score ≤ 2, no subscore >1) at Wk 8. Secondary endpoints were the proportion of patients in response (reduction in Mayo score of ≥ 3 and ≥ 30 % with a decrease in the rectal bleeding score of ≥1 or a rectal bleeding score ≤1), proportion of patients with mucosal improvement (endoscopy score ≤1), and the change in Mayo score. Safety assessments included ECG, Holter monitoring, pulmonary function testing, optical coherence tomography and adverse events (AEs).

Results: 95% of patients completed the induction portion of the study. The proportion of patients achieving clinical remission was 16.4% for HD (p=0.0482 vs. PBO), 13.8% for LD (p=0.1422), and 6.2% for PBO. The proportion of patients with clinical response was 58.2% for HD (p=0.0140), 53.8% for LD (p=0.0648), and 36.9% for PBO. The proportion of patients with mucosal improvement was 34.3% for HD (p=0.0023), 27.7% for LD (p=0.0348), and 12.3% for PBO. The improvement in Mayo score from baseline was 3.3 points for HD (p=0.0035), 2.6 points for LD (p=0.0986), and 1.9 for PBO.

The AE profiles were comparable between groups, with approximately 31% of patients experiencing a treatment emergent AE (TEAE) across all groups. The most common TEAEs in the study were worsening of ulcerative colitis (HD 1 [1.5%], LD 2 [3.1%], PBO 3 [4.6%]) and anemia/decreased Hgb (HD 0, LD 3 [4.6%], PBO 3 [4.6%]). Only modest effects on heart rate were seen with no notable cardiac, pulmonary, ophthalmologic or malignancy AEs observed. Transient ALT ≥3x ULN occurred in 3 patients (HD 1 [1.5%], LD 2 [3.1%]) and decreased with continued treatment.

Conclusions: Modulation of S1P receptors in patients with moderate to severe UC with RPC1063 1 mg induced clinical remission, clinical response, and mucosal improvement, validating a novel therapeutic approach for the treatment of UC. The positive efficacy and the safety/tolerability results from this study suggest a favorable risk-benefit profile of RPC1063 that supports a Phase 3 UC program.

OP025
A randomized, double-blind placebo-controlled phase 2a induction study of MEDI2070 (anti-p19 antibody) in patients with active Crohn's disease who have failed anti-TNF antibody therapy

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Background: IL-23 is implicated in the pathogenesis of Crohn's disease (CD). Previous studies of antibodies targeting the p40 subunit common to IL-12 and IL-23 suggested benefit in patients with CD who had failed treatment with anti-tumor necrosis factor (TNF) therapy. We studied the efficacy and safety of MEDI2070, a fully human IgG2 monoclonal antibody that selectively binds the p19 subunit of IL-23, in patients with active CD who had failed or were intolerant to anti-TNF therapy.

Methods: Subjects were 18-65 years old with active CD (Crohn's Disease Activity Index [CDAI] score ≥ 220 and ≤ 450) and active inflammation (C-reactive protein [CRP] ≥ 5 mg/L, or fecal calprotectin [FCP] ≥250 mcg/g, or endoscopic evidence of inflammation within 12 weeks of screening). All subjects had received ≥1 anti-TNF agent, with primary nonresponse, loss of response, or intolerance. Stable doses of 5-aminosalicylates, prednisone ≤20 mg/d, budesonide ≤ 6 mg/d, antibiotics for CD for at least 2 weeks, or immunomodulators (IMM) for at least 8 weeks, were permitted. Using concealed allocation, subjects were randomized blindly to MEDI2070 700 mg IV or placebo at Weeks 0 and 4, with stratification by number of prior anti-TNF agents (1 vs. >1), and followed to week 12. Primary analysis was comparison of the proportion of subjects receiving at least one dose of study medication who achieved clinical effect, defined as clinical response (≥100 point drop from baseline CDAI) OR clinical remission (CDAI <150) at week 8 (W8). Assuming clinical effect of 20% with placebo, 54 subjects per arm provided 87% power to detect a 25% treatment difference using a 2-sided significance level of 0.1.

Results: 121 subjects (61 placebo, 60 MEDI2070) were randomized, with 1 subject per arm not dosed. 57 placebo and 55 MEDI2070 subjects completed W8. Baseline characteristics were similar, with mean (SD) baseline CDAI 319 (58), 71.4% with CRP ≥5, and 75.9% with FCP ≥250. 31.1% had 1 prior anti-TNF agent; 68.9% had ≥2. 38.7% had primary anti-TNF failure. With MEDI2070, 49.2% had clinical effect at W8 vs. 26.7% with placebo (P=0.010). At W8, clinical remission was noted in 27.1% with MEDI2070 vs. 15.0% with placebo (p=0.102) and clinical response in 45.8% and 25.0%, respectively (p=0.017). A composite outcome of clinical effect AND ≥50% reduction from baseline FCP or CRP was achieved in 42.4% with MEDI2070 vs. 10.0% with placebo (p<0.001). No increased rate of adverse events with active treatment was observed over 12 weeks as compared to placebo.

Conclusions: MEDI20170, a specific anti-IL-23 antibody, demonstrates clinical effect in patients with active CD who have failed anti-TNF therapy, and has a favourable safety profile over 12 weeks.

OP026
Post-operative use of anti-TNFα agents in patients with Crohn's disease and risk of re-operation - a nationwide cohort study

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Background: Up to 80% of patients with Crohn's disease (CD) will at some time require surgery. Surgery is not curative and recurrence is typical. An advantageous role of post-operative anti-tumour necrosis factor-alpha (anti-TNFα) agents has been suggested in observational and small clinical studies. In a nationwide cohort study, we examined the magnitude of risk of reoperation in CD patients treated postoperatively with anti-TNFα agents.

Methods: Association between postoperative anti-TNFα agents and reoperation was studied in two cohorts of CD patients undergoing first time operation. Cohort 1: patients not treated with anti-TNFα agents within 6 months before operation; Cohort 2: patients treated with anti-TNFα agents at least once within 6 months before operation. We defined postoperative exposure to anti-TNFα agents as at least one treatment within 6 months after first time operation (exposed cohort), reference cohort was patients not treated with anti-TNFα agents within 6 months after first time operation. Patients were followed from 6 months after first operation until date of reoperation, death, emigration or end of follow-up (5 years). We used Cox proportional-hazards regression to compute crude and adjusted hazard ratios (aHR) with 95% confidence intervals (95% CI). Adjustment was made for age, sex, co-morbidity (Charlson Index), duration of CD, use of immunosuppressive agents within 6 months after operation. Data were retrieved from nationwide Danish health registries.

Results: In cohort 1, patients not treated with anti-TNFα agent before operation (n=2446), only 31 (1.3%) received anti-TNF α agent within 6 months after operation (exposed cohort), 2415 (98.7%) were not treated (reference cohort). Compared to those not treated with anti-TNFα agent after operation, the aHR of reoperation among those treated was 3.14 (1.45-6.81). In cohort 2, patients who were treated with anti-TNFα agent before operation (n=387), 63 (16.3%) were treated with anti-TNFα agent within 6 months after operation (exposed cohort), and 324 (83.7%) were not treated (reference cohort). Compared to those not treated with anti-TNFα agent after operation, the aHR of reoperation among those treated was 1.79 (0.94-3.40).

Conclusions: Postoperative use of anti-TNF α agent was low in anti-TNFα agents naïve patients (1.3%), while 16.3% of the patients pre-operatively exposed to anti-TNFα received this therapy post-operatively. Postoperative anti-TNFα treatment did not reduce the need for subsequent surgery compared to patients not treated. Thus, a reduced rate of surgery after post-operative anti-TNFα treatment could not be documented; however, confounding by indication may contribute to the results obtained.

OP027
The rising incidence of early-onset paediatric inflammatory bowel disease (Paris A1a) in Scotland since 1981: a national, population-based, cohort study

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Background: Although worldwide data has clearly shown the persistent rise in paediatric inflammatory bowel disease (PIBD), trends in the incidence of early-onset PIBD (i.e. diagnosed before their 10th birthday; Paris A1a) are not yet clear. Recent administrative data suggests that A1a PIBD has shown a dramatic rise in recent years [1] , however robust population-based incidence data are lacking. We aimed to evaluate the incidence of PIBD A1a disease in Scotland across four decades using a complete national cohort study.

Methods: National data from previously published incident cases of PIBD in Scotland during the periods 1981-1995 and 2003-2008 were examined to determine those diagnosed less than 10yrs of age; prospectively collected incident cases from 2009-2013 were also included. A1a cases were divided into two sub-groups for further analysis (0-5yrs and 6-9yrs at diagnosis). Incidence rates were calculated using publicly available population data from the Scottish government and trends across cohorts calculated using Poisson regression analysis.

Results: A total of 402 A1a PIBD patients were identified during the study periods. There was a steady increase in incident cases across epochs: 39 (1981-1985), 54 (1986-1990), 63 (1991-1995), 112 (2003-2007) and 134 (2008-2013) cases respectively. The crude incidence of A1a PIBD rose from 1.2/100,000/yr (1981-1985) to 4.0/100,000/yr (2008-2013) ($p<0.001$). The crude incidence of those diagnosed at 0-5yrs of age rose from 0.7/100,000/yr (1981-1985) to 2.0/100,000/yr (2008-2013) ($p=0.017$) compared to an incidence of 2.0/100,000/yr (1981-1985) to 7.2/100,000/yr (2008-2013) ($p<0.001$) for those diagnosed at 6-9yrs of age. The incident rate ratio between the first and last epochs were 2.9 (95% CI 1.5-6.4) and 3.6 (95% CI 2.3-5.8) for the 0-5yr and the 6-9yr age group respectively, demonstrating a three-fold increase in both groups across the study period.

Conclusions: Using population-based Scottish data from the previous four decades we have shown that early-onset PIBD (A1a) has shown a significant rise in incidence, with three-fold increases seen in both the very-early-onset (0-5yr) and 6-9yr age groups. Further examination of these young children, especially with regard to epigenetics and environmental exposures may provide clues to IBD aetiopathogenesis.

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OP028

Oral delivery of a new class of non-antibody protein scaffold Nanofitins targeting TNF-alpha shows a strong preventive and curative anti-inflammatory effect in models of inflammatory bowel diseases.

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Background: Despite a remarkable efficacy, treatment of inflammatory bowel diseases (IBD) using systemic administration of anti-TNF-alpha antibodies remains associated with serious adverse effects. Oral administration of such therapeutics would benefit from a better targeting to the site of inflammation in the gut while decreasing their systemic exposure and related side effects. To this aim, the SADEL FP7 European project has been developing oral formulation of anti-TNF-alpha Nanofitins (NF), a novel alternative scaffold derived from the sac7d protein found in an extremophilic archeabacterium and stable enough to survive the hostile environment of the gut.

Methods: Screening of anti-TNF-alpha NF hits was done in vitro using surface plasmon resonance and in vivo by evaluating their anti-inflammatory effects in preventive mode after intrarectal instillation (10 mg/kg) in TNBS-induced model of colitis (C57Bl6 mice), using 5-ASA at optimal dosage (30 mM) for comparison. NFs providing reduction of inflammation similar or superior to 5-ASA were engaged in a dose-range finding study in the same model, and the optimal dose has been confirmed in DSS-induced model of colitis (Balb/C mice). Oral efficacy was performed in TNBS-induced model of colitis by oral gavage of the NF leads, in preventive mode with a dose escalation (10, 100 and 400 mg/kg) and/or in curative mode at a single dose (100 mg/kg).

Results: 3 out of the 9 anti-TNF-alpha NFs screened at 10 mg/kg by intrarectal instillation in TNBS-induced model of colitis have demonstrated remarkable anti-inflammatory effects, with the lead NF candidate decreasing 30 % ($p = 0.0008$) of the lesions (5-ASA, 35 %) and 62 % of TNF-alpha expression (5-ASA, 46 %). The preventive effect of the NFs appeared to be directly correlated with their respective binding characteristics to TNF-alpha. The therapeutic efficacy of these 3 NFs in TNBS model has been improved again at the optimal dosage of 100 mg/kg, and has been further confirmed in DSS-induced model of colitis. Their anti-inflammatory efficacy was fully retained upon oral delivery without the need for a specific formulation as for the lead NF at 100 mg/kg decreasing 65 % (preventive, $p < 0.00001$) or 37 % (curative, $p = 0.047$) of intestinal inflammations.

Conclusions: The extreme stability of the NF scaffold allowed the generation of anti-TNF-alpha therapeutics with a powerful preventive and curative anti-inflammatory action after oral administration. The use of the oral route is expected to prevent from systemic-related side effects; making anti-TNF-alpha NFs a promising new avenue for the treatment of IBD. The drug development of the lead NFs is pursued in collaboration with a pharmaceutical partner within the SADEL FP7 European project.

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Digital Oral Presentations

Digital Oral Presentations

DOP Session 1 - Imaging IBD: Endoscopy, radiology or histology?

DOP001
Comparison of rectosigmoidoscopy and colonoscopy for assessment of endoscopic activity in ulcerative colitis

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Background: Endoscopy limited to the rectum and sigmoid has been the standard to measure mucosal healing (MH) rates in ulcerative colitis (UC) clinical trials. The objective of this study was to evaluate whether rectosigmoidoscopy adequately represents endoscopic activity of the more proximal colon.
Methods: Four central readers from 2 sites determined Mayo endoscopic subscores (MES) of the rectosigmoid region and proximal colon in 331 endoscopic videos (2 readers/video) from EUCALYPTUS, a Phase 2 induction study of etrolizumab in UC. Videos were obtained at baseline, day 43, and day 71. MH (MES≤1) and MES based on the rectosigmoidoscopy were compared with those based on colonoscopy when available. A third, independent central reader adjudicated discrepancies in scoring of MH between two readers.
Results: Among the 331 videos, 239 had examinations beyond the rectum and sigmoid. Of the 239 examinations, 230 had agreement with regards to presence of active disease (MES≥2) or MH (205 and 25, respectively) by rectosigmoidoscopy and colonoscopy. Of the remaining 9 examinations, the presence of activity was only detected in segments proximal to rectosigmoid. The overall correlation between rectosigmoidoscopy and colonoscopy for assessment of endoscopic activity was good/excellent (r=0.84). Table 1 summarizes the proportion of patients achieving MH between treatment groups and study visit by evaluation with rectosigmoidoscopy and colonoscopy. In 9 of 34 videos with mucosal healing in the rectum and sigmoid, endoscopy detected the presence of lesions in the proximal colon with a higher proportion of patients in the placebo group which had an impact on efficacy assessment at Day 71.
Conclusions: The overall correlation for presence of endoscopic activity between rectosigmoidoscopy and colonoscopy was good/excellent. However, in this study, greater persistence of proximal lesions in the placebo group had an impact on evaluation of mucosal healing and efficacy analyses. This finding should be confirmed in an independent study before full colonoscopy is recommended for clinical trials.

Table 1 Proportion of patients with mucosal healing (MH — Mayo 0 or 1) by treatment group, visit, and extent of evaluation. n= No. of patients with mucosal healing; N= total no. of patients with evaluable videos. P values: vs placebo.

		Placebo	etrolizumab 100mg	etrolizumab 300mg+LD
MH rectosigmoidoscopy at Day 43	n/N (%)	2/35 (5.7%)	6/34 (17.6%)	7/37 (18.9%)
	p-value		0.15	0.15
MH colonoscopy at Day 43	n/N (%)	2/35 (5.7%)	5/34 (14.7%)	5/37 (13.5%)
	p-value		0.26	0.43
MH rectosigmoidoscopy at Day 71	n/N (%)	5/37 (13.5%)	11/36 (30.5%)	8/36 (22.2%)
	p-value		**0.09**	0.37
MH colonoscopy at Day 71	n/N (%)	3/37 (8.1%)	10/36 (27.8%)	7/36 (19.4%)
	p-value		**0.03**	**0.19**

DOP002
The impact of magnetic resonance enterography and capsule endoscopy on the classification of disease in patients with known Crohn's disease: A PROSPECTIVE ISRAELI IBD RESEARCH NETWORK (IIRN) STUDY

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Background: The phenotypic classification of Crohn's disease (CD) (Montreal classification) is important in prediction of the disease course and selection of management strategy. The classification is usually determined at initial diagnosis and is frequently based on ileocolonoscopic and radiologic data. Advanced endoscopic and imaging techniques such as video capsule endoscopy (VCE) and magnetic resonance enterography (MRE) provide additional data regarding the extent of luminal disease and extraintestinal manifestations. Our aim was to prospectively evaluate the impact of MRE and VCE in patients with known small bowel CD (SBCD) on disease classification as compared to the original assessment.
Methods: Seventy six consecutive patients with known SBCD in clinical remission or mild disease (CDAI<220) were prospectively recruited and underwent MRE, and if patency was proven by patency capsule, VCE. Montreal classification was determined upon recruitment and compared to the classification based on the results of the diagnostic evaluation.
Results: Seventy six patients underwent MRE. VCE was performed in 53. Both tests were performed in average of 5.7 years (range 19-0.3) after original diagnosis. VCE and MRE detected new disease location in 56% and 39% of patients, respectively(p=0.27). New proximal disease was detected with VCE and MRE in 50% and 30%, respectively (p=0.13). New colonic disease was identified in 6 cases

(8%), 3 cases with each modality. Twenty seven percent of patients originally diagnosed with a benign phenotype (B1) were reclassified as having an advanced phenotype (B2/B3). MRE and VCE reclassified the phenotype in 26% and 10% of cases, respectively (p=0.11). Overall, according to findings of both tests the original Montreal classification was altered in 49\76 patients (64%). Capsule altered classification in 47% mostly by changing the extent of actual disease and MRE changed the classification in 50%, evenly by changing the phenotype and extent.

Conclusions: Video capsule endoscopy and magnetic resonance enterography alter the Montreal classification in a significant percent of Crohn's patients in complete remission. Video capsule endoscopy was significantly more sensitive for detection of proximal small bowel disease. Magnetic resonance enterography was significantly more sensitive in detection of changes in disease phenotype, mostly due to exclusion of patients with severe stricturing disease from performing video capsule endoscopy. The described changes in the disease classification may have an important impact on both clinical management and long-term prognosis in these patients.

DOP003
Diffusion-weighted magnetic resonance entero-colonography is highly effective to detect endoscopic ulcerations in ileocolonic Crohn's disease

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Background: Close monitoring of Crohn's disease (CD) patients is essential in the era of biologics. The need to repeat colonoscopies makes use of mucosal healing, as a therapeutic target, difficult to apply in daily practice. Diffusion-weighted magnetic resonance entero-colonography (DW-MREC)has shown good accuracy to detect and assess inflammatory activity in CD[1] [2].

We aimed to assess the correlation between endoscopic lesions and DW-MREC parameters i.e. Apparent Diffusion Coefficient (ADC) and Clermont score(CS) [2] .

Methods: In this prospective study, all the patients underwent consecutively DW-MREC without bowel cleansing, without rectal enema [2] and colonoscopy within 4 weeks (mean interval=17±11 days). Radiologists were not aware of endoscopic findings and vice versa. Results are given in mean±standard deviation.

Results: Among the 43 CD patients, 9 (20.5%) had previous intestinal surgery. CDAI, CRP and fecal calprotectin value were 179±93, 31.1±8.0g/L and 1172.9±730.3µg/g, respectively. The CDEIS, SES-CD and CS were 6.8±7.1, 9.2+/-8.0 and 15.8±10.7, respectively. Mean ADC was inversely correlated with CDEIS (rho=-0.40; p=0.0067) and SES-CD (rho=-0.33; p=0.032).

Considering the 194 segments (ileum=37,colorectal=159), ADC inversely correlated with segmental CDEIS (-0.48; p<0.001) and segmental SES-CD (-0.44; p<0.001). MRI directly visualized ulcerations with poor efficacy: sensitivity (Se)=0.29, specificity (Spe)=0.92. In contrast, ADC values were lower in the segments with deep ulcers (1.30±0.23) or superficial ulcerations (1.75±0.64) than in the segments without ulceration (2.15±0.5)(p=0.001). Using a ROC curve, we determined that segmental ADC<1.88 detected endoscopic superficial ulcerations with Se=0.64 and Spe=0.75. Segmental ADC<1.42 detected endoscopic deep ulcers with Se=0.91 and Spe=0.83 (AUC=0.84; p<0.001). Segmental ADC decreased with the ulcerations size increase: no ulceration (2.17±0.5), ulceration < 5mm (2.09±0.04), 6-20mm (1.79±0.65) and >20mm (1.50±0.53) (p=0.0001).

Regarding to the 37 ileal segments, CS correlated with ileal CDEIS (0.62; p<0.001) and ileal SES-CD (0.58; p< 0.001). CS was higher in the ulcerated segments (23.3±8.4) than in the segments without ulceration (12.4±10.0) (p=0.006). CS >18.9 detected ulcerations with Se=0.79 and Spe=0.73. CS increased with the ulceration size (p=0.012).

Conclusions: Although MRI correlated moderately with endoscopic scores, DW-MREC using ADC and Clermont score was highly effective to indirectly detect endoscopic ulcerations in CD. Thus DW-MREC could lead to define MRI healing as a new treatment goal in CD, which could be use both in daily practice and in clinical trials.

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DOP004
Early transabdominal ultrasonography to assess intestinal wall thickness and vascularity appears to predict long-term outcome in Crohn's disease patients undergoing infliximab therapy: A prospective study

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Background: Infliximab (IFX) is known to be effective in Crohn's disease (CD) patients, but there is a need to identify predictive factors for its efficacy. Transabdominal ultrasonography (TAUS) is a minimally-invasive approach for assessing transmural activity in CD lesions by looking at intestinal wall thickness and vascularity. This study was to investigate if TAUS can help to predict clinical response and long-term outcome in CD patients receiving IFX.

Methods: A prospective case-control study was undertaken in 26 CD patients who had undergone remission induction therapy with IFX from January 2007 to July 2014. IFX (5mg/kg) was given at weeks 0, 2, 6, and then every 8 weeks as maintenance therapy. TAUS was done at weeks 0, 2, and 6. The main lesion in each patient was identified for intestinal wall thickness, intestinal wall structure and blood flow within the intestinal wall by using color Doppler ultrasound imaging. Wall structure was evaluated semi-quantitatively in terms of preservation, indistinctness, or loss of

the five-layer structure. Blood flow was evaluated semi-quantitatively according to the Limberg score. The TAUS data were compared with CD activity index (CDAI) during IFX therapy up to week 54.

Results: At week 10, non-responders were 4 (15%), and responders were 22. Of the 22 responders, 15 (58%) sustained long-term remission up to week 54, while 7 patients (27%) had experienced loss of response (LOR) by week 54. There was no statistically significant difference in CDAI at week 10 between long-term remission and LOR subgroups (mean CDAI 72 vs. 104; P=0.21). Similarly, there were no significant differences in the wall thickness and wall structure of the affected bowel at weeks 6 between long-term remission and the LOR subgroups (-3.0mm vs. -2.0mm; P=0.33 and 1.1points vs. 1.7points; P=0.23, respectively). However, a significant difference was observed both in blood flow score and reduction rate in blood flow score of the affected bowel at week 6 between the two groups. The blood flow score was reduced by 2.7 points when compared to baseline in patients with long-term remission, but by 1.2 points in patients with LOR (P=0.014).

Conclusions: Transabdominal ultrasonography to assess intestinal wall thickness and vascularity at CD lesions revealed that both blood flow score and the reduction rate of blood flow score at week 6 may predict loss of response to infliximab at 12 months. Therefore, patients with residual vascularity at week 6 should be monitored closely for changing the treatment at an early stage to avoid LOR.

DOP005
Large bowel mucosal dysplasia in the original specimen influences on severity of pouchitis and higher risk of J-pouch dysplasia

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Background: Restorative proctocolectomy (RPC) is current gold standard procedure for most patient diagnosed with ulcerative colitis (UC). The incidence rate of J-pouch dysplasia or adenocarcinoma is low. The aim of the study was to investigate the correlation between large bowel mucosal dysplasia in the original specimen and the severity of pouchitis based on Pouchitis Disease Activity Index (PDAI) as well as the incidence of dysplasia in the J-pouch reservoir.

Methods: A total of 276 patients diagnosed with ulcerative colitis and undergoing RPC in our institution between 1984 and 2009 were analyzed. Mean follow-up was 9.7 years (range 1-23). Results of histological examinations of both original specimen and biopsies from the J-pouch taken during endoscopic examination were evaluated.

Results: Analyzing the original specimen, fifty six lesions of low grade dysplasia (LGD), twenty five lesions of high grade dysplasia (HGD) and five adenocarcinoma (Ca) lesions were revealed. Pouchitis was diagnosed in 66 of 276 patients (23,9%). In group of patients with pouchitis, in the original specimen 31 LGD were found, 19 HGD were revealed and 3 adenocarcinoma were found, whereas in remaining patients (n=13) there were neither dysplasia nor adenocarcinoma in the original specimen. Evaluating the PDAI score regarding the presence of dysplasia in the original specimen, the average PDAI scores were: 5.1 (no dysplasia/adenocarcinoma), 6.47 (group with LGD), 7.56 (group with HGD), 7.6 (group with Ca) with statistically important differences. All patients with dysplasia (n=8) or Adenocarcinoma (n=1) in J-pouch reservoir were positive for dysplasia in the original specimen. LGD of J-pouch (n=5) was associated with primary lesions of 3 HGD, 1 LGD, 1 Adenocarcinoma in the original specimen, whereas HGD of J-pouch reservoir (n=3) was associated with 2 HGD and 1 LGD in the original specimen. One patient with adenocarcinoma in J-pouch reservoir was diagnosed with adenocarcinoma found in the original specimen.

Conclusions: Dysplasia or adenocarcinoma in J-pouch reservoir is rare. Patients with dysplasia or adenocarcinoma in the original specimen are more susceptible to develop dysplasia in the J-pouch reservoir. The higher dysplasia in the original specimen, the higher PDAI resulting in severity of pouchitis. Precise follow up in group of patients with dysplasia lesions of original specimen should be recommended because of higher risk of neoplastic transformation.

DOP006
Histological normalisation is associated with superior clinical relapse free survival compared to histological activity and histological quiescence in ulcerative colitis

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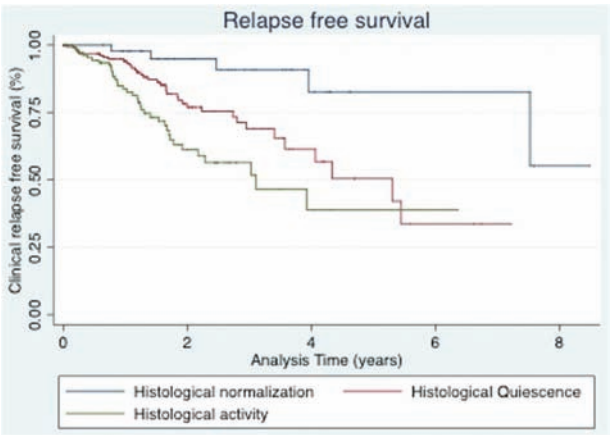
Background: We have recently shown that complete histological normalisation (CHN) of mucosa in ulcerative colitis (UC) patients is possible in the current era of disease-modifying therapies. This study examines if CHN is associated with reduced risk of clinical relapse (CR) in UC patients compared to those with histological activity (HA) or histological quiescence (HQ).

Methods: Patients with confirmed UC and baseline colonoscopy with biopsies taken in each segment of the colon (rectum, left and right-side) and follow-up colonoscopy more than one year later were identified. Those in clinical remission at final colonoscopy who had more than 6 months clinical follow-up were included. Demographic and clinical data was collected from case records. Each colonic segment of the final colonoscopy was evaluated for endoscopic mucosal healing (MH) and histological activity. The primary outcome was clinical relapse (CR) defined by an SCCAI > 2, sub-score of > 1 for stool frequency or rectal bleeding, medication escalation or hospitalization secondary to disease activity. CR-free survival was compared



"Clinical relapse free survival: Histological normalisation v histological quiescence v histological activity"

between patients with CHN without any crypt architectural distortion, HA with the presence of any residual histological inflammation, and HQ with crypt architectural distortion but no acute activity in all bowel segments. Predictors of CR-free survival were determined using Kaplan Meier analysis, log-rank test and Cox proportional hazard model.

Results: 310 patients (50% male, 60% pancolitis) were identified; 45 (15%) had CHN, 108 (35%) had HA, and 157 (51%) had HQ. 77 (25%) patients experienced CR at a median time of 1.3 years (range 0.06-7.52). On univariate analysis CHN (p=0.0001) was associated with improved CR-free survival.

MH (p=0.0077) and segmental histological normalisation (normal mucosa in bowel segment previously shown to have active UC) (p= 0.015) were also associated with improved CR-free survival. No other demographic, disease or medication related characteristics were significantly associated with CR. On multivariate analysis, only CHN was associated with improved CR-free survival. Hazard ratios for CR were 1.2 (95%CI: 1.11–10.30), p = 0.033 for patients who had evidence of HQ compared to CHN and 5.63 (95%CI:1.69–18.76, p = 0.005) for those with HA compared to those with CHN.

Conclusions: In UC patients, CHN is associated with improved CR-free survival compared to both histological quiescence and histological activity and is more predictive than MH. We describe a level of "deeper remission" with associated superior clinical outcomes.

DOP007
Mucosal healing in ulcerative colitis: when zero is better

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Background: Ulcerative colitis (UC) is a chronic inflammatory bowel disease characterized by a relapsing and remitting course. Extensive evidence has underlined the importance of mucosal healing, defined as the resolution of visible inflammation and ulceration at endoscopy, as a treatment aim for UC, and represents the gold standard for assessing disease activity . Currently, both endoscopic Mayo scores 0 (normal mucosa) and 1 (mild erythema, decreased vascular patterns) are accepted endpoints for UC mucosal healing.

We aimed to assess whether there was a difference in the incidence of clinical relapse at 12 months between UC patients with endoscopic Mayo scores 0 and 1.

Methods: Retrospective study, including all patients in corticosteroid-free remission between 2008 and 2013 and follow-up of at least one year with endoscopic Mayo score of 0 or 1 assessed during colonoscopy. We assessed clinical (age, gender, disease duration, therapy) as well as laboratorial values (haemoglobin, leukocytes, platelets, ferritin, CRP, ESR) at baseline colonoscopy and during a 12 month follow-up. Clinical relapse was defined as need for induction treatment, treatment escalation, hospitalization or surgery.

Statistical analysis was performed with SPSS v21.0, using chi-square test and a multivariate regression model; a p value < 0,05 was considered statistically significant.

Results: Included 138 patients, 72 (52,2%) female, with mean age 48,9 years (SD: 13,9; range 17-78). UC was classified as proctitis in 64 (46,4%) patients, left-sided colitis in 38 (27,5%) and pancolitis in 35 (25,4%), and mean disease duration was 8 years (range 1-31). Endoscopic Mayo score was classified as 0 in 61 (44,2%) patients and 1 in 77 (55,8%) patients. Clinical relapse during follow-up occurred in 28 (20,3%) patients, and was significantly more frequent in patients with Endoscopic Mayo Score-1 (27,3 vs 11,5%; p=0,022). This association was additionally encountered in the subset of patients with left-sided colitis or pancolitis (29,7 vs 11,1%; p=0,049), but not in patients with UC localized to the rectum (p=n.s.). In the multivariate analysis, endoscopic Mayo Score 1 was the only factor significantly associated with the risk of relapse during a 12 month follow-up (OR=2,89 CI 95% 1,14-7,36; p=0,026).

Conclusions: In patients with ulcerative colitis in corticosteroid-free remission, particularly those with left sided colitis or pancolitis, endoscopic Mayo Score 1 was significantly associated with a threefold increased risk of relapse compared to endoscopic Mayo Score 0. Our results support the use of endoscopic Mayo score 0 as the most suitable treatment endpoint to define mucosal healing in patients with ulcerative colitis.

DOP008
Plexitis as a predictive factor for early post-operative endoscopic recurrence in patients with Crohn's disease undergoing a right hemicolectomy with ileocolonic anastomosis: Results from a prospective, single center trial.

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Background: Many Crohn's disease (CD) patients will experience post-operative endoscopic recurrence (ER) within one year after surgery. Prediction of early ER is warranted, to advocate the initiation of post-operative prophylactic therapy. In retrospective studies, plexitis was proposed as a predictive factor for early post-operative ER and we aimed to confirm this in a prospective setting.

Methods: A prospective cohort of 74 patients (30 male; median age 45 years) undergoing a right hemicolectomy with ileocolonic anastomosis for confirmed CD was studied. As a control group, 19 patients with ulcerative colitis and 19 patients with a tumour of the caecum were included. Active smoking (n=21), fistulising disease (n=39) and previous bowel resections (n=28) were selected as predefined potential clinical confounders. The proximal resection margin of every surgical specimen was histologically investigated on three consecutive slides by a pathologist. Inflammatory cells were counted stepwise within and appositioned to every ganglion of both the myenteric and submucosal plexus. Eosinophils were counted on haematoxylin-eosin stained slides, lymphocytes and mast cells on immunohistochemically CD45 and tryptase stained slides, respectively. All patients underwent ileocolonoscopy six months after surgery, and endoscopic recurrence was defined as a Rutgeerts score of ≥i2b. Statistical analyses were performed using SAS software and were based on application of Bayes' rule.

Results: At six months, ER was seen in 37 of 74 patients (50%). Prediction of ER based on the clinical confounders led to an area

under the curve (AUC) of only 0.547 (95%CI:0.415-0.678). When looking at the counts, the mean count of submucosal and myenteric lymphocytes, as well as submucosal mast cells was significantly higher in CD-patients compared to the control groups (P<0.0001). Furthermore, the submucosal lymphocyte count could discriminate between ER and no ER with an AUC of 0.640 (0.513-0.767). Adding these submucosal lymphocyte counts to the clinical parameters, resulted in a significantly higher AUC of 0.703 (0.584-0.821) (P=0.047) compared to the use of clinical information alone. Simplifying these analyses by looking only at the percentage of non-zero counts resulted in a comparable result with an AUC of 0.677 (0.554-800).

Conclusions: Submucosal lymphocytic plexitis in the proximal section margin was significantly related with the risk for ER after right hemicolectomy. In clinical practice, the use of the percentage of non-zero counts can be used to predict the risk for early post-operative ER. Furthermore, our data suggest that blocking lymphocyte trafficking in the post-operative bowel by anti-adhesion molecules may prevent early post-operative ER.

DOP009
Development of a Simplified histological Geboes Score for ulcerative colitis

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Background: The presence of histological activity in patients with clinical and endoscopic quiescent ulcerative colitis (UC) has been related to a higher risk of relapse. The Geboes histological Score is the most used in UC, but its complexity limits its applicability. [1] As it was previously developed to assess the effect of topical therapy, some aspects have become redundant in the era of biologicals. We therefore aimed to create a Simplified Geboes Score (SGS) and determine its accuracy to predict UC relapse.

Methods: Only variables linked to active inflammatory activity were taken from the original Geboes Score: neutrophils/eosinophils in the lamina propria and neutrophils in the epithelium were reduced to 3 subcategories, and epithelial injury at crypts and surface was combined into

"Proposed Simplified Geboes Score"

Simplified Geboes Score			
	Relapse	**Non-relapse**	**P value**
Grade 1: Basal plasma cells			**0.004**
1.0 No increase	7 (12%)	51 (88%)	
1.1 Mild increase	5 (56%)	4 (44%)	
1.2 Marked increase	3 (37%)	5 (63%)	
Grade 2: Lamina propria neutrophils and eosinophils			
Eosinophils			0.09
2A.0 No increase	12 (18%)	56 (82%)	
2A.1 Mild increase	2 (33%	4 (67%)	
2A.2 Marked increase	1 (100%)	0 (0%)	
Neutrophils			0.12
2B.0 No increase	13 (19%)	54 (81%)	
2B.1 Mild increase	1 (14%)	6 (86%)	
2B.2 Marked increase	1 (100%)	0 (0%)	
Grade 3: Neutrophils in the epithelium			0.17
3.0 None	10 (16%)	52 (84%)	
3.1 <50% crypts involved	4 (36%)	7 (64%)	
3.2 >50% crypts involved	1 (50%)	1 (50%)	
Grade 4: Epithelial injury			**0.02**
4.0 None	7 (12%)	50 (88%)	
4.1 Marked attenuation	1 (33%)	2 (67%)	
4.2 Probable destruction – Probable erosions	1 (25%)	3 (75%)	
4.3 Unequivocal crypt destruction – Unequivocal erosion	4 (67%)	2 (33%)	
4.4 Ulcer or granulation tissue	2 (40%)	3 (60%)	
Total Simplified Geboes Score			**0.11**
1.0	5 (12%)	37 (88%)	
1.1	0 (0%)	2 (100%)	
1.2	0 (0%)	3 (100%)	
2A.1	1 (50%)	1 (50%)	
2A.2	0	0	
2B.1	0 (0%)	3 (100%)	
2B.2	0	0	
3.1	1 (25%)	3 (75%)	
3.2	0	0	
4.1	1 (25%)	3 (75%)	
4.2	1 (25%)	3 (75%)	
4.3	4 (77%)	2 (23%)	
4.4	2 (40%)	3 (60%)	

one category. Additionally, basal plasmacytosis was included as a scoring variable (see Table). [2] All histological slides from a previous study evaluating UC patients with complete mucosal healing (Mayo 0) were then re-read by two independent readers. [3] UC relapse (clinical Mayo Score ≥ 3) was recorded in these patients over a 12-month follow-up period.

Results: Seventy-five UC patients (40 men, median age 40 years) with endoscopic healing were included. Histological activity was observed in 33/75 (44%) patients: 17 (23%) presented basal plasmacytosis (SGS grade 1), in 7/75 (9%) eosinophils (SGS grade 2A) were observed and in 8/75 (11%) neutrophils (SGS grade 2B) were identified in the lamina propria. Crypts were involved in 13/75 (17%) cases (SGS grade 3) and epithelial injury (SGS grade 4) was diagnosed in 18/75 (24%) patients. During follow-up 15 patients (20%) experienced a clinical relapse, and histological activity at baseline was observed in 10 of these (67%). Basal plasmacytosis (SGS grade 1, p=0.004) and epithelial injury (SGS grade 4, p=0.02) were significantly associated with UC relapse (see Table) and identified as predictors of relapse in univariate regression analysis (SGS grade 1 OR 6.5 [1.9-22], p=0.003; SGS grade 4 5.7 [1.7-19], p=0.005). After multivariate regression analysis, only epithelial injury was withheld as a UC relapse predictor (OR 6.9 [CI 1.9-24], p=0.003.

Conclusions: 67% of UC patients in endoscopic remission still showed histologic activity. We simplified the histological Geboes score and demonstrate that epithelial injury is a significant risk factor for relapse in these patients. Further studies should now be designed to validate this score.

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Digital Oral Presentations

DOP Session 2 – Epidemiology of IBD

DOP010
Incidence of inflammatory bowel diseases in the Faroe Islands from 1960-2014: a 54-year overview from a population-based cohort

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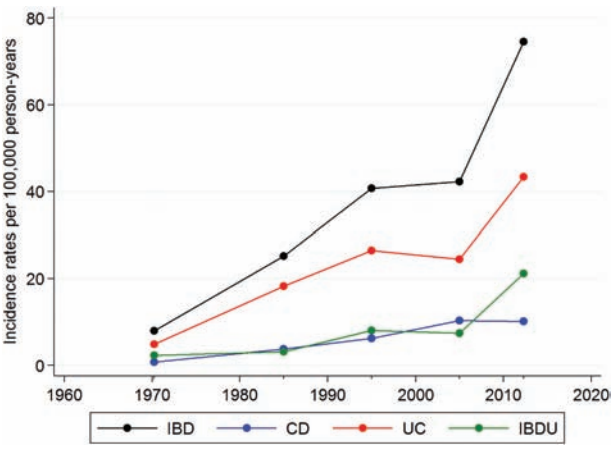
Background: Inflammatory bowel disease (IBD) consists of Crohn's disease (CD), ulcerative colitis (UC) and IBD unclassified (IBDU). In 2010 and 2011, the European Crohn's & Colitis Organization's Epidemiological Committee study (ECCO-EpiCom) found the highest incidence rate in the world on the Faroe Islands of 83 per 100,000 person-years (1). In the present study we assessed the long-term time trends in IBD incidence in the Faroese population of approximately 49,000 inhabitants.

Methods: Data were retrieved from the national patient registry at the Medical Department at the National Hospital of the Faroe Islands and included all cases of CD, UC and IBDU from July 1960 to July 2014. Patients of all ages who where diagnosed with IBD in the Faroe Islands were included. Diagnoses were determined according to the Copenhagen Diagnostic Criteria.

Results: A total of 664 patients have been diagnosed with IBD in the last 54 years on the Faroe Islands, 114 with CD, 417 with UC and 133 with IBDU. In 1960-79, a total of 55 persons were diagnosed; 105 in 1980-89; 166 in 1990-99; 179 in 2000-09, and 159 persons from 2010 until the end of July 2014. This represents an increase in the age-standardised IBD incidence rate (European Standard Population, ESP) from 8, 25, 41, 42, to 75 per 100,000 person-years. The age-standardised incidence rate (ESP) was also calculated for CD, UC and IBDU. For CD, the rate increased from 1 to 10, for UC from 5 to 43 and for IBDU from 2 to 21 per 100,000 person-years (figure 1).



"Figure 1 Incidence rates for IBD, CD, UC and IBDU for the periods 1.7.1960-31.12.1979, 1.1.1980-31.12.1989, 1.1.1990-31.12.1999, 1.1.2000-31.12.2009 and 1.1.2010-31.7.2014 in the Faroe Islands."

Conclusions: The highest incidence of IBD in the world is found on the Faroe Islands. The increase in the IBD incidence over the last 54 years has been dramatic, from 8 in 1960-79 to 75 in 2010-14 per 100,000 person-years. Such a rapid change is most likely linked to not only increased diagnostic awareness but also to so far unidentified environmental factors.

[1]

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DOP011
The ongoing rapid and significant rise of incident paediatric-onset inflammatory bowel disease in Scotland

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Background: The worldwide incidence of paediatric-onset inflammatory bowel disease (PIBD) is rising, with Scotland having the highest rate in the UK. Scottish PIBD data over the last 40 years has shown a consistent increase, including a 76% rise over 13 years around the millennium [1] . The aim of this study was to calculate current PIBD incidence rates in Scotland and to determine if the temporal trend of significant increase has been maintained.

Methods: Historical data from 2003-2008 (cohort 1) was compared to prospective, nationwide data of all incident cases diagnosed in paediatric services (under 16 years of age) from 2009-2013 (cohort 2). Age-sex adjusted incidence rates were calculated using population data from the General Registrar's Office for Scotland. Cases were classified as Crohn's disease (CD), ulcerative colitis (UC) or inflammatory bowel disease unclassified (IBDU) and diagnosed according to the Porto criteria. Statistical analysis was performed using Poisson regression.

Results: A total of 436 patients were diagnosed with PIBD over six years in cohort 1 (265 CD, 115 UC, 56 IBDU) compared to 478 children over five years in cohort 2 (286 CD, 126 UC, 66 IBDU). Median age at diagnosis in cohort 2 (60% males) was 12.3 years, similar to cohort 1 (58% males) at 11.9 years. The adjusted incidence rate increased from 7.8/100,000/year (95%CI 7.1-8.6) in cohort 1 (2003-2008) to 10.4/100,000/year (95%CI 9.6-11.5) in cohort 2 (2009-2013) (p<0.001). This significant increase was also seen individually for CD (4.7/100,000/year [95%CI 4.2-5.4] compared to 6.3/100,000/year [95%CI 5.6-7.0][p<0.0001]) and UC (2.1/100,000/year [95%CI 1.7-2.5] compared to 2.7/100,000/year [95%CI 2.3-3.3][p=0.009]). There was a non-significant increase in IBDU from 1.0/100,000/year (95%CI 0.7, 1.3) in cohort 1 to 1.4/100,000/year (95%CI 1.1, 1.8) in cohort 2 (p=0.07).

Conclusions: There continues to be an ongoing rise in incident PIBD (and both CD and UC) in 2009-13 in this national, population-based study compared to recent historical data, with a further significant rise of 33%. The reasons behind this continued increase remain unclear and further research is needed to elucidate potential factors in aetiopathogenesis.

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DOP012
Incidence and risk factors of cutaneous manifestations in pediatric-onset Crohn'sdisease: A population-based study

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Background: Cutaneous manifestations (CM) are common in adult patients with Crohn's disease (CD), but their incidence in pediatric-onset CD is unknown. The aims of our study were in a population-based pediatric-onset CD cohort: i) to determine the cumulative incidence of CM, including aphtous stomatitis (AS), erythema nodosum (EN) and pyoderma gangrenosum (PG); and ii) to identify the socio demographic and clinical factors at CD diagnosis associated with a higher risk of developing CM during the CD course.

Methods: Clinical data at diagnosis and at maximal follow-up were recorded in a population-based pediatric-onset CD cohort (n=537, <17 years at CD diagnosis) diagnosed from 1988 to 2004. Data on CM were reviewed by a dermatologist. Cumulative incidence and risk factors of CM were estimated by survival analysis and by Cox models, respectively.

Results: Median age at CD diagnosis was 14.6 years (Q1=12.2; Q3=16.1) and 53.6% of patients were males. At CD diagnosis, CM were present in 87 patients (16.2%) of whom 26 had (30%) at least 2 CM. After a median follow-up of 11 years (Q1=7; Q3=15), 148 patients (28%) had developed a total of 175 CM, including 110 (63%) AS, 59 (34%) EN, and 6 (3%) PG. Cumulative incidence of CM was 21% [17.7 -24.6], 25% [21.6-29.0], 27% [23.5-31.2] and 28% [24.3-32.3] at 1, 5, 10 and 15 years, respectively. In multivariate analysis, female gender (HR=2.6 [1.4-4.6]; p=0.002), age at diagnosis <15 years (HR=2.2 [1.3-3.8]; p=0.003) and L4 location at diagnosis (HR=2.2 [1.3-3.6]; p=0.002) were associated with a higher risk of developing CM during the CD course.

Conclusions: In this population-based pediatric-onset CD cohort, CM are frequent both at diagnosis and during CD course, and are associated with female gender, age <15 years and L4 location at CD diagnosis. These results emphasize the need for a close collaboration between dermatologists, pediatric gastroenterologists and gastroenterologists in pediatric-onset CD in order to optimize the management of these patients.

DOP013
Increase of Inflammatory Bowel Disease incidence in teenagers in a prospective population-based-study over a 21-year period (1988-2008)

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Background: Few data are available on recent temporal trends in the incidence of pediatric-onset inflammatory bowel disease (IBD) in industrialized countries. The aim of this prospective study was to assess the change in incidence and clinical presentation of pediatric-onset IBD over a 21-year period.

Methods: Pediatric-onset IBD was defined by an age at diagnosis <17 years. Data at diagnosis were extracted from the population-based IBD study in Northern France (Epimad Registry) between 1988 and 2008. Age groups and location at IBD diagnosis were defined according to the Paris classification (1) with age: <10 yrs or ≥ 10 yrs and location as follows: 1) for CD: pure small bowel involvement (L1); pure colonic involvement (L2); ileocolonic involvement (L3); 2) for UC: proctitis (E1); left sided colitis (E2); extensive colitis (E3); pancolitis (E4

Results: During this 21-year period, 1147 incident pediatric-onset IBD cases were recorded (8% of all IBD) including 846 CD (73.8%), 271 UC (23.6%) and 30 IBD unclassified (IBDU) (2.6%) cases. Median age at diagnosis was similar in CD (14.5 years [Q1=11.9-Q3=16.1]) and UC (14.1 years [11.0-16.0]) and did not change over time. There were significantly more males in CD than in UC (53.4% vs 45.0%; p=0.02). Median time between onset of symptoms and IBD diagnosis was stable over time at 3 months [1-6]. Mean incidence was $4.0/10^5$ for IBD as a whole (3.0 for CD, 0.9 for UC and 0.1 for IBDU). During this 21-year period a dramatic increase of both CD and UC incidence was observed in teenagers

[10-16 years]: for CD from 4.3 in 1988-90 to 9.6/10^5 in 2006-08 (+123%; p<10-3) and for UC, from 1.6 to 2.9/10^5 (+81%; p<10-3) in both genders. IBD location did not change over time in both CD and UC; for CD: L1=12.2%, L2=14.5% and L3=73.3% and for UC: E1=31.1%, E2=25.4%, E3=10.5% and E4=33%.

Conclusions: In this large population-based study the incidence of both CD and UC dramatically increased in teenagers over a 21-year period with no modification of age, location at diagnosis and time between onset of symptoms and diagnosis. These results suggest that a strong environmental factor predisposing to IBD is at work in this population.

(1) Levine et al Inflamm Bowel Dis 2011

DOP014
Dietary patterns and risk of Inflammatory Bowel Disease in Europe: Results from the EPIC study

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Background: Diet is suspected to be an environmental factor involved in the etiology of inflammatory bowel disease(IBD). Epidemiological studies have examined associations between intake of specific nutrients or foods and risk of ulcerative colitis (UC) and Crohn's disease (CD)(1).However in several diseases,to assess the impact of overall diet and correlations between groups of foods and risk of disease, a dietary pattern approach have been used (2). For the first time, we prospectively investigated the global impact of diet to identify dietary patterns associated with UC and CD risks.

Methods: In this case-control study nested within the European Prospective Investigation Into Cancer and Nutrition (EPIC), we included all individuals who developed incident UC or CD during follow up and two matched controls. At recruitment, dietary intake from country-specific food frequency questionnaires and lifestyle factors were recorded(3-4). Conditional logistic regression models with adjustment for potential confounders were used to estimate incident rate ratios (IRRs) of developing UC and CD associated with the Mediterranean diet score and a posteriori dietary patterns produced by factor analysis.

Results: A total of 256 individuals were diagnosed with UC and 117 with CD. A "high sugar and soft drinks" pattern was associated with a higher risk of UC, particularly in cases diagnosed at least two years after dietary assessment (IRR for the fifth vs. first quintile 1.68 (0.98-2.87); ptrend = 0.03). Individuals with high sugar and soft drinks intakes were at high risk of UC only when they had low intakes of vegetables, legumes and fruit. No dietary pattern was associated with CD. The Mediterranean diet score was not associated with UC or CD.

Conclusions: In this large European prospective study a dietary pattern characterized by high sugar and soft drinks, and low vegetable, fruit, and legume consumptions was associated with UC risk. These findings must be confirmed in other populations, and experimental data are needed to explore the effect of such a dietary pattern on the composition and activity of the gut microbiota and other pathways involved in the pathogenesis of IBD. If confirmed, the increasing shift towards a diet rich in sugar and soft drinks could have contributed to the increased incidence of UC in the US and Europe over the past 50 years and more recently in Asia.

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DOP015
Inflammatory bowel diseases in Israel: High prevalence suggested by health maintenance organizations administrative databases

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Background: There are four Health Maintenance Organizations (HMOs) in Israel, all with centralized paperless electronic clinical charts. Use of health administrative databases is the most efficient method for constructing population-based cohorts but it is prone to misclassification which could result in over-or underestimation of the target population. Correct societal allocation of resources to treat IBD patients requires proper knowledge of the prevalence in the population. Current estimates in Israel are based on outdated studies on biased selected cohorts. We aimed here to determine the accuracy of the ICD-9 codes in identifying inflammatory bowel diseases (IBD) patients within the HMOs databases and to estimate the prevalence of IBD in Israel.

Methods: We constructed a standardized system to combine uniform data from the four Israeli HMOs databases, covering 98% of the 8,180,000 residents of Israel. Records on HMO members with at least one IBD-related ICD-9 code were retrieved from each HMO database (2000-2013; excluding deceased subjects). Charts of a random sample of 1200 subjects who had only 1-3 ICD-9 codes in total were retrieved in order to estimate the rate of false-positives (FP). Additionally, a cohort of 5,235 confirmed IBD patients treated in hospital-based IBD centers across Israel was assembled (i.e. true-positives (TP)). The rate of IBD patients who did not have any codes within the HMO databases (i.e. false-negative (FN)) was detected by chart abstraction.

Results: 64,215 subjects in Israel had at least one IBD-related code in their clinical chart. The rate of FN was only ~1% while the accuracy of identifying IBD patients among subjects with 1, 2 and 3 IBD-related codes (i.e. TP) was 6-25%, 36-42%, and 54-64%, respectively (range is between HMOs). Applying these rates, the total number of IBD patients in Israel is estimated at 38,453 (473 per 100,000 or ~0.4%).

Conclusions: This is the first validated estimated prevalence of IBD in Israel. The 0.4% estimated prevalence is among the highest reported worldwide. Simple search of IBD patients in the HMO databases by ICD-9 codes has only 60% positive-predictive value but 99% specificity. This supports the underway development and validation of novel search algorithms within the HMOs databases, which will provide a methodological infrastructure for performing population-based research using the HMOs administrative databases.

On behalf of the Israeli IBD Research Nucleus (IIRN).

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DOP016
Are extraintestinal manifestations associated with disease outcomes in Crohn's Disease? Results from a population based inception cohort between 1977-2012

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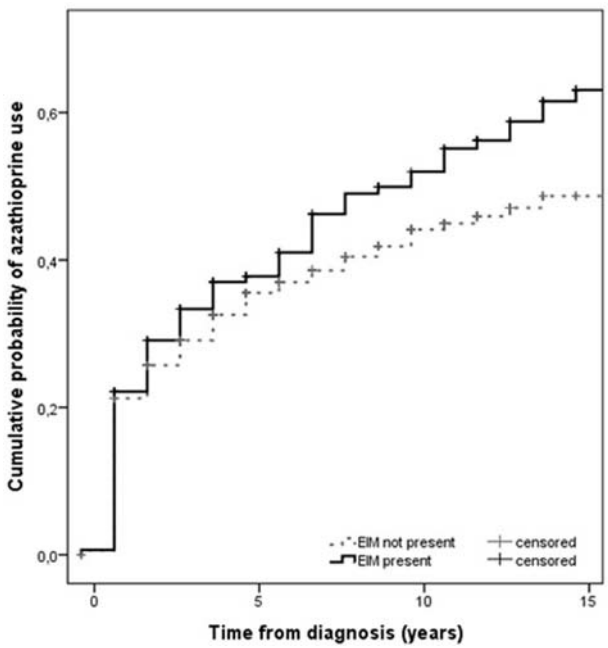
Background: Association between extraintestinal manifestations (EIM) and disease activity suggest a common pathogenic link. Limited data are available on the effect of EIMs on the long-term disease course in Crohn's disease. The aim of this study was to analyze the association between the presence of EIMs (joint, skin, eyes) and treatment steps and long term disease outcomes in the population-based CD inception cohort in the Veszprem province database between 1977 and 2012.

Methods: A well-characterized Hungarian cohort of 506 incident cases with Crohn's disease (male/female: 251/255, age at diagnosis: 31.5 years, SD 13.8 years) diagnosed between January 1, 1977 and December 31, 2008 were included. Follow-up data were collected until December 31, 2012. Both in- and outpatient records were collected and comprehensively reviewed.

Results: EIMs (Joint, skin and eyes) were present in 32.2%. Presence of EIMs was associated with female gender (OR: 1.59, 95%CI: 1.09-2.32; p= 0.01), location (p=0.009) and smoking (OR: 2.08, 95%CI: 1.40-3.07, p<0.001), but not with disease behavior, change of disease behavior or surgery. Presence of EIMs was associated with the need for azathioprine (OR: 2.13, 95%CI: 1.45-3.11, p<0.001; pmulti <0.001), anti-TNF therapy (OR: 3.20, 95% CI 1.71-5.95, p<0.001; pmulti<0.03) and steroid use (OR: 3.54, 95%CI 2.19-5.71, p<0.001; pmulti<0.001) in both univariate analysis and logistic regression analysis. In Kaplan-Meier analysis, there was a tendency of higher cumulative azathioprine use in patients with EIMs during follow up (pLogRank= 0.07), but not with time-to hospitalization, behavior change or surgery.

Conclusions: Presence of EIM was associated higher maximum treatment steps during the disease course including need for steroids, azathioprine and anti-TNF therapy.



"Figure 1 Cumilative probability of azathioprine use according to the presence of extraintestinal manifestations"

DOP017

Disease behaviour in Crohn's disease patients diagnosed in the biological era - A Dutch population-based IBD-SL cohort study

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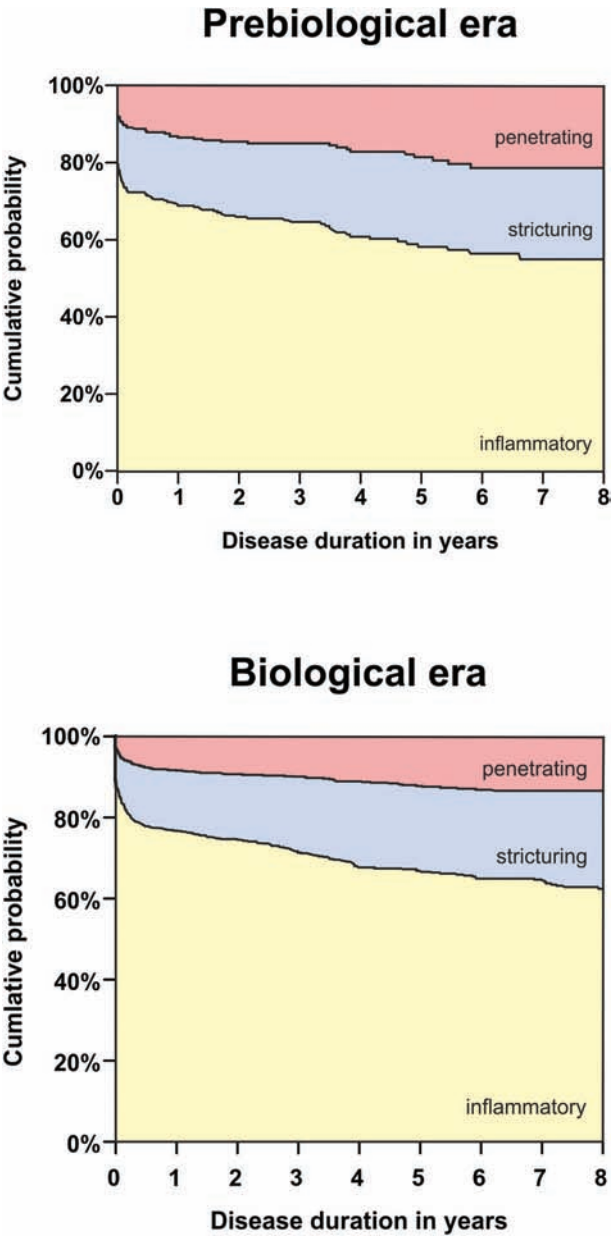

"Disease phenotype in the pre-biological and biological era"

Background: In Crohn's disease (CD), chronic inflammation can result in the development of strictures and fistulas. It has been suggested that progression to disabling phenotypes can be prevented by adequate treatment of (subclinical) inflammation. In the last decades, treatment modalities in CD have changed with the introduction of biological agents and an increased and earlier use of immunomodulators. It is, however, unknown whether disease phenotype progression had attenuated. The aim of this study was to compare disease behaviour between the pre-biological and biological era in a population-based cohort of CD patients.

Methods: Since 1991, incident IBD cases in the South-Limburg (SL) area are included in our population-based IBD-SL cohort, with over 93% completeness. All CD patients were divided in two time cohorts. The pre-biological cohort comprised patients diagnosed between 1991 and 1998, followed until 1999 (registration of biological therapy for CD). The biological cohort comprised patients diagnosed between 1999 and July 2011, followed until 2014. Disease behaviour was classified at diagnosis and during follow-up according to the Montreal classification as B1 (non-stricturing, non-penetrating), B2 (stricturing), or B3 (penetrating). Data were analysed with a Kaplan-Meier survival curve, and hazard ratios (HR) were calculated using a Cox regression model.

Results: In total, 342 patients in the pre-biological and 820 patients in the biological era were included. Mean follow-up was 4.0 (SD 2.5) and 6.4 (SD 3.6) years, respectively. At diagnosis, B2 or B3 phenotype were less often observed in the biological era (12.8% vs. 22.0%, HR 0.52; 95%CI 0.38-0.73), especially B3 phenotype (3.6% vs. 8.2%, HR 0.41; 95%CI 0.24-0.71) (Figure). Disease progression from B1 to B2 or B3 occurred in 29.7% in the pre-biological era and 28.3% in the biological era, HR 0.95; 95%CI 0.70-1.29. In both eras, ileal or ileocolonic disease was associated with phenotype progression (HR 4.85; 95%CI 3.06-7.67).

Conclusions: In this population-based CD cohort, patients diagnosed in the pre-biological and biological era had a similar risk of developing stricturing or penetrating disease. These findings indicate that disease phenotype progression has not changed, despite changes in CD management.

DOP018

A 17-year prospective cohort study of paediatric inflammatory bowel disease patients diagnosed less than 10 years of age (Paris A1a)

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Background: The Paris classification of paediatric inflammatory bowel disease (PIBD) highlights that patients diagnosed before their 10th birthday (Paris A1a) have a different clinical phenotype at presentation than those diagnosed aged 10-16 years (A1b). However, data regarding accurate incidence rates, disease natural history, medication use and surgery is required.

Methods: All A1a PIBD patients within our prospective, regional PIBD database from South-East Scotland diagnosed from 08/97-07/14 had data recorded regarding demographics, phenotype, details of medical therapy and surgery; data at last paediatric follow-up (FU) was also collected. Accurate incidence data was

generated using publicly available population data. Statistics were performed in R with Poisson regression analysis for incidence data.

Results: 121 A1a PIBD patients (77 Crohn's disease [CD], 28 ulcerative colitis [UC] and 16 IBD-unclassified [IBDU]) were identified (32% of PIBD cohort); 52% were male. Total FU was 816 patient-years; median FU was 7.1yrs (IQR 3.6-9.6). The incidence of A1a PIBD was 4.4/100,000/yr (CD 2.8/100,000/yr; UC 1.0/100,000/yr; IBDU 0.6/100,000/yr); there was no significant increase in incidence between 2000-2006 and 2007-2013 (p=0.577). One patient was diagnosed <2yrs (male UC requiring 5-ASA treatment), 34 at 2-5yrs and 86 at 6-9yrs. At diagnosis 20% of CD patients diagnosed aged 2-5yrs had panenteric disease, 36% isolated colonic disease, and 16% had isolated oral and/or perianal disease; all had inflammatory behaviour. At a median of 8yrs FU phenotype was similar. In the older CD cohort (diagnosed 6-9yrs) 41% had panenteric disease at diagnosis (45% at FU); 25% had isolated colonic disease; and 17% of this group progressed to penetrating/fistulising disease at follow-up. The younger age-group were less likely to have panenteric disease at diagnosis (p=0.002) or progress to penetrating disease (p<0.001). 73% of UC patients had E3 disease at diagnosis; this figure was 77% at a median of 5.5yrs follow-up. 61% had exposure to thiopurines, 27% to methotrexate (82% remission at 16 weeks), and 25% to anti-TNF therapy (57% remission achieved). 20 patients (17%) had IBD-related surgery; 16 CD patients and 4 UC patients.

Conclusions: A third of patients diagnosed with PIBD present before 10 years of age, with the incidence of very early-onset disease remaining stable over time. The requirement for immunosuppression, especially biological therapy, is significant. Intriguingly, differences exist between those diagnosed <6 years of age with older children more likely to have panenteric CD at diagnosis and to progress to penetrating disease.

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Digital Oral Presentations

DOP Session 3 – Safety first

DOP019
Opportunistic infections in inflammatory bowel disease (IBD): relevance of immunosuppressive therapy and mortality

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Background: Opportunistic infection (OI) is a main cause of death in IBD. There is controversy if the risk of OI is related to immunosuppressants (IMMS) or the disease itself.
AIMS: To evaluate: 1. The type of OI found in IBD under IMMS or biologicals (IMM/Biol), 2. The relationship of OI with IMM/Biol, 3. The mortality associated to OI and the impact of morbidity in OI associated mortality.
Methods: We performed a retrospective study of IBD patients that presented a relevant infection (requires hospitalisation, causes death or is life-threatening, causes IMM/Biol treatment withdrawal, or is a recurring condition). 183 cases were identified from the prospectively maintained ENEIDA local database from 6 Catalan hospitals (5736 patients - 3419 patients requiring IMM/Biol at any given point). For each patient four periods of infection exposure were analysed (P): P1 (median: 406 months): IBD pre- diagnosis, P2 (median: 59 months): from IBD diagnosis to IMM/Biol initiation, P3 (median: 57 months): during IMM/Biol, and P4 (median: 30 months): after IMM/Biol withdrawal/de-intensification; P3- P4 until end of follow-up or death.
Results: 292 infections were found in 183 patients. **P1 (n = 183)**: 9 infections. **P2 (n= 183)**: 15 infections: 10 patients with 1 OI and 2 with ≥ 2 OI. 2. **P3 (n=183/index infection)**: 1 OI in 96 patients, 2 in 41 and ≥ 3 in 46 patients. Median time from IMM/Biol treatment beginning and OI: 22 months. 88 patients received monotherapy, 87 COMBO, and 8 required 3 or more IMM/Biol. **P4 (n = 55)**: 1 infection in 10 patients (8 with IMMS monotherapy). **Types of infections:** 23 bacteremia / viremia, 46 urinary tract infection/pielonephritis/prostatitis, 85 respiratory infections, 49 colitis due to CMV /Clostridium difficile /other germs, 31 herpes virus (HSV, VZV), 13 tuberculosis (all except 1 patient had a recommended screening of latent tuberculosis and 2 patients presented tuberculosis after an appropriate tuberculostatic treatment), 5 papilloma virus infections (1 penis neoplasia), 21 skin/ENT infections, 17 liver/biliary tract infections, 3 bacterial meningitis, 5 vulvovaginitis , 2 endocarditis , 2 HIV, 1 leishmaniasis. **Comorbidity:** 80 patients had no concomitant diseases, 103 patients with one or more major comorbidity. The overall **mortality** was 4.3 % and associated to infection was 3.3 %. Mortality associated to infection was not related to comorbidity.
Conclusions: OI is a major cause of death in IBD irrespective of comorbidity. The risk of infection appears to be related to immunosuppression and not due to IBD itself. An intensive surveillance and awareness of OI in IBD patients requiring IMM/Biol should be performed, particularly for tuberculosis.

DOP020
The prevalence of autoimmune diseases in a nationwide paediatric inflammatory bowel disease cohort

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Background: Autoimmune diseases (AIDs) affect up to 10% of individuals living in Europe, so are a significant cause of morbidity. High rates of immune-mediated comorbidity and familial clustering suggest that genetic predisposition underlies AI disease susceptibility, yet few clinical studies have defined the prevalence rates of co-morbid AIDs in specific paediatric populations. We aimed to document the occurrence of Juvenile Idiopathic Arthritis (JIA) and other AIDs in a Scotland-wide cohort of paediatric inflammatory bowel disease (PIBD; diagnosed <17 years of age) patients.
Methods: The Paediatric-onset IBD Cohort and Treatment Study (PICTS) is a nationwide Scottish study of incident and prevalent PIBD patients, collecting a wide range of data, including rigorous phenotyping, with continuous long-term follow-up. The PICTS database was interrogated to identify patients enrolled up to 30/06/12 (follow-up to 30/06/14) with a diagnosis of at least one associated AID by last follow-up. Cases believed to be related to use of anti-TNF α treatment were excluded.
Results: Of 809 patients in the PICTS cohort, 43 had one or more associated AID, an overall co-morbid immune disease rate of 5.3%; 49% (21/43) male. There were 44 AIDs in 43 patients; one patient had dual AIDs (psoriasis [PSOR] and spondyloarthropathy [SPA]) co-existing with IBD. Otherwise, there were 7 cases of JIA, 3 cases of SPA and 9 cases of PSOR. Additionally there were 4 cases of coeliac disease, 2 of thyroiditis and 2 cases of type 1 diabetes. No

cases of Systemic Lupus Erythematosus (SLE) were identified. There were 15 cases of autoimmune liver disease (Primary Sclerosing Cholangitis [PSC], Auto-Immune Hepatitis [AIH] and Autoimmune Sclerosing Cholangitis [ASC]) in this cohort, accounting for 35% of all PIBD-associated AID.

Conclusions: Over 5% of PIBD patients in this large cohort study have associated AIDs. Autoimmune liver disease is the commonest AID in this cohort of PIBD patients; psoriasis accounted for 23% and JIA 16% of PIBD-associated AID.

DOP021
Risk of liver fibrosis in Crohn's Disease patients treated with methotrexate: A case-control study

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Background: Methotrexate (MTX) is the treatment of choice for many immune-mediated systemic disease as psoriasis or rheumatoid arthritis. In Crohn's disease (CD) the use of MTX is limited in part for their potential risk of liver fibrosis. However, the availability data in CD is very limited.Aims: To assess the prevalence of liver fibrosis in CD patients and identify associated risk factors.

Methods: All CD patients treated in any time with MTX (cases) in 2 referral centres of inflammatory bowel disease and patients with CD never exposed to MTX (controls) were prospectively included. Demographic characteristics, body-mass index (BMI), metabolic syndrome or liver disease risk factors (alcohol use, diabetes mellitus, dyslipemia, hypertension and HCV and HBC infection), duration and route of treatment administration and cumulative dose of MTX were obtained. Biological data were also collected (AST, ALT, INR and platelet levels) and the APRI and FORNS score were calculated. Liver stiffness was assessed by transient elastograhy (TE). Liver fibrosis was defined by TE > or =7,9 KPa, APRI >1,5 or FORNS >6,9

Results: A total of 84 patients were included (56 cases and 28 controls), 56% with inflammatory behaviour, 26% with penetrant behaviour, 43% with previously intestinal resection and 31% with perianal disease. 93% of patients not have routine alcohol consume, 9% have obesity and 37% have overweight. Only 5% of patients have diabetes and 13% dyslipemia. There are no differences in basal characteristics between the two groups. The mean cumulative dose of MTX received was 1.545mg (IIQ 730-2755) with a mean duration of 29 months (IIQ 12-60). 77% of patients received MTX subcutaneously, 50% with induction dose of 25 mg weekly for 16 weeks and all of them received acid folic supplementation. The mean values of TE, APRI and FORNS scores were 4,9 ± 1,9 KPa, 0,22 ± 0,1 and 3,2 ± 1,6 respectively in cases and 5,8 ± 2,9 KPa, 0,22 ± 0,2 and 3,7 ± 2,2 in controls, without differences between the two groups. Liver fibrosis by TE as previously defined was only detected in 3 cases (10,7%) and 4 controls (7,1%) (P=ns). Routine alcohol use, diabetes mellitus and major mean age were associated to liver fibrosis in the multivariate analysis.

Conclusions: The risk of liver fibrosis in CD patients treated with MTX is low and not seems superior compared with patients never exposed to MTX.

DOP022
Incidence of and risk factors for thromboembolism in Inflammatory Bowel Disease: Results from a population-based inception cohort

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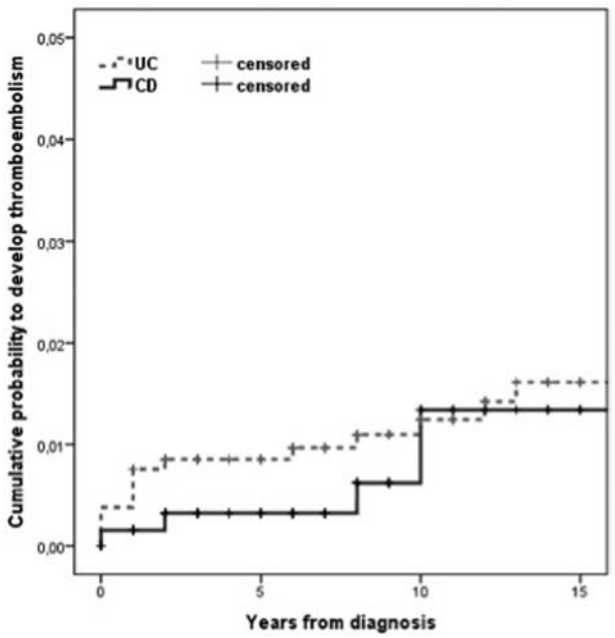
Background: Patients with inflammatory bowel disease (IBD) were reported to have an increased risk for venous thromboembolism (VTE), particularly when hospitalised. The estimated risk varies considerably among studies, primarily due to differences in cohort type and methodology. The aim of the present study was to analyze the incidence and risk factors of VTE in a population based inception cohort in the Veszprem province database between 1977 and 2012.

Methods: A total of 1708 incepted IBD patients were included (male/female: 879/829; CD (Crohn's disease): 648, age at onset: 29, IQR: 22-39; UC (ulcerative colitis): 1060, age at onset: 36, IQR: 26-50 years). Both in- and outpatient records were collected and comprehensively reviewed and followed-up until the 31st of December 2012 for a total of 21369 patient-years.

Results: Twenty-two VTE events were identified in 19 patients (6 events in 5 CD and 16 in 14 UC patients) - 15 deep vein thrombosis (DVT), 5 pulmonary embolism (PE) and 2 mesenterial thrombosis, 81.2% of the events occurred in patients with active disease. Four patients had a VTE event also prior to IBD diagnosis. The incidence rate of VTE was 1.03 per 1000 patient-years. Incidence was higher in males (1.34 per 1000 patient years, p=0.03, IRR: 2.94, 95%CI: 1.06-8.15) compared to females (0.73 per 1000 patient years). The



"Figure 1. Cumulative probability to develop venous thromboembolic events in patients with Crohn's disease and ulcerative colitis"

cumulative probability of VTE in IBD after 5-, 10- and 15-years after the diagnosis was 0.7%, 1.2% and 1.5%, similar in both CD and UC (Figure 1.).

Median age at VTE event was 37 (IQR: 29–46) years, with 6 and 10 patients below 30 and 40 years-of age at VTE. The risk of VTE in UC was associated with extensive location (OR: 3.25, 95%CI: 1.13–9.35), presence of fulminant episode during the disease course (OR: 4.15, 95%CI: 1.28–13.5), smoking (OR: 3.46, 95%CI: 1.14–10.5) and need for steroids (OR: 2.97, 95%CI: 0.99–8.92). Similarly, in CD all but one patients with VTE were smokers.

Conclusions: The incidence of VTE was lower than previously reported. VTE developed during active disease, a quarter of the patients had also prior VTE before the IBD diagnosis. The incidence was higher in males and in UC it was associated with extensive disease, fulminant episodes, corticosteroids-requiring disease and smoking, but not with age at onset.

DOP023
Evaluation of global coagulation profiles in patients with acute severe colitis: Implications for thromboprophylaxis

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Background: Venous thromboembolism (VTE) is an extraintestinal manifestation of inflammatory bowel disease (IBD). Guidelines recommend thromboprophylaxis for hospitalised patients with acute severe ulcerative colitis (ASC), but not after discharge. Population-based studies suggest the ambulatory out-patient period following a flare is the greatest at-risk period for VTE. We aimed to characterise global markers of coagulation in patients with ASC during hospitalisation and their evolution up to 12 weeks after admission.

Methods: Consecutive patients hospitalised with ASC, as well as age/gender matched controls with extensive ulcerative colitis (UC) in remission were enrolled. Serial blood samples were taken from ASC patients at days 1 and 5 during admission, then at weeks 4 and 8-12. In addition to standard laboratory tests (inflammatory markers, factor and fibrinolytic assays), global assays of coagulation were recorded at each timepoint including thrombin generation (TG) on platelet poor plasma (calibrated automated thrombinography) and thromboelastography on whole blood (ROTEM®). Clinical indices, endoscopic findings, interventions and clinical outcomes were recorded.

Results: 14 patients with ASC were enrolled and followed up to week 12 (mean age 36.9 yrs, 9 males, Montreal Severity S3) as well as 13 controls with quiescent UC (mean age 35.8 yrs, 8 male, all score S0). ASC patients had significantly elevated median CRP at days 1 (71.4 mg/L) and 5 (10.7 mg/L) compared to controls (median CRP 0.2 mg/L; p<0.0005). Compared to controls, procoagulant factor VIII was significantly elevated at days 1, 5 and week 4 (p<0.005), and von Willebrand factor remained elevated (vWF) up to week 12 (p<0.005). Endogenous thrombin potential (ETP) was significantly elevated at all timepoints up to week 12. For ROTEM®, rate of clot formation (reflecting rapidity of polymerization between platelets and fibrinogen) and maximum clot strength was elevated up to week 4, most likely driven by high circulating levels of fibrinogen in ASC patients.

Conclusions: Global assays of coagulation and factor assays demonstrate that ASC is a hypercoagulable disease state. Although this hypercoagulable profile improves over time it is still present up to 8-12 weeks after admission compared to control patients with quiescent, extensive UC. The at-risk period of developing VTE appears to persist for several weeks after presentation with ASC, at a time when thromboprophylaxis is routinely discontinued.

DOP024
Allogeneic bone marrow-derived mesenchymal stromal stem cells for the treatment of refractory perianal Crohn fistulas: a dose-escalating placebo-controlled study

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Background: Mesenchymal stromal cells (MSCs) have potential as cellular treatment for perianal Crohn's disease (pCD), because of their ability to regenerate damaged tissue and to regulate immune responses.

Table

	Medians with P-values for comparison to control group				
Coagulation parameter	**Day 1**	**Day 5**	**Week 4**	**Week 8–12**	**Controls**
Fibrinogen g/L	5.6 (<0.0001)	3.9 (0.017)	4 (0.34)	3.3 (0.11)	3.1
FVIII U/ml	2.21 (<0.0001)	2.3 (<0.0001)	1.57 (0.0027)	1.355 (0.296)	1.29
vWF IU/ml	1.67 (<0.0001)	1.495 (<0.0001)	1.32 (0.0001)	1.225 (0.0035)	0.79
ETP nM.min	1777 (0.0003)	1815 (0.0003)	1714 (0.0192)	1732 (0.0056)	1368
Extem MCF mm	47.5 (<0.0001)	48 (0.0001)	55 (0.0319)	56 (0.18)	68.5
Extem MCF mm	74.5 (<0.000)	71 (0.0008)	69.5 (0.0516)	68.5 (0.22)	67
Extem α °	80.5 (<0.0001)	80 (<0.0001)	78.5 (0.0139)	79 (0.0531)	76
Fibtem MCF mm	36 (<0.0001)	27 (<0.0001)	21.5 (0.0028)	20 (0.0079)	16

Patients and methods: In a prospective double blind phase I-II trial 21 CD patients with draining perianal fistulas (total 32 fistulas, max 3 external and max 2 internal openings), but without active luminal disease and not responding to current therapy modalities, were randomized (5:2) to receive either protocolized local injections of 10, 30 or 90x10^6 (cohort 1, 2 or 3) allogeneic bone marrow-derived MSCs (bmMSC) or placebo. Treatment, preceded by endoscopy, MRI and removal of the seton, consisted of curettage and closure of the internal opening of the fistulous tract and standardized local injection of the study drug at the internal opening. Follow-up visits were at 6, 12 and 24 weeks. Primary endpoints were safety and preliminary efficacy of bmMSC treatment. Secondary objectives were a.o. the changes in CRP, disease activity (PDAI), and quality of life scores (sIBDQ and SF-36). A complete healed fistula (CHF) was defined as no discharge upon pressure at physical examination.

Results: Local infusion of bmMSC was safe as no serious adverse events were detected. After bmMSC therapy CHF was reached in 60% of the patients at week 6, in 40% at week 12 and in 80% at week 24 in cohort 1, and in 67% (6/9) of the fistulas. In cohort 2, 80% of patients had CHF at all three follow-up visits, and in 86% (6/7) of the fistulas. In cohort 3 this was 20% and 29% (2/7), respectively, at any time point. Placebo resulted in CHF in 17% of the patients at week 6 and in 33% at week 12 and 24, for the fistulas this was 22% (2/9) and 33% (3/9) resp. Seton drainage was needed in 2 patients after bmMSC therapy (1 in cohort 1; 1 in cohort 3) and in 1 patient after placebo. Abscess drainage was needed in 1 patient in cohort 2 at 16 weeks after bmMSCs, however, this fistula was completely healed at week 24. PDAI scores at week 0, 12 and 24 coincided perfectly with therapy efficacy: in cohort 1 changing from 4.4 to 3.0 and 2.0, respectively. In cohort 2 from 3.8, 0.8 to 1.3, and in cohort 3 from 5.0, 3.8 to 4.2 as opposed to 5.2, 5.5 and 3.8 in the placebo group. No major differences were observed in other secondary endpoints.

Conclusions: Local administration of allogeneic bmMSC is safe and feasible in patients with refractory pCD. Local treatment with bmMSC showed superior fistula healing compared to placebo with 30x10^6 bmMSC dose having the best response rates, a low dose had good and the highest dose rather poor CHF results.

DOP025
Description of colorectal cancers detected in the Dutch population based IBD-SL cohort

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Background: Patients with ulcerative colitis (UC) or Crohn's Disease (CD) are considered to have an increased risk of colorectal carcinoma (CRC). Studies in non-IBD patients have suggested that procedural factors may contribute to CRC development after endoscopy. In IBD patients, data on this topic are scarce. We therefore described all CRCs diagnosed in our population based IBS-SL cohort, and assessed the contribution of procedural factors to the development of interval CRCs.

Methods: Since 1991, incident IBD cases are included in the population based IBD-SL cohort, with over 93% completeness. Clinical records were cross-linked with data from the National Pathology Database and Dutch Cancer Registry. We built on the interval CRC nomenclature of the World Endoscopy Organization, which classifies CRCs into: screen-detected (CRC diagnosed during scheduled screening/surveillance exam in an asymptomatic patient) and non-screen detected, categorized into interval CRC (CRC diagnosed <5year after colonoscopy which excluded CRC) and CRC in a patient who did not undergo screening/surveillance. Then, procedural factors of interval CRCs were evaluated in terms of time from previous colonoscopy to CRC diagnosis, stage of CRC at diagnosis and findings at previous colonoscopy [Figure].

Results: Twenty-three IBD-CRC cases were identified in 2835 IBD patients (1162 CD, 1673 UC) covering 24290 person years of follow-up (0.9 CRC/1000 person years). Mean age at CRC diagnosis was 66 year (SD 13), 48% were males. Eleven CRCs (48%) were located in the proximal colon and 5 (22%) were early stage (T1-2N0M0). Six (26%) were poorly differentiated, 4 (17%) mucinous adenocarcinomas and 1 (4%) contained serrated features. Four CRCs (17%) were screen-detected and 17 (74%) non-screen detected (9 (39%) interval CRCs and 8 (35%) CRCs in patients who did not undergo screening/surveillance). Interval CRCs were diagnosed on average 35 months (SD 18) after previous colonoscopy. Six of 9 interval CRCs were ascribed to missed lesions, 3 to newly developed CRCs and none to incomplete resection. Four of 6 patients with interval CRCs attributable to a missed lesion, had active colitis during the previous colonoscopy [Figure].

Conclusions: In this population-based study, 39% of the CRCs diagnosed in IBD patients were interval CRCs. Missed cancers/precursors likely explained the majority of the interval CRCs. Our findings highlight the importance of high quality colonoscopy and strict adherence to surveillance recommendations to overcome challenges to prevent CRC in IBD patients.

DOP026
Increased cancer risk in Dutch Crohn's disease patients: Results from the population based IBD-SL cohort

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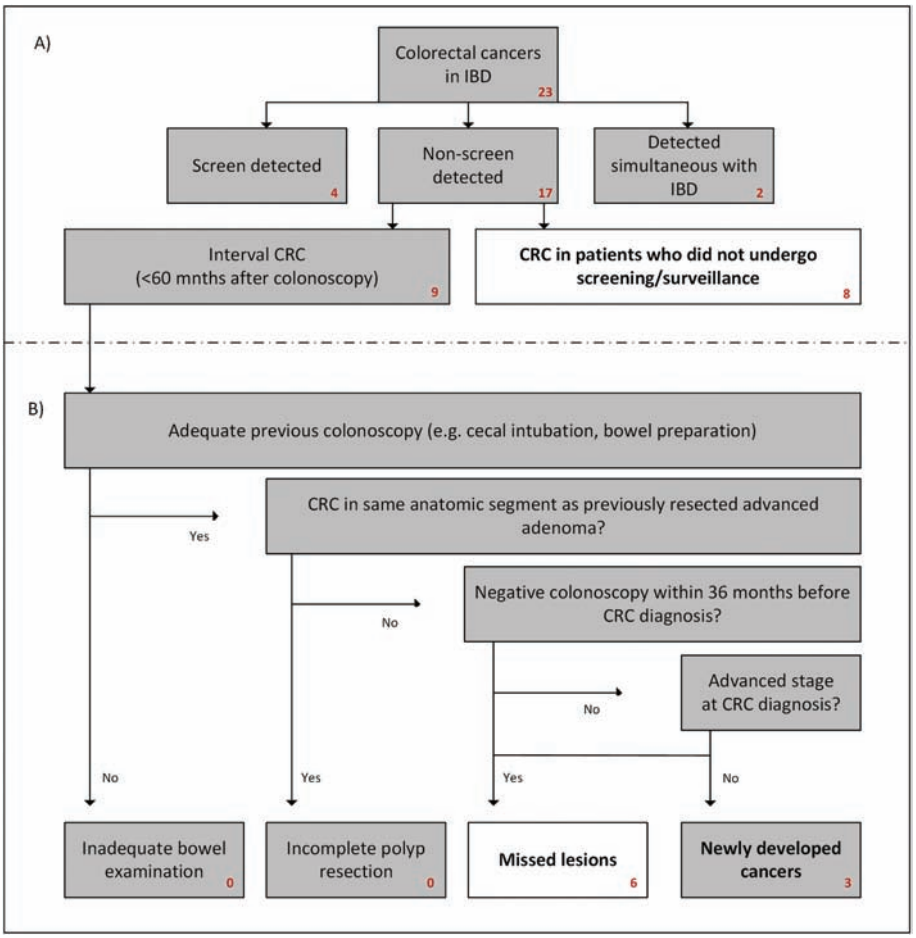

Figure A) Classification of CRCs diagnosed in IBD patients. B) Evaluation of the etiology of interval CRCs

Table: Standardized cancer incidence ratios of patients from the population based IBD-SL cohort, and of medication based sub groups

	Total IBD-SL cohort				Immunosuppression naïf -no thiopurines use -no anti-TNF use		Thiopurines -minimum 12 months use -no anti-TNF		Anti-TNF -minimum 12 months use -regardless of thiopurines use	
Number patients	1162				452		273		293	
Patient years	10705				4373		1917		1425	
	O	**E**	**SIR**	**95%CI**	**SIR**	**95%CI**	**SIR**	**95%CI**	**SIR**	**95%CI**
Overall	62	46.48	1.33	**1.02-1.71***	1.37	0.94-1.94	1.41	0.70-2.53	2.03	0.93-3.86
Overall (inc. BCC)	79	61.64	1.28	**1.01-1.60***	1.38	0.99-1.86	1.15	0.59-2.00	1.80	0.90-3.22
CRC	11	5.65	1.95	0.97-3.48						
Upper GI	5	2.71	1.84	0.59-4.30						
Prostate	1	4.42	0.23	0.01-1.26						
Lung	9	5.90	1.53	0.70-2.90						
Breast	1	8.71	0.11	**0.00-0.64***						
Skin (inc. BCC)	32	20.59	1.55	**1.06-2.19***	1.67	0.97-2.68	1.10	0.30-2.83	2.63	0.96-5.72
BCC	17	14.75	1.15	0.67-1.85	1.46	0.70-2.69	0.37	0.00-2.07	2.45	0.66-6.26
SCC	10	2.61	3.83	**1.83-7.04***	2.74	0.74-7.02	7.16	**1.44-20.92***	4.28	0.06-23.83
Melanoma	5	2.75	1.81	0.59-4.24	2.68	0.54-7.82	0	NA	2.69	0.04-14.98
Hematologic	8	3.31	2.41	**1.04-4.76***	1.79	0.36-5.24	1.74	0.02-9.68	0	NA

O, number of observed cancers/ E, number of expected cancers/ SIR, standardized incidence ratio/ 95%CI, 95% confidence interval (by Byar's approximation, alpha=0.05) / BCC, basal cell carcinoma/ CRC, colorectal cancer/ SCC, squamous cell carcinoma/ *, statistical difference / NA, Not applicable

Background: Both chronic inflammation and use of immunosuppressive agents can increase the risk of malignancies. Whether (extra) intestinal cancers occur more frequently in Crohn's disease (CD) remains controversial, partly because population based studies on cancer risk are scarce. We studied the cancer risk of CD patients in a Dutch population based IBD cohort (IBD-SL). Secondly, we

aimed to confirm the previously reported increase of skin and hematologic cancer risk in immunosuppression users.

Methods: All CD patients, diagnosed in South Limburg between 1991 and 2011, were followed until 2012 and cross-linked with the Dutch Cancer Registry. Observed cancers (O) and age- sex- and calendar year based expected cancers (E) were used to calculate standardized incidence ratios (SIR) for overall cancer risk, common cancers (i.e. colorectal- (CRC), upper gastro-intestinal-, lung-, breast- and prostate cancer) and possible immunosuppression related cancers (i.e. overall hematologic and skin cancer, basal cell cancer (BCC), squamous cell cancer (SCC) and melanoma). Sub analyses were performed for patients without immunosuppression, those ever on thiopurines (>12 months use, without anti-TNF) and ever on anti-TNF (>12 months, regardless of thiopurines). In the last two groups, only patient years after medication start were included in analysis.

Results: In total, 1162 CD patients (37% male) contributed to 10705 person years at risk. SIRs are shown in the table. Overall, CD patients had a 33% increased risk (SIR 1.33; 0.95%CI 1.02-1.71) of developing cancer compared to the general population. CRC risk was not significantly increased (1.95; 0.97-3.48). Overall skin cancer (1.55; 1.06-2.19), SCC (3.83; 1.83-7.04) and hematologic cancer (2.41; 1.04-4.76) were increased, while breast cancer (0.11; 0.00-0.64) was decreased. In the sub analysis, patients ever on thiopurines had an increased risk to develop SCC (7.12; 1.44-20.92).

Conclusions: In the population based IBD-SL cohort, the overall cancer risk for CD patients was higher compared to the general population. This finding can be attributed to an increased risk for hematologic and skin cancer, which was most pronounced for SCC in longterm thiopurine users. The risk of gastro-intestinal cancers was not increased and the risk of breast cancer was even strongly decreased. The above findings underline the increased cancer risk of immunosuppression use in IBD patients and point to the relevance of regular screening, especially for dermatological cancers.

DOP027
Survival in inflammatory bowel disease related colorectal cancer

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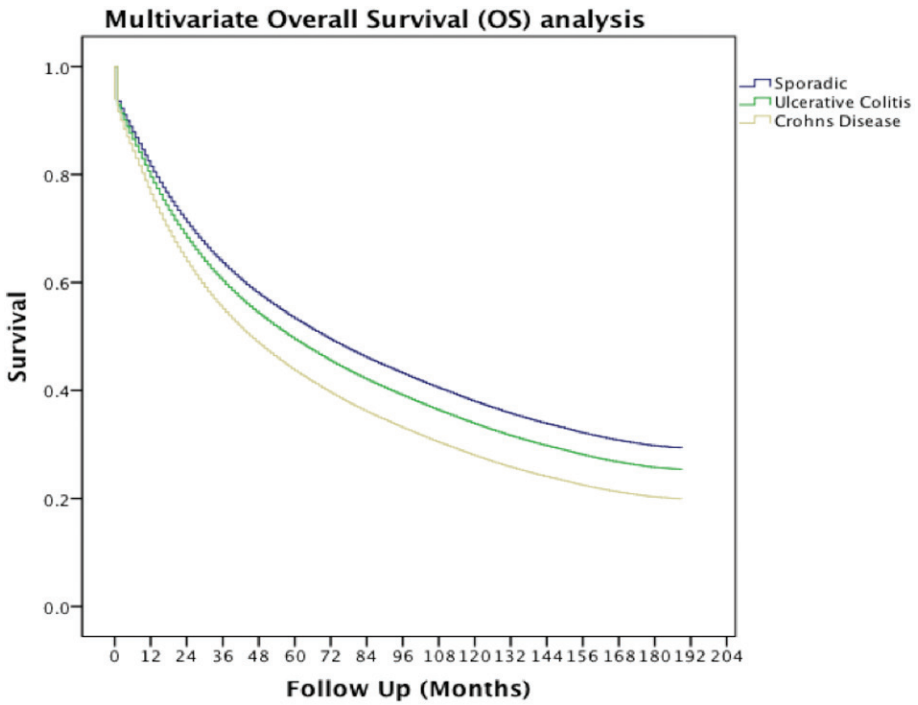

"Cox Regression analysis comparing Crohn's and Ulcerative Colitis CRC compared to sporadic CRC"

Background: Inflammatory Bowel Disease (IBD) is a risk factor for Colorectal Cancer (CRC). The aim of this national study is to determine whether there are differences in outcomes and survival between sporadic and IBD related CRC.

Methods: A national study was carried out using the Hospital Episode Statistics (HES) database between the years of 1997 to 2012. Chi squared analysis was undertaken to determine differences in demographics. Multivariate Cox regression analysis was used to examine survival differences between IBD and sporadic CRC.

Results: A total of 286,591 underwent surgery for colorectal cancer in England. Of these, 1,546 patients (0.5%) had Ulcerative Colitis (UC) and 776 (0.3%) had Crohn's Disease (CD). Patients with IBD-CRC are younger (median age 64 years) than those with sporadic CRC (median age, 71 years). Inflammatory Bowel Disease was an independent predictor of 30-day re-intervention (OR 1.32 CI 1.12-1.56, p=<0.001). Cox Hazard Regression demonstrated the UC CRC group to have a reduced overall survival (HR 1.12, CI 1.04-1.20, p=0.003). However, CD patients had an even worse survival compared to sporadic CRC patients (HR 1.32, CI 1.20-1.45, p=<0.01). There was no difference in survival between patients with UC undergoing segmental colectomy and subtotal/total colectomy (HR 1.10, CI 0.90-1.34, p=0.354).

Conclusions: Colorectal cancer patients who have concurrent IBD have a worse overall survival compared to patients with sporadic CRC. This is particularly the case in Crohn's Disease patients.

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Digital Oral Presentations

DOP Session 4 – Controlled & uncontrolled trials in IBD

DOP028
Efficacy and safety of retreatment with vedolizumab in patients with ulcerative colitis

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Background: Retreatment with a biologic agent in symptomatic patients with ulcerative colitis (UC) after a drug holiday is often necessary given the recurrent nature of UC. Vedolizumab (VDZ), a monoclonal antibody to α4β7 integrin, has proven efficacy and safety in the treatment of UC (GEMINI 1, NCT00783718).[1] This interim analysis (22 May 2009 - 27 June 2013) of data from the ongoing, open-label GEMINI long-term safety (LTS) study (NCT00790933) evaluated the effects of VDZ retreatment in UC patients who rolled over from the double-blind, placebo (PBO)-controlled GEMINI 1 study.
Methods: In GEMINI 1, after 6 weeks of induction therapy, VDZ responders were re-randomised to PBO or VDZ every 8 or 4 weeks (Q8W or Q4W) during the 46-week maintenance period (maintenance intent-to-treat [ITT] population). Patients from GEMINI 1 who completed the study (n=199) or withdrew early (due to sustained non-response, disease worsening, or the need for rescue medication; n=131) were eligible to enrol into GEMINI LTS to receive open-label VDZ Q4W. Here we evaluate rates of clinical response and remission with VDZ retreatment in these rollover patients in GEMINI LTS (prespecified analyses). Rates were calculated based on the number of patients at week 0 of GEMINI LTS. Adverse event (AE) and serious adverse event (SAE) rates were also evaluated.
Results: In GEMINI LTS, patients retreated with VDZ after up to 1 year of drug holiday following re-randomisation to PBO during weeks 6 to 52 of GEMINI 1 (PBO completers) or due to loss of response or sustained non-response (VDZ Q8W and Q4W early terminators) regained response (Table). Similar trends were observed with VDZ retreatment in the subpopulations of completers or early terminators with prior tumour necrosis factor antagonist failure. No increase in AEs or SAEs was observed with VDZ retreatment in completers/early terminators.
Conclusions: Patients with UC from GEMINI 1 who responded to VDZ induction treatment and then had a drug holiday for up to 1 year were safely retreated with VDZ Q4W in GEMINI LTS and experienced clinical benefits.

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References:

[1] Feagan BG, (2013), Vedolizumab as induction and maintenance therapy for ulcerative colitis, N Engl J Med, 699-710

DOP029
Ustekinumab efficacy and safety in Crohn's disease patients refractory to conventional and anti-TNF therapy: a multicenter retrospective experience.

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Background: Ustekinumab is a human monoclonal antibody against the p40 subunit of interleukin-12 and interleukin-23. It has been shown to be effective in Crohn's disease (CD) patients refractory to anti-TNF in a phase II trial (Sandborn WJ et al N Engl J Med. 2012). The aim of the present study was to assess subcutaneous ustekinumab benefits and safety, and to identify predictive factors of clinical response in a multicenter cohort of anti-TNF refractory CD patients.
Methods: A retrospective observational study was conducted in French tertiary centers from the GETAID, including all consecutive patients who received subcutaneous ustekinumab for refractory CD to conventional and anti-TNF therapy and having a follow-up of more than 3 months. The primary objective was ustekinumab clinical benefit at 3 months, defined by a significant improvement

Table: Rates of clinical response and remission by GEMINI 1 treatment group (maintenance ITT population of GEMINI 1 completers and early terminators)

	GEMINI 1 Completers			GEMINI 1 Early Terminators[a]		
Visit	PBO[b] (n=45)	VDZ Q8W (n=74)	VDZ Q4W (n=80)	PBO[b] (n=67)	VDZ Q8W (n=32)	VDZ Q4W (n=32)
Number (%) of patients with clinical response[c]						
GEMINI 1						
Week 6	41 (91.1)	69 (93.2)	71 (88.8)	62 (92.5)	30 (93.8)	26 (81.3)
Week 26	43 (95.6)	68 (91.9)	76 (95.0)	19 (28.4)	3 (9.4)	3 (9.4)
Week 52	31 (68.9)	62 (83.8)	65 (81.3)	NA	NA	NA
GEMINI LTS						
Week 0	31 (68.9)	67 (90.5)	79 (98.8)	14 (20.9)	6 (18.8)	5 (15.6)
Week 28	35 (77.8)	60 (81.1)	74 (92.5)	39 (58.2)	17 (53.1)	12 (37.5)
Week 52	30 (66.7)	58 (78.4)	66 (82.5)	38 (56.7)	13 (40.6)	10 (31.3)
Week 84	24 (53.3)	45 (60.8)	47 (58.8)	32 (47.8)	8 (25.0)	6 (18.8)
Week 108[d]	7 (15.6)	32 (43.2)	23 (28.8)	26 (38.8)	6 (18.8)	6 (18.8)
Number (%) of patients with clinical remission[e]						
GEMINI 1						
Week 6	31 (68.9)	48 (64.9)	47 (58.8)	36 (53.7)	14 (43.8)	17 (53.1)
Week 26	38 (84.4)	61 (82.4)	63 (78.8)	16 (23.9)	3 (9.4)	1 (3.1)
Week 52	25 (55.6)	57 (77.0)	57 (71.3)	NA	NA	NA
GEMINI LTS						
Week 0	21 (46.7)	65 (87.8)	70 (87.5)	4 (6.0)	2 (6.3)	1 (3.1)
Week 28	34 (75.6)	56 (75.7)	71 (88.8)	30 (44.8)	8 (25.0)	8 (25.0)
Week 52	29 (64.4)	55 (74.3)	65 (81.3)	26 (38.8)	9 (28.1)	8 (25.0)
Week 84	23 (51.1)	47 (63.4)	45 (56.3)	26 (38.8)	6 (18.8)	5 (15.6)
Week 108[d]	7 (15.6)	32 (43.2)	22 (27.5)	23 (34.4)	4 (12.5)	4 (12.5)

Abbreviations: ITT, intent-to-treat; LTS, long-term safety; NA, not applicable; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; VDZ, vedolizumab.

[a] Patients withdrew because of sustained non-response, disease worsening, or the need for rescue medication.

[b] The PBO groups received 2 doses of VDZ during the induction phase of the study. PBO completers received PBO for weeks 6 to 52. Time off drug before retreatment in GEMINI LTS varied in ITT PBO early terminators.

[c] Clinical response was defined as a decrease in the partial Mayo score of ≥2 points and ≥25% from baseline, with a decrease in rectal bleeding subscore of ≥1 point from baseline or absolute rectal bleeding subscore of ≤1 point.

[d] At Week 108, the number of patients in the study was 7, 32 and 24 for PBO, VDZ Q8W and VDZ Q4W completers and 28, 7 and 8 for PBO, VDZ Q8W and VDZ Q4W early terminators, respectively.

[e] Clinical remission was defined as a partial Mayo score of ≤2 with no individual subscore >1.

as judged by the physician leading to continue the treatment with complete steroids weaning if given at inclusion. Ustekinumab safety and clinical benefit at 6, 12 months and end of follow-up were also recorded.

Results: Ninety-seven CD patients (27 males, mean age 35.1 ± 11.6 years) received at least one subcutaneous ustekinumab injection in 16 centers. At baseline, median (IQR) disease duration was 11.9 (7.3-16.2) years; 97 (100%) patients experienced previous failure or intolerance to thiopurines or methotrexate and to at least one anti-TNF agent (infliximab or adalimumab, with 85 (87%) who received both anti-TNFs) and 59 (61%) patients underwent prior intestinal resection. Ustekinumab was given for luminal CD in 88 (91%) patients and for perianal disease in 9 (9%). Median follow-up duration was 39.2 ± 32.8 weeks. Mean cumulative dose of ustekinumab given for induction from week 0 to 4 was 148.5 ± 65 mg (range: 45-396 mg). At inclusion, 15 patients received corticosteroids and 12 patients concomitant immunosuppressant (IS). Clinical benefit at 3 months was observed in 69 (71%) patients in the whole population and in 8/9 of patients with perianal CD. Among the primary ustekinumab responders, 78% and 86% experienced clinical benefit at 6 and 12 months, respectively. Concomitant IS and absence of corticosteroids at time of ustekinumab introduction were associated, but non-significantly, with clinical response to ustekinumab at 3 months (p=0.09). No serious adverse effects related to ustekinumab were reported.

Conclusions: In patients with highly refractory CD, a clinical benefit to subcutaneous ustekinumab was observed in 71% at 3 months and was maintained in the majority of patients for up to 12 months. Along this, ustekinumab could be considered as a rescue therapy in

CD patients who experienced prior failure or intolerance to conventional IS and to anti-TNF agents.

DOP030
GLPG0974, an FFA2 antagonist, in ulcerative colitis: efficacy and safety in a multicenter proof-of-concept study

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Background: Free fatty acids (FFA) act as inflammatory signaling molecules through receptors such as FFA2, which is activated by short chain fatty acids (SCFA). Through FFA2, SCFAs induce neutrophil activation and migration. In IBD patients, FFA2 expression is up-regulated in the colon.

GLPG0974 is a potent and selective antagonist of FFA2, inhibiting SCFA-induced neutrophil migration and activation *in vitro*. In healthy volunteers, GLPG0974 is safe, and shows good pharmacokinetics (PK) and pharmacodynamics, with maximal inhibition of SCFA-induced neutrophil activation at 200 mg b.i.d.

Methods: The safety and efficacy of GLPG0974 in mild to moderate UC (Mayo score 4-10 with an endoscopic subcore of ≥1) was evaluated in a double-blind exploratory study, in 45 patients (aged 18-75) treated for 4 weeks with 200 mg b.i.d. GLPG0974 or placebo (2:1 randomization; NCT01829321). A stable background of 5-aminosalicylates/ immunosuppressants was allowed but not steroids. Mayo scores and biopsies for Geboes scores and myeloperoxidase (MPO) positive cells (immunohistochemistry) were collected at baseline (BL) and week 4. Fecal calprotectin (FC) and subscores for partial Mayo and PK were evaluated at BL, week 1, 2 & 4.

Results: Baseline characteristics, including Mayo score (8.0), FC (550 µg/g), MPO positive cells (8.1%) and expression of FFA2 in colon biopsies, were similar in both groups. GLPG0974 was well tolerated and safe, with no serious infections and a low frequency of common infections favoring GLPG0974 (n=1) over placebo (n=3). The percentage of MPO-positive cells in the lamina propria of colon biopsies, indicating neutrophil influx, was reduced by GLPG0974 (median change from BL: GLPG0974: -33%; placebo: -5%). The proportion of patients showing a reduction of MPO positive cells was larger with GLPG0974 (61%) than with placebo (28%). FC was reduced by GLPG0974 (median % change from BL: -30 %), whereas it increased in the placebo group (median % change from BL: +24%). (Partial) Mayo score and individual subscores improved over time, but without a differentiation between GLPG0974 and placebo. There were no differences in clinical response, clinical remission or mucosal healing rates. Patients showed a good PK exposure with average plasma concentrations within the range of exposures in healthy volunteers.

Conclusions: In this 4-week, first-in-UC study with an FFA2 antagonist in mild to moderate UC patients, GLPG0974 was well tolerated and safe. Biomarkers (MPO and FC) indicate that GLPG0974 reduces neutrophil activation and influx, suggesting a role for FFA2 in neutrophil migration in UC. The reduction in neutrophil influx is not sufficient to induce a measurable clinical difference between GLPG0974 treated patients and placebo within 4 weeks.

DOP031
Phase I study of intraperitoneal administration of autologous tolerogenic dendritic cells for refractory Crohn's disease.

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Background: Ex vivo generated autologous tolerogenic dendritic cells (tolDCs) can restore immune tolerance in experimental colitis. In humans, autologous tolDCs have been safely administered in type 1 diabetes patients. The aim of this study was to determine the safety and tolerability of intraperitoneal injection of autologous tolDCs in refratory Crohn's disease (CD) patients.

Methods: A phase-I, single-center, sequential-cohorts, dose-range-finding study was designed (EudraCT: 2007-003469-42, PEI-08-049). Refractory CD patients underwent apheresis to collect peripheral mononuclear cells. Stable tolDCs were generated ex-vivo following a previously developed protocol and administered by sonography-guided intraperitoneal injection. Six sequential cohorts of patients (2 per cohort) were established: the first 3 cohorts received a single peritoneal tolDCs at escalating doses ($2x10^6/5x10^6/10x10^6$) and the last 3 cohorts were treated with 3 intraperitoneal injections at weeks 0, 2 and 4 at escalating doses ($2x10^6/5x10^6/10x10^6$). Safety was assessed sequentially in every cohort by an external safety committee. Clinical and endoscopic activity, health-related quality of life, and biomarkers were evaluated over 12 weeks after tolDCs administration. Patients were followed over 1-year period to assess safety.

Results: Nine patients were included in the study. No adverse effects were detected during tolDCs injection and 1-year follow-up. Three patients withdrew from the study before week 12 because of CD worsening. Clinical activity assessed by CDAI decreased from 280/60 (mean/SD) at week 0 to 233/115 at the end of the study (p=0.3): 1 (11%) patient reached clinical remission (CDAI<150) and 2 (22%) presented clinical response (CDAI decrease ≥100). Endoscopic activity measured by CDEIS decreased from 18/5 to 11/8 (p=0.4). Endoscopic lesions improved markedly in 3 patients (33%) at week 12 examination. IBDQ changed from 125/27 at week 0 to 131/38 at the end of the study (p=0.7): in 1 case (11%) remission was reached (IBDQ at week 12 ≥170) and in 2 (22%) a response was observed (IBDQ score increase ≥16 points). No change in biomarkers was observed. Clinical activity amelioration correlated with endoscopic activity improvement in 2 cases. Higher or multiple doses of DCs were not related to clinical or endoscopic changes.

Conclusions: Autologous tolDCs were administered for the first time in CD patients. Intraperitoneal administration of autologous tolDCs appears safe and feasible for the treatment of refractory CD. No clear signal of efficacy was observed in this pilot study. Further studies should be developed in order to test a potential clinical benefit, to determine the optimal administration route and dose, and to monitor the immune responses.

DOP032
Fistula treatment with adipose derived mesenchymal stem cells - prospective study on experimental model of perianal Crohn's disease

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Background: Conservative and surgical treatment of perianal fistulas in patients with Crohn's disease (CD) is effective in about 40-60% (1). Local administration of adipose tissue derived stem cells (ADSCs) or biomaterials represents new approach in human fistula treatment with mixed results (2). In vivo bioluminescence imaging using firefly luciferase can clarify the distribution and viability of the ADSCs after implantation.

The aim of the study was to evaluate the fistula healing after local application of ADSCs in comparison with other surgical and non-surgical techniques

Methods: Coecostomy was used as a fistula model in Lewis rats. The inguinal adipose tissue was harvested from transgenic donor expressing firefly luciferase (LEW-Tg(Rosa-luc)11Jmsk; Jichi Medical School, Japan). Using collagenase technique suspension of vital ADCSs (1-2*106 cells/ml) was obtained.

Rats were randomized into the following interventional groups:

Group A (N=12) - fistula tract ligation

Group B (N=16) - perifistular application of ADSCs

Group C (N=12) - intrafistular application of flowable cross-linked collagen and glycosaminoglycan matrix - Integra ® followed by perifistular application of ADSCs and external opening suture.

Group D (N=11)- intrafistular application of 70% glucose followed by external opening suture.

Fistula drainage assessment (FDA) was used to evaluate the fistula healing. Rats were imaged in IVIS Lumina XR camera during 30days follow-up. Interventional groups were compared with untreated (N=30) resp. external opening sutured fistulas (N=9).

Results: There was no mortality after interventions. Fistula was healed in 6 (50,0%) animals in group A and 6 (37,5%) in group B, which was significantly more frequent than in untreated animals (spontaneous closure in 1 (3%) case (p< 0,01).In groups C and D the fistula closure occurred in 5 (41,7%) resp. 3 (27,3%) which was similar to the control group - 3 (33,3%), p>0,05. In group B, the bioluminescence signal 30 days after application was higher in animals with closed fistula - 8,23 (1,20 to 16,9)*10^4 vs. 1,74 (0,16-6,9)*10^4 (p = 0,039).

Conclusions: Presence of viable ADCSc after perifistular application was associated with fistula closure. Results of this technique were comparable with surgical treatment (fistula tract ligation). Application of biomaterials or 70% glucose into the fistula tract did not improve healing.

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DOP033
Efficacy and safety of anti-TNF therapy for inflammatory bowel disease (IBD) in liver transplant recipients for primary sclerosing cholangitis (PSC): a multicenter experience.

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Background: The management of IBD after liver transplantation (LT) for PSC is complex due to the immunosuppression background and the risk of IBD worsening after LT. The aim of this study was to assess efficacy and safety of anti-TNF therapy in this population.

Methods: It was a retrospective, descriptive, national multicentric study. All the French adult LT centers have been contacted to indentify and include patients who underwent LT for PSC between January 1985 and December 2012 then treated by anti-TNF therapy for IBD. Medical datas were screened to assess clinical efficacy, endoscopic efficacy and safety after induction and at the end of the treatment.

Results: Eighteen patients (14 men, 4 women), who underwent LT for PSC between 1989 and 2012, followed in 9 of the 20 adult LT French centers have been treated by anti-TNF therapy between 2004 and 2014 for IBD after LT. All patients presented colonic location. The median age at the beginning of the treatment (Day 0) was 37.2 years (24.0-51.9). The median time between LT and Day 0 was 5.9 years (1.1-20.8). The median duration of IBD evolution at Day 0 was 14.1 years (0.4-27.6). Seven patients (38.9%) received infliximab, 7 (38.9) adalimumab and 4 (22.2%) received both successively. The median duration of treatment was 10.4 months (2.7-30.6) and the median follow-up was 20.9 months (5.0-72.5). Six patients (33%) were treated with azathioprine. Seventeen (94.4%) were treated by tacrolimus and 1 (5.6%) by ciclosporine. After induction, 16 patients (88.9%) presented a clinical improvement of which 10 (55.6%) were in clinical remission. At the date of latest news, 12 patients (66.7%) showed clinical improvement of which 7 (38.9%) were in clinical remission. An endoscopic improvement was found in 9 of the 14 patients (64.3%) with endoscopic follow-up. The treatment was continued in 10 of the 18 patients (55.6%). Six patients (33.3%) presented at least one infection during the follow-up. Three patients (16.7%) developed a colon cancer of wich 1 with fatal outcome. They suffered from an IBD with an evolution duration of respectively 14, 27 and 28 years and had been treated by an anti-TNF therapy respectively 7, 2 and 8 months before the cancer diagnosis. One patient developed a cancer of the cervix.

Conclusions: The efficacy of anti-TNF therapy in patients with relapsing IBD after a LT for PSC seems to be similar to that observed in non-transplanted patients. The safety seems acceptable with an infectious risk due to the context and the immunosuppressive regimen. An endoscopic follow-up with a screening for colonic dysplasia is essential in this population.

DOP034
Efficacy of adalimumab in patients with Crohn's disease and symptomatic small bowel stricture: a multicentre, prospective, observational cohort study (CREOLE)

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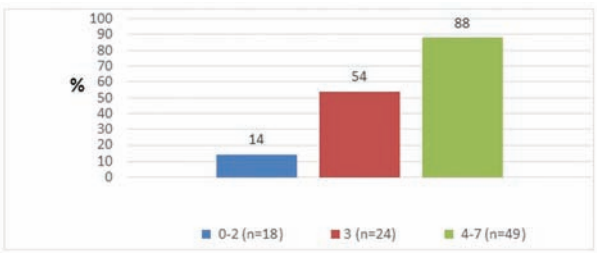
Background: The aim of this study was to estimate the success rate of adalimumab (ADA) in patients with Crohn's disease (CD) and symptomatic small bowel stricture (SSBS), and to identify predictive factors of success.

Methods: We performed a multicentre, prospective, observational cohort study in patients with CD and a SSBS (defined by a CD obstructive score (CDOS) ≥3 on a scale from 0 to 6 and taking into account obstructive symptoms during the 8 previous weeks). Patients who were exposed to an anti-TNF within the last 12 months were not eligible. Included patients received 160 mg of ADA at W0, 80 mg at W2, and then 40 mg every 2 weeks. MR enterography (MRE) was performed at baseline. The primary endpoint was ADA success at W24 (no corticosteroids after the 8th week following inclusion, no other anti-TNF, no endoscopic dilation, no bowel surgery, no severe adverse effect (SAE) leading to ADA discontinuation and no study withdrawal). Baseline factors associated with success were identified using the logistic regression model. Eighty patients were deemed necessary to detect an odds ratio (OR) of success greater than 2.0 or 4.0 with a power of 80%, depending on the rate of ADA success (50 to 70%) and on the proportion of patients in the good prognosis group (25 to 75%).

Results: From January 2010 to December 2012, 117 patients from 21 centers were screened. Nineteen patients were excluded, and 98 were analysed (44 M, median [inter-quartile range (IQR)] age of 36 years (29-46), duration of obstructive symptoms was 4 months [1-11]). At W24, 61/98 (61%) patients achieved success. A clinico-radiological prognostic score was built from items evaluated at the time of ADA initiation, and independently associated with success. It was obtained by adding 1 point for immunosuppressant (p=0.027), obstructive symptoms for less than 5 weeks (p=0.036), CDOS ≥***4 (p=0.018), severe T1 delayed enhancement intensity at MRE (p=0.007), no fistula (p=0.007) and of 2 points for maximal proximal diameter above the stricture from 18 to 29 mm (p<0.0001).
59% of patients who were in success at W24 were still in success at year 2 with a median (±SE) follow-up of 1.97 ± 7.6 years after W24. Serious adverse events were noted in 11/98 (11%). None was considered related to the study drug.

Conclusions: In this prospective cohort of CD patients with SSBS, ADA success was observed in 60% of cases at W24, and predicted by a simple score. This score needs to be validated in an independent cohort.



Probability of success at W24 in 94 patients with CD and SSBS treated with ADA according to the prognostic score

"Figure CREOLE"

DOP035
Anti-TNF withdrawal in IBD: Relapse and recapture rates and predictive factors from 160 patients in a pan-UK study

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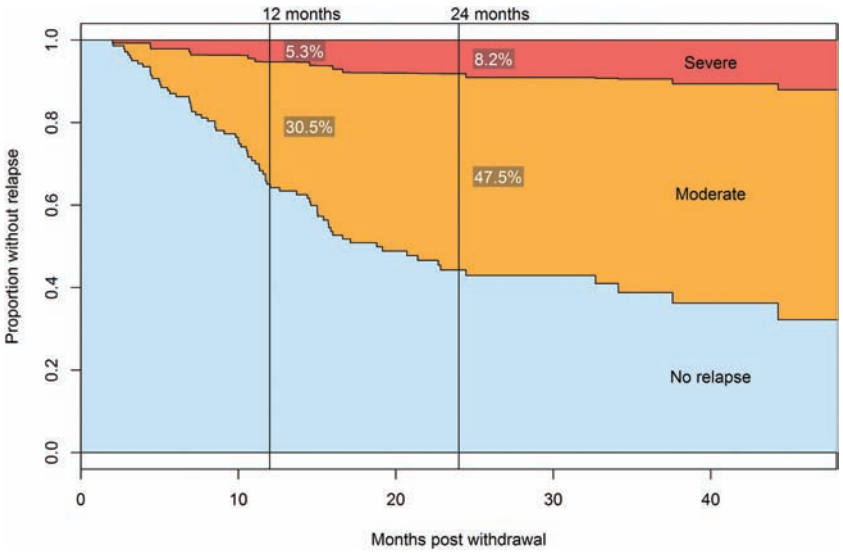

"Figure 1 - Relapse following withdrawal of anti-TNF in Crohn's disease"

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Background: Infliximab and adalimumab have established roles in IBD therapy. UK regulators (NICE and SMC) mandate reassessment of disease activity after 12 months of therapy. The guidelines mandate that therapy should ordinarily be discontinued where clinical remission and mucosal healing has been achieved. However, there are presently insufficient data to inform on the outcomes of anti-TNF withdrawal.

Methods: We conducted a retrospective clinical audit of outcomes following withdrawal of anti-TNF therapy. Inclusion criteria were confirmed diagnosis of IBD; ≥12m continuous anti-TNF therapy; primary withdrawal reason sustained clinical remission (no corticosteroids for 6m). Relapse was defined as moderate (oral steroids, immunomodulators, recommencement of anti-TNF agent) or severe (hospitalisation, iv steroids, surgical resection). All UK centres were invited to participate. Demographic and phenotypic data, clinical, laboratory and endoscopic parameters were recorded onto standardised proformas.

Results: 160 cases (130 infliximab; 30 adalimumab) with a median follow-up time of 25m post withdrawal were included in this analysis. 141 (88%) had Crohn's, the remainder UC/IBDU. 54% were female and the median age at drug withdrawal was 31y. All were in clinical remission at withdrawal; 62.5% (100/160) had normal laboratory parameters (Hb, WCC, plts, Albumin, CRP, FC); 87.3% (89/102) had complete mucosal healing where endosocpy was performed pre-withdrawal. Relapse rates for Crohn's disease were 36% at 1 year and 56% at 2 years (figure 1); for UC/IBDU, they were 44% at 1 year and 50% at 2 years. Younger age at diagnosis (p=0.003) and elevated WCC (p=0.044) were predictive of relapse. Anti-TNF therapy was re-introduced in 59/81 patients following relapse and was successful in 92%.

Conclusions: Planned withdrawal of anti-TNF therapy for sustained clinical remission is associated with a moderate-to-severe relapse of Crohn's disease in over half of patients by 2 years. Prediction of relapse in a group carefully selected for clinical remission remains difficult.

DOP036
PYRAMID registry: an observational study of adalimumab in Crohn's disease: Results at year 6

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Background: This study evaluated the long-term safety of adalimumab (ADA), as used in routine clinical practice, for up to 6 years in patients with moderately to severely active Crohn's disease (CD) enrolled in the global observational registry PYRAMID.

"Table 1. Cumulative incidence of treatment-emergent adverse events (AEs) excluding prior exposure in other CD ADA trials"

AE	Year 3 8174.7 PY Events (E/100PY)	Year 5 13351.8 PY Events (E/100PY)	Year 6 13924.3 PY Events (E/100PY)
Any AE	2301 (28.1)	4673 (35.0)	5106 (36.7)
Serious AE	1827 (22.3)	3389 (25.4)	3604 (25.9)
AE leading to discontinuation	266 (3.3)	530 (4.0)	610 (4.4)
AE leading to death	15 (0.2)	46 (0.3)	47 (0.3)
Serious infection	340 (4.2)	596 (4.5)	682 (4.9)
Opportunistic infection (excluding oral candidiasis and TB)	4 (<0.1)	17 (0.1)	25 (0.2)
TB	5 (<0.1)	15 (<0.1)	13 (<0.1)[a]
Any malignancy, including non-melanoma skin cancer	48 (0.6)	90 (0.7)	104 (0.7)
Lymphoma	3 (<0.1)	6 (<0.1)	9 (<0.1)
Demyelinating disorder	1 (<0.1)	6 (<0.1)	7 (<0.1)

[a] Changes in the adjudication process between year 5 and 6 resulted in the decrease in TB events

Methods: All patients entering the multi-centre, non-interventional registry PYRAMID were to be followed for up to 6 years. Adverse events (AEs) were collected from the first dose to up to 70 days after the last dose of ADA or through the cutoff of 1 December 2013. AE rates are reported as per 100 patient-years (PY).

Results: A total of 5061 patients (57.1% female, mean age 37.8 years, median duration of CD 8.2 years) have enrolled in PYRAMID, totaling 13924.3 PY of ADA exposure, excluding prior exposure in CD ADA clinical trials. As of 01 Dec 2013, 2885 patients (57%) were still participating and 297 patients (5.9%) had at least 6 years of ADA exposure. A total of 2600 patients (51%) received biologic therapy prior to enrollment (98.3% infliximab, 5.6% certolizumab, 1.4% natalizumab, 0.5% other). During the study, concomitant corticosteroids (CS), immunosuppressants (IMM), and IMM + CS were used by 29.4%, 35.6%, and 11.6% of patients, respectively. A total of 682 patients (4.9/100 PY) experienced serious infections, of which 265 patients (5.1/100 PY) were on combination therapy with IMM and 417 patients (4.8/100 PY) were on ADA monotherapy. A total of 104 patients (0.7/100 PY) experienced any malignancy, of which 50% had received combination therapy with IMM. Thirty-eight treatment-emergent deaths (0.3/100 PY) were reported, of which 7 were considered possibly related to ADA. Overall, adalimumab exposed patients did not have an increased mortality versus the general population. The table shows an overview of exposure-adjusted registry treatment-emergent AEs for years 3, 5, and 6.

Conclusions: After up to 6 years of observation, long-term ADA exposure continued to be well-tolerated in patients with moderately to severely active CD. No new safety signals were identified. AE rates remained stable over time.

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Digital Oral Presentations

OXFORD

DOP Session 5 – Drug levels & biomarkers

DOP037
Initial Adequate Trough Concentrations during Induction Therapy Correlate with Sustained TNF Suppression and Predict Remission with Adalimumab in Anti-TNF Naïve Crohn's Disease Patients

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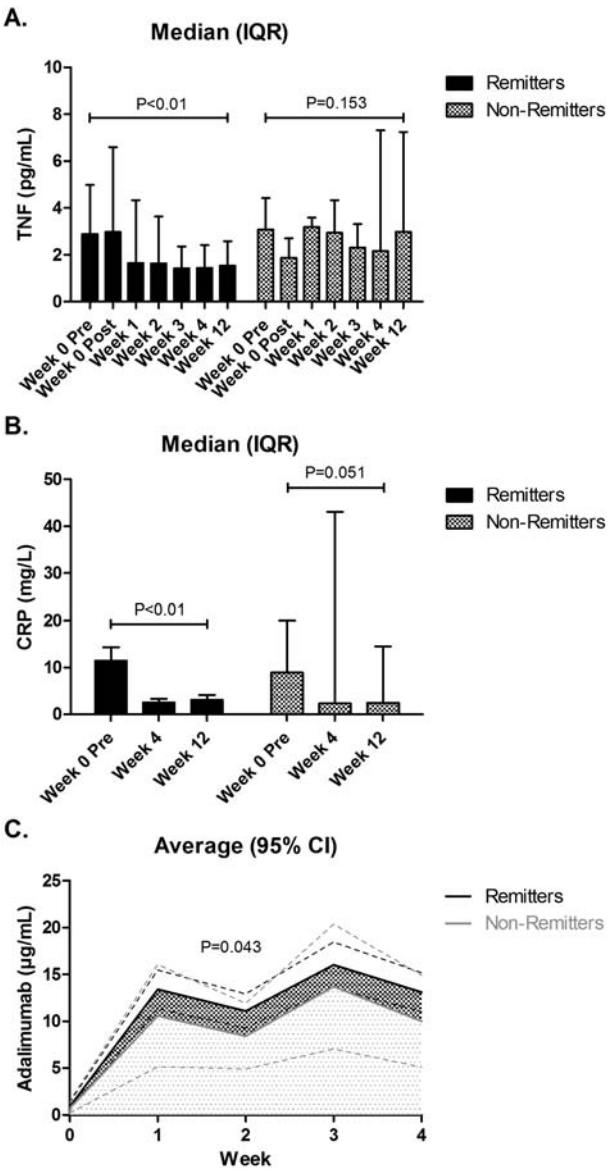
Background: Adalimumab (ADM), a fully human TNF antagonist, is effective for treating patients with Crohn's disease (CD). A correlation between concentration and effect was observed at distinct time points. Our aim was to evaluate the correlation of early longitudinal measurements of ADM with different biological markers for disease activity and induction of clinical remission.

Methods: Prospective two-centre open-label study in 23 anti-TNF naïve patients with moderate to severe CD induced with ADM 160/80 mg at week 0 and 2 and 40 mg every 4 weeks in monotherapy. Serum samples were taken pre and post first injection and at weeks 1, 2, 3, 4 and 12. Clinical remission was evaluated at week 12 and was defined as a Harvey-Bradshaw index (HBI) ≤4. True primary non-responders, defined as a lack of clinical response despite adequate drug exposure, were excluded from longitudinal analyses. [1] Concentrations of ADM were measured with the Leuven assay (lower limit of quantification, LLOQ 0.3 µg/mL) and antibodies to ADM with a drug tolerant homogenous mobility shift assay (LLOQ 1.7 U/mL).

Results: Of the 23 patients, 16 (70%) achieved clinical remission at week 12. Median (IQR) HBI in remitters (R) and non-remitters (NR) was 7 (5-9) vs. 7 (5-9) at week 0 (P=0.840); 1 (0-5) vs. 7 (5-9) at week 4 (P=0.020) and 1 (0-2) vs. 6 (5-7) at week 12 (P=0.001). CRP and TNF concentrations at baseline were similar in R and NR: respectively 6.9 vs. 8.9 mg/L (P=0.504) for CRP and 2.9 vs. 2.9 pg/mL (P=0.973) for TNF and decreased significantly in R but not in NR (Fig.1A&B). Drug exposure as defined by area under the curve ($AUC_{(week\ 0\text{-}4)}$) of ADM was significantly greater for R than NR (Fig.1C). One patient had an ADM exposure level in the 95th percentile and was excluded as a true primary non-responder; this patient also had low TNF at baseline (0.56 pg/mL). Trough concentrations of ADM were better associated with clinical remission at week 12 than peak concentrations; ROC curve analysis at week 2 revealed a cut-off of >9.7 µg/mL (100% specificity, 69% sensitivity, AUROC 0.87, P< 0.01) and at week 4 of >11.0 µg/mL (100% specificity, 69% sensitivity, AUROC 0.88, P<0.01). One patient developed antibodies to ADM (detectable at week 12) and was in clinical remission at that time.

Conclusions: Primary (non-)response to ADM is not associated with immunogenicity even during monotherapy. Our results indicate that adequate exposure to ADM drives response and that in relation to TNF concentration, this might be predictive of effective disease suppression.



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DOP038
Faecal calprotectin measurement and infliximab trough levels predict therapeutic evolution CD patients in clinical remission

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Background: The deep remission notion (clinical remission and mucosal healing) is an important objective for patients under treatment. The appearance of inflammation and pharmacological biomarkers could be a non-harmful way of predicting the evolution of Crohn's disease (CD). The aim of our study was to offer a predictive model for relapse in CD patients presenting clinical remission undergoing infliximab (IFX) treatment.

Methods: It was a prospective monocentric study that included all CD patients on IFX maintenance treatment (5mg/kg) and in clinical remission (CDAI< 150) for at least 16 weeks, between 2011 and 2014. On the day of the IFX infusion, all of these patients underwent a faecal calprotectin assay (Buhlmann technique), a CRP assay and pharmacological assays of IFX (ELISA , Theradiag). TLI (> 2µg/ml) were considered therapeutic as well as CRP levels < 5mg/l and faecal calprotectin levels < 250mg/g of stools. All of the patients included were followed up for a minimum of nine months. A CDAI score was calculated at each IFX infusion. A patient was defined in loss of response to IFX (LOR) when the CDAI was above 220, resulting in a change of treatment deemed necessary by the physician (IFX optimisation, change of medical treatment including the use of corticosteroids, surgery).

Results: 119 patients (mean age: 34 years, M:F sex ratio 1.2, mean duration of the disease 7.8 years) were included. The mean follow-up period was 20.4 months. 17% of the patients were on combotherapy (IFX and azathioprine). During follow-up, 37 patients (31.1%) out of the 119 relapsed, 78% within the first 6 months (mean period: 4.6 months). While the clinical characteristics of the relapsed and non-relapsed patients were similar, a univariate analysis isolated four significant factors predicting LOR: (CRP > 5mg/l (p=0.043), ATI > 20ng/ml (p< 0.001), LTI > 2 µg/ml (p< 0.001) and calprotectin > 250 µg/g stools (p<0.001)). After logistic regression, two independent factors were linked to a loss of clinical response: LTI < 2µg/ml (OR: 4,34 ; 95% CI: 1.28-10.7; p=0.001) and faecal calprotectin > 250µg/g stools (OR: 3.5; 95% CI: 1.5-8.7; p=0.001). In light of these results, a training cohort of 55 patients was isolated randomly in order to implement a predictive model for LOR in patients on IFX and in clinical remission. The combination of calprotectin > 250µg/g stools and TLI < 2µg/ml enabled to be predicted LOR in 95% of the cases within 6 months. This model was validated on the test cohort of 64 patients with a PPV of 95% and an NPV of 95%.

Conclusions: In IFX-treated CD patients and in clinical remission, a combination of TLI (< 2µg/ml) and faecal calprotectin (>250µg/g of stools) enable the prediction of LOR within 6 months in 95% of cases.

DOP039
Early therapeutic drug monitoring for prediction of short-term mucosal healing in patients with ulcerative colitis treated with infliximab

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Background: Mucosal healing is currently a primary goal of anti-TNF therapy in inflammatory bowel disease (IBD). Mucosal healing is an independent predictor of sustained clinical remission in patients with ulcerative colitis (UC) treated with infliximab (IFX). Although trough concentrations (TC) of both IFX and adalimumab have been associated with mucosal healing during the maintenance treatment in IBD, there are only limited data regarding the role of therapeutic drug monitoring during the induction phase.We investigated whether IFX TC during the induction phase can predict short-term, mucosal healing (STMH) in patients with UC.

Methods: This was an observational, retrospective, single-center study. Patients who received scheduled induction therapy (week 0-2-6) and had an endoscopic evaluation both at baseline and after induction therapy (week 10-14) were eligible to be included in the study. STMH was defined as a Mayo endoscopic sub-score of 0 or 1, assessed after the induction therapy, with a baseline sub-score of 2 or 3. Infliximab TC were evaluated in prospectively collected serum samples at weeks 0, 2, 6 and 14 after IFX initiation using an in-house developed and clinically validated ELISA.

Results: From an electronic database of 411 UC patients treated with IFX, 101 were finally included in the study. Patients with STMH had higher IFX TC at weeks 2, 6 and 14 compared to those without (Table). A receiver operating characteristic (ROC) curve analysis identified a cut-off of 22.5 µg/ml at week 2 (AUC: 0.642, p=0.016) and 12.8 µg/ml at week 6 (AUC: 0.691, p=0.001), as predictive values for STMH. Univariate (chi-square) analysis identified IFX TC> 22.5 µg/ml at week 2 [p=0.013, OR: 3.1 (95%CI: 1.3-7.3)], IFX TC >12.8 µg/ml at week 6 (p=0.002, OR: 3.9 (95%CI: 1.7-9.1)], female gender [p=0.039, OR: 2.5 (95%CI: 1.1-5.9)] and azathioprine (AZA) at start of IFX [p=0.009, OR: 3 (95%CI: 1.3-6.9)], as parameters predicting STMH. Multiple logistic regression analysis retained IFX TC>12.8 µg/ml at week 6 [p=0.004, OR: 3.6 (95%CI:

Median (IQR) IFX TC (μg/ml)	STMH (n=55)	No STMH (n=46)	p (Mann-Whitney U test)
w2	22.7 (15.9–31.6)	17.6 (8.5–22)	0.016
w6	17.3 (9.6–25.3)	9.3 (3.6–13.6)	0.001
w14	7.4 (3.4–11.2)	1.5 (0.7–3.2)	<0.001

1.5-8.6)] and AZA at IFX initiation [p=0.024, OR: 2.7 (95%CI: 1.1-6.6)] as independent factors predicting STMH.

Conclusions: This study reflecting real-life clinical practice indicates that early therapeutic drug monitoring may be of great significance for guiding therapeutic decisions in UC patients treated with IFX, while concomitant immunomodulators may play an important role towards STMH.

DOP040
Relationship between vedolizumab pharmacokinetics and endoscopic outcomes in patients with Ulcerative Colitis

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Table1: Mucosal Healing by Measured VDZ $Conc_{trough}$ Quartile at Wk 6 in Patients With UC in GEMINI 1

		$Conc_{trough}$ Quartile			
	PBO[a]	Q1	Q2	Q3	Q4
Wk 6 VDZ $conc_{trough}$, mcg/mL		≤17.1	>17.1 to 25.0	>25.0 to 35.7	>35.7 to 140.0
n	133	169	173	172	175
Percentage of patients with mucosal healing[b] at wk 6 (95% CI)	27.8 (20.2, 35.4)	20.1 (14.1, 26.2)	32.4 (25.4, 39.3)	44.8 (37.3, 52.2)	62.9 (55.7, 70.0)

Four patients had a VDZ $conc_{trough}$ below the limit of quantitation and were excluded from the quartile analysis.
[a] PBO data are provided for comparative reference.
[b] Mucosal healing was defined as a Mayo Clinic ES ≤1. Patients missing an ES were counted as not achieving mucosal healing.

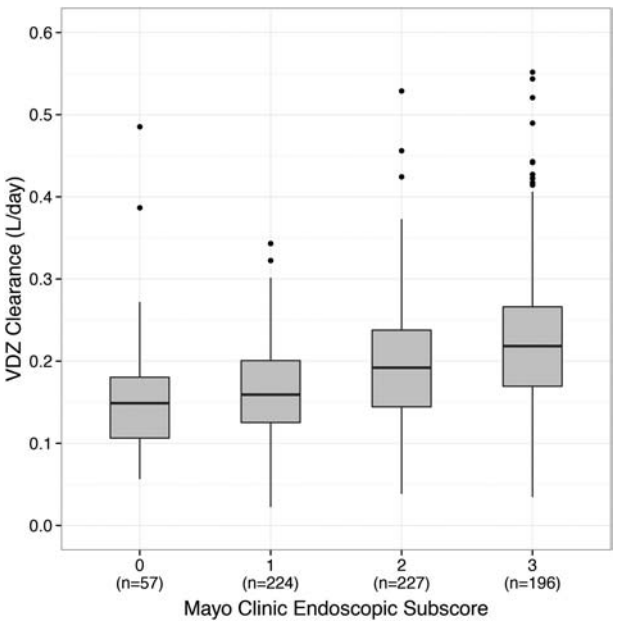

Figure 1. XXXXXXX

Background: Higher serum levels of tumor necrosis factor antagonists have been associated with mucosal healing in ulcerative colitis (UC). We studied the pharmacokinetics (PK) of vedolizumab (VDZ, 300 mg), an $alpha_4beta_7$ integrin antagonist, in relation to endoscopic outcomes.

Methods: In GEMINI 1, patients with UC received double-blind placebo (PBO) or VDZ (cohort 1) or open-label VDZ (cohort 2) at weeks (wks) 0 and 2 (induction).[1] Wk 6 VDZ responders were rerandomised to PBO or VDZ every 4 or 8 wks during maintenance (wks 6-52); induction PBO patients and wk 6 VDZ nonresponders continued on PBO and VDZ every 4 wks, respectively. Endoscopy was performed and blood for PK analysis was collected periodically. For VDZ-treated patients from cohorts 1 and 2 with a wk 6 Mayo Clinic endoscopic subscore (ES), the median wk 6 VDZ serum trough concentration ($conc_{trough}$) was determined for each ES (range, 0-3; higher scores suggest more active disease). Wk 6 VDZ $conc_{trough}$ quartiles and associated rates of mucosal healing (ES≤1) were calculated. VDZ clearance (CL) values for VDZ-treated patients with a wk 6 ES were estimated via population PK modelling.[2]

Results: At wk 6, mucosal healing was more common in patients with higher measured VDZ $conc_{trough}$ (Tab. 1).

Wk 6 median measured VDZ conctrough values were 34.5, 30.4, 24.0, and 19.6 mcg/mL for ESs of 0 (n=55), 1 (n=223), 2 (n=224), and 3 (n=188), respectively (ES unavailable, n=3). Notably, the median wk 6 measured VDZ conctrough in those with an ES of 3 (n=188) was below the overall GEMINI 1 wk 6 median (25.6 mcg/mL). A trend toward greater estimated VDZ CL in patients with higher ESs was noted (Fig. 1).

Conclusions: At wk 6, mucosal healing was more common and ESs were lower in patients with higher measured VDZ $conc_{trough}$ values than in those with lower values. The apparent association between higher ES and faster VDZ CL also could be due to confounding factors.

Clinical study funded by Millennium Pharmaceuticals, Inc. (d/b/a Takeda Pharmaceuticals International Co. [TPI]). Medical writing assistance provided by E. Barton of MedLogix Communications, LLC, and supported by TPI. S. Abrol assisted with figures.

References:

[1] Feagan BG, et al., (2013), Vedolizumab as induction and maintenance therapy for ulcerative colitis, N. Engl J Med., 699-710

[2] Rosario M, et al., (2014), Population pharmacokinetic modelling of vedolizumab in patients with ulcerative colitis or Crohn's disease, J Crohns Colitis, S225-S226

DOP041
Etrolizumab population pharmacokinetics (Pop PK) and covariate analysis in patients with moderately to severely active ulcerative colitis (UC)

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Background: Etrolizumab is a humanized IgG1 monoclonal antibody that specifically binds the beta(β)7 subunit of alpha(α)4β7 and αEβ7 integrins. Clinical activity of etrolizumab has been observed in patients with moderate to severe UC in a Phase 2 trial. The objective

of this Pop PK analysis was to characterize covariate effects on the PK profile of etrolizumab.

Methods: This analysis included data from 145 etrolizumab-treated patients from 3 studies: a Phase 1 dose-escalation study (single doses at 0.3, 1, 3 or 10 mg/kg intravenously [IV], 3 mg/kg subcutaneously [SC] or 3 monthly doses at 0.5, 1.5 or 3 mg/kg SC or 4 mg/kg IV); a Phase 2 efficacy and safety study (2 SC dose cohorts of 100 mg at weeks 0, 4 and 8 or 420 mg at week 0 followed by 300 mg at weeks 2, 4 and 8); and a Phase 2 open-label extension study (300 mg SC monthly). A stepwise forward addition and backward elimination approach was used to evaluate the impact of the following baseline covariates on etrolizumab PK: age, sex, body weight (BW), Mayo Clinic Score, albumin, C-reactive protein, faecal calprotectin, prior use and response to anti-tumour necrosis factor alpha biologics and concomitant treatment with steroids or immunosuppressants. The Pop PK analysis was performed using NONMEM 7.1.2.

Results: A 2-compartmental model with first-order absorption and elimination kinetics described etrolizumab PK well. BW and baseline serum albumin were identified as significant covariates for clearance (CL; $P < 0.001$); each explained 16% and 30% of the interindividual variability (IIV) of CL, respectively. Simulation showed similar exposure variability for a BW-based or fixed dose. No other covariates were found to have a significant impact on etrolizumab PK. The final model estimated the typical population CL value and central volume of distribution to be 0.245 L/day and 3.2 L, respectively. The elimination half-life and SC bioavailability were estimated to be 11 days and 53%, respectively. The IIV of evaluated PK parameters ranged from 19% to 67%. Pop PK simulation estimated that 105 mg every 4 weeks, the proposed Phase 3 dose regimen, can maintain a steady-state trough concentration of >1.7 µg/mL in 85% of patients (1.7 µg/mL is the observed minimum drug level associated with full β7 receptor occupancy in peripheral blood and colonic tissue).

Conclusions: Etrolizumab exhibited linear PK at the target therapeutic dose. Based on the available data, BW and baseline serum albumin were identified as statistically significant covariates for CL. However, given the favourable safety and efficacy profiles for etrolizumab, the impact of these covariates on the therapeutic outcome is expected to be minimal and not clinically relevant.

DOP042
Clinical response and remission with vedolizumab across a range of baseline fecal calprotectin levels in ulcerative colitis: Results from GEMINI 1

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Background: Calprotectin is a neutrophil granule protein released during inflammation. In ulcerative colitis (UC), fecal calprotectin (fCal) concentration varies with endoscopic activity and is believed to reflect intestinal inflammation. Vedolizumab (VDZ), an anti-$\alpha_4\beta_7$ integrin monoclonal antibody, reduces gastrointestinal inflammation by inhibiting migration of gut-homing memory T cells into the gastrointestinal tract. In GEMINI 1, a phase 3 study of VDZ in UC, fCal concentrations were measured to document degree of inflammation and to evaluate any correlation with response to VDZ.

Methods: In GEMINI 1, patients with moderately to severely active UC were randomly assigned to receive double-blind placebo (PBO) or VDZ 300 mg (induction ITT population) or open-label VDZ at weeks 0 and 2. Response was measured at week 6 using the Mayo Clinic score. Each patient collected a stool sample (~20 g) at baseline and week 6 for determination of fCal. Per the test kit (PhiCal quantitative enzyme-linked immunosorbent assay), fCal >150 µg/g stool reflects active UC. This post hoc analysis evaluates the effect of VDZ induction therapy on fCal concentrations and clinical response and remission. Baseline fCal cut-offs of ≤250 and >500 µg/g stool were used, reflecting the degree of disease activity in this population.

Results: At baseline, PBO- and VDZ-treated patients had similar degrees of inflammation as determined by fCal concentrations and percentage of patients with fCal ≤250 or ≥500 µg/g (Table). At week 6, response and remission rates were numerically higher with VDZ than PBO regardless of baseline fCal (Table), and a 69% and 32% decrease in geometric mean of fCal was observed for VDZ and PBO-treated patients, respectively (P=0.0011). Overall safety data have been previously reported. [1]

	PBO n=149		VDZ n=225	
Baseline fCal, µg/g stool Median (min, max)	1006 (24, 16444)		1112 (24, 20000)	
Baseline fCal Category	**≤250 µg/g n=27**	**>500 µg/g n=92**	**≤250 µg/g n=37**	**>500 µg/g n=156**
Clinical Response* at Week 6, n (%) patients	8 (30)	23 (25)	20 (54)	75 (48)
Clinical Remission** at Week 6, n (%) patients	2 (7)	6 (7)	7 (19)	27 (17)

* Reduction of ≥3 points and ≥30% from baseline in complete Mayo Clinic score, with a decrease in rectal bleeding subscore of ≥1 point or absolute rectal bleeding subscore ≤1. ** Complete Mayo Clinic score ≤2 and no individual subscore ≥1.

Conclusions: In this post hoc analysis, VDZ induction therapy for UC reduced fCal levels at week 6, a marker of mucosal inflammation, significantly more than PBO. Response and remission rates were higher with VDZ regardless of baseline fCal concentration.

Clinical study funded by Millennium Pharmaceuticals, Inc. (d/b/a Takeda Pharmaceuticals International Co.).

References:

[1] Feagan BG, et al., (2013), Vedolizumab as induction and maintenance therapy for ulcerative colitis, N Engl J Med, 699-710

DOP043
Faecal calprotectin as a tool for relapse prediction in clinical routine in Crohn's Disease patients – preliminary Results from the prospective, population-based FIRE study

S. Nikolaus*[1], D. Lang[2], B.M. Wittig[2], M. Schwarz[2], S. Schreiber[1]

Table: FC levels at different study visits

		N		Median	Mean ± SD	Percentiles	
		valid	missing			25	75
FC levels at BL [µg/mL] (p = 0.019)*	Total	362	0	147.5	416.5 ± 614.2	59.6	417.5
	"Relapser"	79	0	186.0	549.3 ± 709.7	75.9	729.4
	"Remitter"	283	0	133.0	379.4 ± 580.8	55.9	371.0
FC levels at 3 months [µg/mL] (p = 0.057)*	Total	261	74	147.5	416.5 ± 614.2	59.6	417.5
	"Relapser"	61	18	236.5	625.2 ± 726.3	68.8	1070
	"Remitter"	200	56	156.5	409.4 ± 586.6	48.9	482.0
FC levels at 6 months [µg/mL] (p = 0.016)*	Total	222	61	135.5	403.7 ± 629.8	51.0	395.0
	"Relapser"	41	13	319.4	735.7 ± 829.6	53.4	1706
	"Remitter"	181	48	116.0	328.5 ± 550.7	50.6	271.5
FC levels at 12 months [µg/mL] (p = 0.593)*	Total	158	58	123.0	371.8 ± 558.9	51.4	391.0
	"Relapser"	23	12	160.0	457.6 ± 700.4	60.4	393.8
	"Remitter"	135	46	116.7	357.2 ± 532.9	47.0	390.0
CRP levels at BL [mg/L] (p = 0.044)*	Total	279	83	4	12.3 ± 37.1	1.6	9.0
	"Relapser"	59	20	5.7	25.3 ± 69.4	1.9	13.0
	"Remitter"	220	63	3.95	8.79 ± 20.3	1.5	8.5

* Mann-Whitney-U-Test; p-value for comparison of "relapser" versus "remitter" group.

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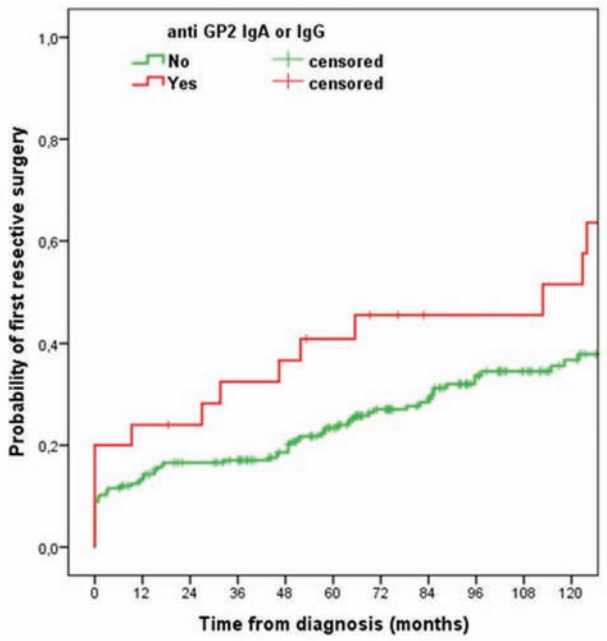
Background: It is difficult to predict the course of Crohn's disease (CD) and until today the gold standards are imaging Methods, primarily endoscopy which is invasive and expensive, and therefore not useful for monitoring patients (pts) in daily routine. The use of faecal calprotectin (FC), which is elevated in pts with IBD and correlates with endoscopic and histological disease activity, may avoid repeated endoscopic examinations. The purpose of the study is to assess the value of routine FC measurement for relapse prediction in CD pts with clinically inactive disease, who receive immunomodulatory treatment.

Methods: FIRE is an ongoing prospective, observational multi–centre study at 103 sites in Germany. Inclusion criteria were status of post moderate–to–severe CD flare which required treatment with steroids, immunosuppressants (IS) and/or TNF antagonists, current remission status (Harvey-Bradshaw index [HBI<5]) and ileocecal and/or colonic disease. Every 3 months until occurrence of moderate–to–severe clinical relapse (HBI≥7), or until 24 months of follow–up, whichever comes first, the following information is collected for each patient: FC level (measurement at central lab), HBI, and current IBD treatment. This sub–analysis aimed to investigate the value of FC in predicting mild–to–severe clinical CD relapse (HBI≥5).

Results: For 362 of 525 pts with available 1–yr follow–up data baseline (BL) FC values and HBI results were analysed. The median age of the population (57.5% female) was 35 yrs, with median disease duration of 6.75 yrs. With current IBD treatment the majority of pts did not experience mild–to–severe clinical CD relapse (HBI≥5), i.e. 79 pts with clinical relapse ("relapser") vs. 283 pts without relapse ("remitter") within 1–yr follow–up. At BL 48.3% of pts had a HBI of 0. A significantly higher median HBI (2.0 vs. 0, p<0.001), CRP and FC level (see table) were observed for "relapser" as compared to "remitter" at BL. During 1–yr follow–up higher FC levels were seen for "relapser" than for "remitter" (see table). In multivariate regression analysis, female gender (p<0.023) and HBI≥1 at BL (p<0.001) were identified as prognostic factors for subsequent flare (HBI≥5), but not higher FC level.

Conclusions: FIRE is one of the largest, prospective FC studies thus far. The data suggest that an increase in FC levels precedes subsequent clinical relapse in CD. Further analysis will examine the clinical value of FC to flare prediction in a confirmatory analysis.

DOP044
Presence of anti-MZGP2 IgG and IgA antibodies assessed by 2 different ELISA assays is associated with younger age at onset, stricturing disease behavior, need for surgery and ASCA/anti-OMP PlusTM positivity in Crohn's Disease



"Association between the presence of anti-GP2 IgA or IgG antibodies and time to resective surgery"

M. Papp*[1], N. Sipeki[1], G.L. Norman[2], Z. Shums[2], D. Roggenbuck[3], P. Antal-Szalmas[4], G. Veres[5], P.L. Lakatos[6]

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Background: Major pancreatic zymogen granule membrane glycoprotein 2(MZGP2 or GP2) is essential for host-microbial interaction and the initiation of bacteria-specific mucosal immune responses in the gut. The aim of the present study was to determine the predictive potential of the anti-MZGP2 antibodies in the determination of disease phenotype, therapeutic strategy and long-term disease course in a prospective referral CD cohort.

Methods: 271 consecutive CD patients(median follow-up:131 months) were included. Anti-MZGP2 IgA and IgG were determined by 2 different ELISA Methods(Inova Diagnostics and Generic Assays) and also ASCA IgG/IgA and anti-OMP PlusTM IgA. Detailed clinical phenotypes were determined prospectively during the follow-up by reviewing the patients' medical charts.

Results: 10.2% and 12.2% of the CD patients were positive for anti-GP2 IgA/IgG and anti-MZGP2 IgA/IgG, respectively. Agreement between assays was good (K=0.56). At diagnosis, 45% of the patients had ileocolonic disease and 79.7% had inflammatory behavior, while 52% had complicated disease behavior and 41.1% had at least one resective surgery at last follow-up. Exposure to steroids, azathioprine(AZA) or anti-TNFs was 88.2%, 73.8% and 41.7%, respectively. Presence of anti-MZGP2 IgA/IgG was associated

with pediatric onset (A1:26.9%, A2:11.6% and A3:6.1%,p=0.02), colonic or ileocolonic location (p=0.035), stenosing disease behavior at diagnosis (B1:10.8%, B2:27.3%, B3:4.5%,p=0.015), penetrating disease behavior at last follow-up(p=0.03), need for AZA (p=0.025, OR:3.74), need for surgery(p=0.02, OR:2.38), ASCA (p<0.001) and anti-OMP (p=0.004) positivity. Similarly, anti-GP2 IgA/IgG positivity was associated with pediatric onset (p=0.053), complicated disease phenotype (p=0.005) and lack of perianal disease (p=0.05) at diagnosis, need for surgery (p=0.017, OR:2.77) and with ASCA (p=0.003) and anti-OMP (p=0.01) positivity. None of the antibodies were associated with the time to initiation of steroids, AZA, anti-TNFs or behavior changes overall in patients with initial inflammatory disease in a Kaplan-Meier analysis. In contrast, both anti-MZGP2 and anti-GP2 IgA/IgG positivity was associated with the time to surgery(p=0.038 and p=0.046).

Conclusions: Presence of anti-MZGP2 IgG/IgA antibodies was associated with disease phenotypes identifying patients at a younger age at onset, ileocolonic location, stricturing/complicated disease behavior, need for surgery and ASCA/anti-OMP positivity in this prospective referral CD cohort. The agreement between the two anti-GP2 assays was good.

DOP045
pANCA and ASCA in > 400 children with IBD-unclassified (IBD-U), Crohn's Colitis and Ulcerative Colitis (UC) - a longitudinal report from the Porto pediatric IBD group of ESPGHAN

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Diagnostic utility of serology to differentiate IBD-U from Crohn's colitis (CC) and UC

	Sensitivity %	Specificity %	PPV %	NPV %
IBD-U vs. CC (pANCA-/ ASCA+)	33%	83%	96%	13%
IBD-U vs. UC (pANCA+/ ASCA-)	65%	66%	94%	38%
CC vs UC pANCA+/ ASCA-	65%	77%	55%	79%
pANCA-/ ASCA+	33%	97%	90%	40%

Background: Serology can help differentiate Crohn's disease (CD) from UC, but the bigger clinical challenge is differentiating IBD-U from isolated Crohn's colitis (CC) and UC. No study to date has longitudinally evaluated ANCA and ASCA in pediatric IBD-U as compared with CC. In this largest study to date, we aimed to explore the diagnostic utility of the serological profile in these IBD subgroups and to assess whether serology can predict disease severity and long term outcomes.

Methods: This was a multicenter retrospective longitudinal study including 406 IBD children from 19 centers affiliated with the Porto IBD-working group of ESPGHAN (mean age 10.5 ± 3.9, 221 (54%) males); 118 (29%) with CC, 142 (35%) with UC and 146 (36%) with IBD-U, classified by the Porto criteria. Median follow-up period was 2.8 [IQR 1.6-4.2] years when outcomes and the last diagnosis was recorded.

Results: The most prevalent serologic profile in IBD-U was pANCA-/ ASCA- 37 (41%), followed by pANCA+/ ASCA- 31 (34%) and pANCA-/ ASCA+ 15 (17%). They had a high PPV but very low NPV to differentiate IBD-U from either CC or UC (table):

UC patients with pANCA+/ASCA- had less often mild disease at diagnosis than those negative for this profile (36 (62%) vs 22 (38%), p=0.033) and had more often severe disease course, defined as the need for calcineurin inhibitors, biologics or colectomy (25 (80%) vs 6 (20%), p=0.026). In contrast, pANCA-/ ASCA+ profile was not associated with disease progression or severity in the CC group.

Conclusions: In this first comparison of serology in IBD-U and isolated CC, serology seems less accurate than previously reported when comparing UC vs. CD, with high PPV and very low NPV for disease phenotype. Moreover, whereas serology profile was predictive of severe disease course in UC, this was not demonstrated in CC, questioning the utility of serology testing in clinical practice of children with CC.

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Digital Oral Presentations

OXFORD

DOP Session 6 – Surgical outcomes

DOP046
Surgery and hospitalization rates during the first year after diagnosis in patients with inflammatory bowel diseases from the 2011 ECCO-EpiCom inception cohort

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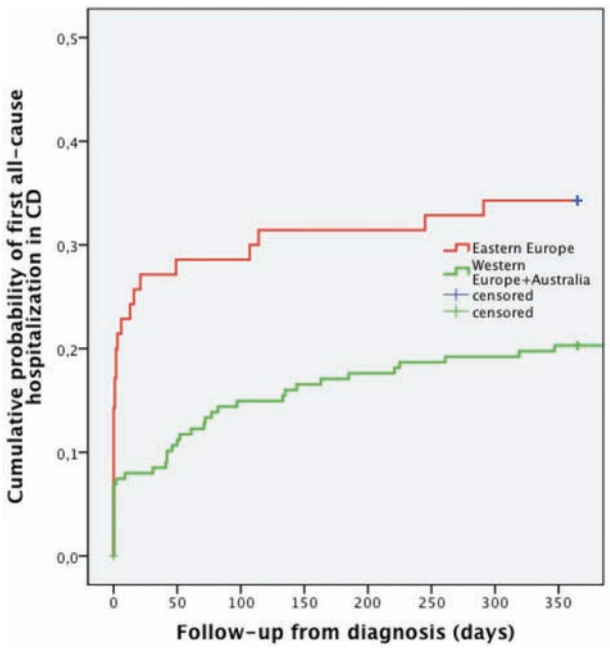
Background: The ECCO-EpiCom study investigates the differences in the incidence, disease characteristics and therapeutical management of inflammatory bowel diseases (IBD) between Eastern and Western Europe. The aim of this study was to analyze the differences in the surgery and hospitalization rates in the 2011 ECCO-EpiCom inception cohort within the first year after diagnosis.

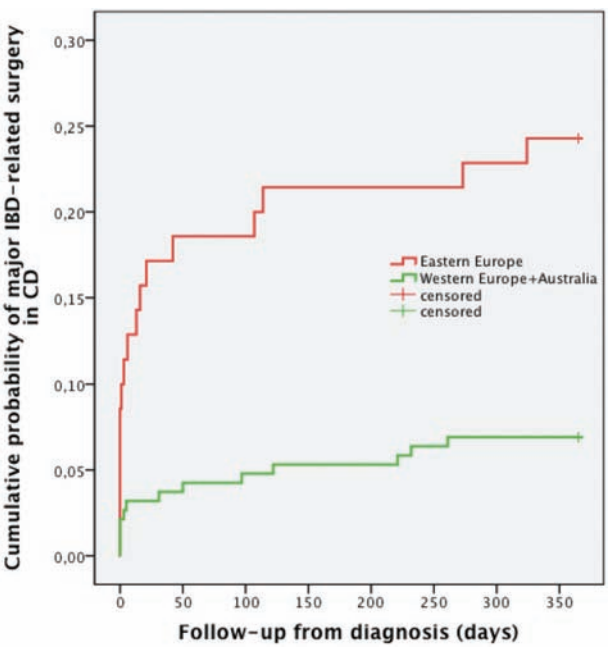
Methods: Fourteen European (9 Western and 5 Eastern European centers) and one Australian center with 258 Crohn's disease (CD), 380 ulcerative colitis (UC) and 71 IBD unclassified (IBDU) patients (65% from Western, 25% from Eastern Europe, 10% from Australia; female/male: 326/383; mean age at diagnosis: 40.9 years, SD: 17.3 years) participated in the one-year follow-up. Patients' data regarding disease characteristics, medical therapy, surgical procedures and hospitalizations were registered and entered in the web-based ECCO-EpiCom database every third month during the first 12 months after diagnosis.

Results: In Eastern Europe, significantly more CD patients were hospitalized compared to Western Europe/Australia within the first year after diagnosis (34% vs. 21%, p=0.02, pLogRank=0.01; Figure 1.).

Patients with L3±L4 (ileocolonic ± upper GI, pLogRankL3=0.007, pLogRankL3+L4<0.00) and complicated disease behavior (pLogRankB1 vs B2/B3<0.001, pLogRankB2 vs B3=0.05) were more frequently hospitalized. In UC, we did not find a geographic difference in the hospitalization rates during the first year (16% vs. 16%, p=0.93). In CD, more Eastern European patients



"Figure 1. Cumulative probability of first all cause hospitalization in Eastern and Western Europe/Australia"



"Figure 2. Cumulative probability of major IBD-related surgery in Eastern and Western Europe/Australia"

underwent a surgical procedure within the first year after diagnosis (pLogRank=0.001; Figure 2.).

Of note, this was associated to ileal only location and stenotic behavior (pLogRankB2=0.09, pLogRankL1=0.008). Overall, the disease behavior was the major driver for both hospitalization and surgery (pLogRankhosp<0.001, pLogRanksurg<0.001). The majority of the surgical procedures were performed within a short time period after diagnosis.
In UC, only 1 patient underwent colectomy.
Conclusions: In Eastern Europe, a significantly higher percentage of CD patients had surgery and were hospitalized compared to Western Europe/Australia within the first year after diagnosis. Disease behavior was the major predictor for both surgery hospitalization. In contrast, both hospitalization rates and risk for colectomy was low in UC.

DOP047
Long Term Outcome of Segmental Resection for Crohn's Colitis: an Observational Study on 200 Patients

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Background: Surgical treatment for segmental Crohn's colitis (CC) is still a subject of debate. Extensive surgery increases the risk for definitive stoma, but the risk for permanent ileostomy after total abdominal colectomy (TAC) and ileo-rectal anastomosis is acceptable. Moreover, total procto-colectomy (TPC) with definitive ileostomy is related to the lowest recurrence risk. The aim of this study is to report the long-term results of segmental resections (SR) for CC in a cohort of 200 patients with a median follow-up of 13.5 years. First endpoint was the risk for TAC after SR; the second was the risk for permanent stoma.
Methods: Patients who underwent surgery for CC were selected from February 1990 to June 2014. Three groups were identified from our database on the basis of surgical option: SR, TAC and TPC. Patients were followed yearly by physical examination, blood test end endoscopy. Only surgical recurrence was considered. Univariate and multivariate analysis were performed in order to identify factors that may affect the risk for total abdominal colectomy and for permanent stoma.
Results: Among 1670 patients operated at our institution for inflammatory bowel disease, 275 were selected. Two hundred received SR, 59 TAC with ileo-rectal anastomosis and 16 total TPC with definitive ileostomy. Mean age at surgery was 37.1 year (±13.9); extension of the disease of more than 3 site was of 31%; this was 15% in SR group and 79.7% TAC group. Among 200 patient treated with SR 130 (65%) never recurred, while 42 (21%) needed a TAC and 28 (14%) an iterative SR. In the subgroup with SR, only 18% needed a definitive stoma. At multivariate analysis only the presence of distal disease resulted statistically significant for TAC (p=0.032). For which concern the risk of permanent stoma, only perianal disease (p=0.0452), distal disease (p=0.0214) and previous use of biologics (p=0.0061) resulted as risk factor for permanent stoma. Median overall surgical recurrence was 6.05 years.
Conclusions: Our study suggests that SR is an effective treatment in case of localized disease with low or absent ano-rectal involvement but patients should be informed of the risk of surgical recurrence leading to TAC and on the risk of permanent stoma during the course of their disease. The risk for TAC after previous SR for Crohn's colitis seems to be related more to the local status of the disease at diagnosis than to other extra-intestinal factors (smoke, familiarity, age, sex or extra-intestinal disease). TPC is required at first surgery only in a very little group of patients, while rectal preservation is possible in more than 80% of cases.

DOP048
Predictors of post-operative endoscopic recurrence in Crohn's disease: a prospective study of the REMIND group

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Background: Post-operative recurrence represents a significant problem for Crohn's disease (CD) patients. After ileocaecal resection, endoscopic recurrence is mainly located on the anastomosis and/or on the neo-terminal ileum. The aim of this study is to identify predictors of post-operative endoscopic recurrence.
Methods: This is a prospective study performed in 9 centres of the REMIND group, collecting data at time of surgery and of endoscopy (performed at 6 months), associated with an extensive bio-banking. Inclusion criteria were: age>18 years old; ileal or ileocecal CD; indication of surgery. Post-operative treatment was given according to a pre-established algorithm. Clinical, biological and endoscopic parameters (description and location of elementary lesions, Rutgeerts score) were collected at month 6. Endoscopic recurrence was defined by a Rutgeerts score>1. Baseline factors (demographic and phenotypic variables) associated with endoscopic recurrence were searched by univariate and multivariate regression analysis.
Results: 210 patients were included. Endoscopy at month 6 was performed in 143 patients at time of analysis (73M/70F). Median age was 32 years old (18-70). Forty-seven were active smokers (33%) and 40 previous smokers (28%) at time of surgery. Median disease duration was 6 years (0-35). Thirty patients (21%) have had perianal lesions. Macroscopic analysis of the surgical specimen showed fistula (with or without stricture) in 58 (41%), and stricture (without fistula) in 77 patients (54%). A treatment with thiopurines or anti-TNF had been given before surgery to 94 (66%) and 81 (57%) patients, respectively. Eighteen patients (38% of active smokers) stopped smoking after surgery. After surgery, 29 (21%) and 46 (32%) patients received thiopurines

and anti-TNF, respectively. An endoscopic recurrence (Rutgeerts score>1) was observed in 63 patients (44%). Women (OR -1,07 IC95% 0,16-0,73), patients with strictures (OR -2,54; IC95% 0,01-0,81) or fistulas (OR -2,49; IC95% 0,01-0,87) had a lower risk of endoscopic recurrence, and active smokers (OR 1,46 IC95% 1,90-9,74) had a higher risk of endoscopic recurrence. Thiopurines and anti-TNF therapies, which were given more frequently to patients at high risk of recurrence (accordingly to the algorithm), had no impact on the rate of recurrence in the whole cohort.

Conclusions: This cohort exhibits the classical characteristics of CD patients undergoing ileocaecal resection. The only reversible factor associated with endoscopic recurrence is smoking behaviour. These results justify the search of predictive biomarkers in this prospective cohort.

DOP049
Involvement of cell fate pathways in early post-surgical recurrence of Crohn's Disease

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Background: The intestinal transcriptomic analysis allowed us to identify alterations in the Notch, Wnt, and Bmp signalling pathways in patients with Crohn's disease (CD) and early post-surgical recurrence (PSR). Although these pathways are involved in defining the final phenotype of many cell types, it is in the intestinal epithelium where they acquire a key role in the maintenance of the barrier function.

Aims: To confirm if the transcriptional changes associated with early PSR are translated at a protein level; and to detect changes between different lineages of intestinal epithelial cells.

Methods: Ileal samples were harvested from the surgical specimens of 14 CD patients undergoing ileo-cecal resection. Follow-up colonoscopies were performed at six, twelve, and eighteen months after surgery. Patients were grouped according to the development (n=5) or not (n=9) of endoscopic recurrence within this period. These tissue samples were used for protein extraction and measurement of those proteins involved in the Notch, Wnt and Bmp pathways (RayBiotech platform, USA). Additionally, samples included in paraffin were used to identify goblet cells (Alcian blue staining), epithelial proliferation (anti- Ki67, Dako, Denmark) and stem cells (anti - Lrg5, LSBio, USA).

Results: The most noticeable changes are the increased production of S100A8, CyclinD1, Notch2, CEA, ADAM17, S100A9 and MUC2 in patients with early PSR. On the other hand, the levels of TGFb1 are reduced comparing PSR to no PSR (p = 0.042). All these proteins are elements of different cell fate pathways. Regarding the detection of changes in epithelial cell lineages, patients with early PSR showed an increased number of goblet cells located at the crypts [44.1 (34.9-48) vs. 29 (25.7-32.3), p = 0.02] and a trend to a lower number of Lrg5 + stem cells [1 (0.76-2.56) vs. 1.4 (0.68-2.31].

Conclusions: Changes in protein elements of cell fate pathways previously seen in the intestinal transcriptome in CD patients who develop early PSR may reflect in changes of cell lineages of the intestinal epithelium.

DOP050
Early thiopurine use is associated with a reduced risk of surgery in children and young people with Crohn's disease but not in ulcerative colitis

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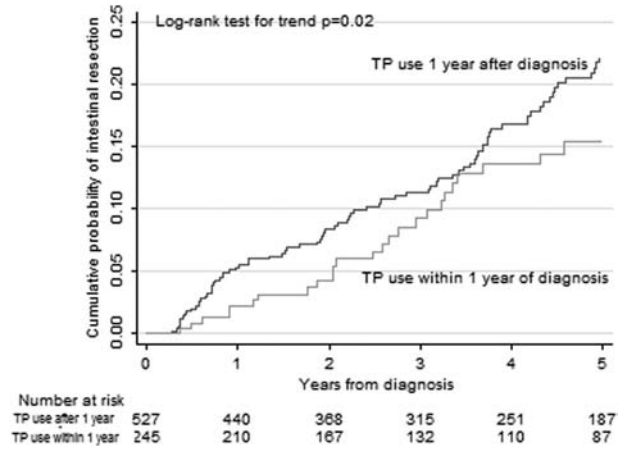
Background: Thiopurine (TP) use can alter phenotypic progression and the risk of surgical intervention in inflammatory bowel disease (IBD) but recent evidence from adult studies has shown little efficacy from its early use in adults. We aimed to quantify the impact of timing and duration of TP use on the risk of first surgery in children and young people with IBD.

Methods: We constructed a cohort of incident cases of children and young people aged <25 years, diagnosed with Crohn's disease (CD) or ulcerative colitis (UC) from 1990-2009 using the Clinical Practice Research Datalink (CRPD), which is a validated research database and represents an 8% sample of the UK population. We stratified TP use by "early use" within the first year after diagnosis and by "duration of use": < 3 month;3-6 months,6-12 months, >12 months. We performed survival analysis using the Kaplan-Meier method to determine the unadjusted 5 year risk of surgery and created a Cox proportional hazards model to determine the impact of early TP use, commenced within a year of diagnosis and duration of TP use on



"Risk of surgery in early (within 1 year) vs late (after 1 year) thiourine use"

risk of first surgery amongst TP users only. We also calculated the numbers needed to treat (NNT) based on the inverse of the absolute 5 year risk reduction for each comparison.

Results: For CD, we identified 1595 incident cases of which 216 had an intestinal resection (13.5%). The 5 year unadjusted cumulative probability of first surgery for those starting TPs within a year of diagnosis compared with those starting after the first year was 15.3% (95% CI:10.5-22.1) versus 22.1% (95% CI:18.1-26.9) respectively (log-rank p=0.02).

The absolute 5 year risk reduction of 6.8% equates to a NNT of 15 patients to prevent one surgery. The early use of TPs was associated with a reduction in risk of first surgery of 39% if started within the first year of diagnosis (HR 0.61, 95% CI:0.41–0.91) and sustained TP use for >12 months duration was associated with a reduction in risk of 71% (HR 0.29, 95% CI:0.20–0.44) although this was apparent after 3 months of use.

For UC, we identified 1175 incident cases of whom 73 (6.2%) underwent a colectomy. There was a 79% risk reduction for colectomy in UC if TPs were used for more than 12 months (HR 0.21, 95% CI:0.10–0.42) but early TP use offered no additional benefit.

Conclusions: Among children and young people using TP therapy, starting early, within the first year of diagnosis, reduces the risk of first surgery by 39% in CD with a NNT of 15. Sustained TP use for 12 months reduces the risk of first surgery by 71% and 79% in CD and UC respectively.

DOP051
Receiving corticosteroid therapy is associated with a poor outcome in patients with elderly-onset ulcerative colitis: a population-based study

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Background: In elderly-onset ulcerative colitis (UC) patients, clinical course has been reported to be mild, with a rare disease extension and a majority of patients never exposed to any immunosuppressant (IS) or anti-TNF-therapy, nor operated. Nevertheless, some patients have poor clinical outcome with early resort to surgery. Along this, the impact of receiving corticosteroid (CS) therapy on the evolution of elderly-onset UC has not been evaluated.

Methods: In a French population-based cohort we identified from 1988 to 2006 473 UC patients >60 years of age at diagnosis with a median follow-up of 6.3 years [Q1=2.3-Q3=10.3]. Clinical outcome of patients undergoing CS (CS group) was compared with patients who never received CS (control group) after adjustment on receiving or not IS and/or anti-TNF therapy (as clinical surrogate marker), on colonic location at diagnosis and disease duration.

Results: Among the 473 UC patients, 157 (33%) received at least once CS therapy (prednisone or prednisolone in 97% of cases). The cumulative probabilities of receiving CS was 21% (95% CI: 17-25) at 1 year, 39% (34-45) at 5 years, and 45% (38-52) at 10 years. Gender, median age and presence of extraintestinal manifestations at diagnosis were not different in CS and control groups. In CS group, proctitis (21%) was less frequent and pancolitis (36%) more frequent compared to control group (32% and 21% respectively, $p<10^{-2}$). At maximal follow-up, 7% and 49% of patients in CS group had proctitis and pancolitis, respectively, compared to 22% and 26% in control group, respectively ($p<10^{-4}$). Colectomy rate was higher in CS group (13%) than in control group (4%, $p=10^{-3}$). Total number of flares and hospitalizations per year but also time spent in hospital were significantly higher in CS group compared to control group ($p<10^{-4}$). The median duration of CS exposure was 4.6 months (2.4-9.0). Thirty-two (20%) patients were CS-dependent, 14 (9%) CS-resistant, and 15 (10%) became intolerant to CS (in which almost 30% of patients developed insulin-dependent diabetes). The cumulative probabilities of developing intolerance to CS was 1.3% (0.0 ; 4.0), 6.7% (2.6 ; 16.4) et 17.3 % (8.1 ; 34.6) at 1, 5, and 10 years respectively. Four patient stopped CS because of intolerance.

Conclusions: In elderly-onset UC, receiving CS therapy is associated with a more pejorative evolution of the disease, with higher rate of surgery, flares and hospitalizations. Moreover, a significant proportion of patients became intolerant to CS with more than one third who developed diabetes. Unlike the majority of cases in elderly-onset UC, IS or anti-TNF treatment should be early considered in patients receiving CS.

DOP052
Lower long-term colectomy rates with IFX than with CsA treatment in moderate to severe UC

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Background: Cyclosporine A (CsA) and infliximab (IFX) are similarly effective in preventing short-term colectomy in patients with moderate to severe ulcerative colitis (UC), but long-term outcomes are lacking. The aim of this study was to compare long-term efficacy of CsA and IFX in moderate to severe UC by analyzing colectomy rates as the outcome parameter for treatment success.

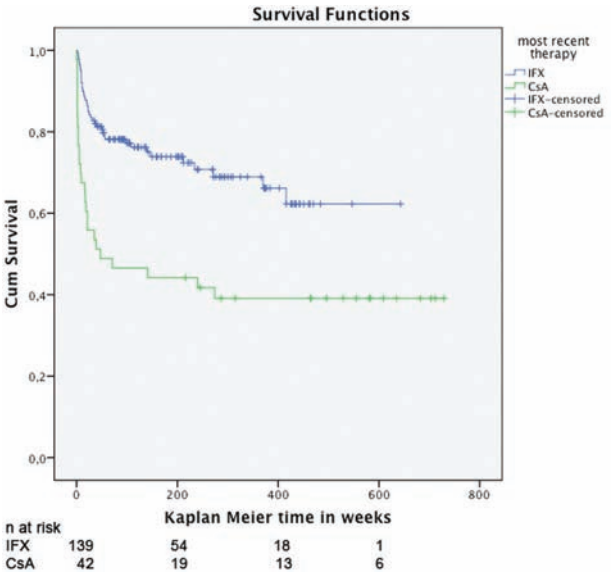
Methods: We retrospectively studied a cohort of patients who had received treatment with CsA or IFX between January 2000 and May 2014 at the Academic Medical Centre in Amsterdam for moderate to severe UC. The primary end point was time to colectomy. Variables such as gender, age, Mayo endoscopic subscore at start of treatment, extent of the disease and concomitant treatments were studied as relevant variables affecting outcome.

Results: 182 patients were studied (CsA group, n=43; IFX group, n=139). Follow-up of at least 6 months was available for all patients. Patient characteristics (age, gender, disease duration, disease extent and severity) were comparable between the two groups, with the exception that the mean follow-up was

significantly longer in CsA treated patients (IFX 61.5 months + 36.8 vs. CsA 124.7 months + 41.5), and steroid use was significantly higher in CsA treated patients (CsA 73% vs. IFX 40%). Colectomy-free survival at different end points was significantly higher in the IFX group as compared to CsA treated patients, as listed in table 1. Colectomy rates for complete follow-up are depicted in a Kaplan Meier survival curve (figure 1). CsA treated patients were at increased risk of undergoing colectomy (HR 2.61, P<0.001). When adding all significant covariates into a multivariate Cox regression model, therapy with CsA or IFX barely not reaches significance anymore (HR 1.84, P=0.084) (table 2).

Table 1: Colectomy-free survival at different time intervals after treatment initiation with CsA or IFX in patients with moderate to severe UC

Colectomy-free survival	CsA	IFX	P (Chi-Square)
1 month	74% (32/43)	98% (136/139)	P<0.0005
6 months	56% (24/43)	84% (117/139)	P<0.0005
12 months	49% (21/43)	80% (108/135)	P<0.0005
36 months	45% (19/42)	67% (67/100)	P=0.015



"Figure 1 Kaplan Meier survival analysis, Log Rank P<0.0005. CsA, Cyclosporine A; IFX, infliximab."

Independent predictors for colectomy were male sex (p=0.022; HR=1.89), younger age (p=0.036; HR 0.98) and endoscopic disease severity (p=0.001; HR 2.59).

Conclusions: IFX treatment is associated with lower colectomy rates compared to CsA in patients with moderate to severe UC.

DOP053
Risk factors of pouchitis after ileal pouch-anal anastomosis in ulcerative colitis: Multivariate analysis

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Background: The standard surgical procedure for ulcerative colitis (UC) has been restorative total proctocolectomy and ileal pouch anal anastomosis (IPAA). Despite the dramatic improvements in medical treatment for UC, a certain portion of patients with UC still requires IPAA. One of the troublesome complications after IPAA is pouchitis. However, the incidence of pouchitis has not been fully elucidated in Asian countries. In the present study, we retrospectively investigated UC patients who underwent IPAA, and elucidate the incidence of pouchitis.

Methods: We retrospectively reviewed 102 patients with UC who underwent IPAA in our institute. Out of 102, 92 patients who received pouch endoscopy after IPAA were included in the analysis. The incidence of pouchitis was calculated by Kaplan Meier curve, and the risk factors for the development of pouchitis were evaluated with cox regression hazard model. Gender, age at disease onset, extent of colitis, indication for IPAA, age at operation, disease duration, the presence or absence of preoperative extra-intestinal manifestations (EIMs), history of smoking, family history of inflammatory bowel disease and postoperative nonsteroidal anti-inflammatory drug (NSAID) use were included as variables for the analyses. The diagnosis of pouchitis was made according to modified pouchitis disease activity index.

Results: A total of 563 pouch endoscopy sessions were conducted for 92 patients. 23 patients (25%) developed pouchitis in our series. The cumulative one, five and ten year pouchitis free survival was 95.4%, 87.4% and 72.0 %, respectively.

Both univariate and multivariate analyses revealed that the presence of preoperative EIMs was a significant risk factor for the development of pouchitis (p=0.02, HR 3.52, 95% CI 1.23-9.65). The cumulative five year pouchitis free survival was

Table 2: Cox regression model. All significant factors with P<0.05 were combined in a multivariate model, as well as steroid use since this factor was significantly different between treatment groups.

Cox regression model	univariate		multivariate	
	HR (C.I.)	P	HR (C.I)	P
Therapy: cyclosporin	2.61 (1.58–4.31)	0.001	1.84 (0.92–3.67)	0.084
Gender: male	1.69 (1.02–2.82)	0.043	1.89 (1.09–3.24)	0.022
Age: years	0.98 (0.96–0.99)	0.015	0.98 (0.96–0.99)	0.036
Follow-up: months	1.01 (1.00–1.01)	0.003	1.01 (0.99–1.01)	0.135
Mayo score: Mayo3	2.46 (1.49–4.09)	<0.001	2.59 (1.51–4.44)	0.001
Disease duration: months	0.99 (0.99-0.99)	0.019	1.00 (0.99–1.00)	0.272
Concomitant treatment: steroids	1.29 (0.79–2.11)	0.31	0.74 (0.43–1.29)	0.285
Disease extend: E3	1.00 (0.99–1.00)	0.45		

90.4% in those without EIMs and 72.9% in those with EIMs, respectively.

Conclusions: The presence of preoperative EIMs is a significant risk factor for the development of pouchitis in Japanese patients with UC who underwent IPAA.

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Digital Oral Presentations

DOP Session 7 – Disease & therapy outcome

DOP054

DOP054 has been converted to a hard copy poster presentation upon author's request – please refer to p. 222 (P289a)

DOP055

Combination therapy with infliximab and azathioprine improves Crohn's disease outcome and infliximab tolerance compared to infliximab therapy alone

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Background: Combination therapy with infliximab (IFX) and azathioprine (AZA) is more effective than IFX alone to induce clinical remission in patients with Crohn's disease (CD). However, the effect of this combination therapy in clinical practice on the long-term outcome of CD is still unknown. The aim of our study was to evaluate the impact of combination therapy with IFX and AZA on CD patient outcome in a tertiary center.
Methods: CD patients receiving IFX alone or in combination with AZA as maintenance therapy between 2007 and 2010 in our center were retrospectively included. Clinical and radiologic activities, mucosal healing (MH), hospitalizations, major abdominal surgeries, treatment modifications and withdrawal of IFX were recorded during the follow-up. MH, defined as the absence of any ulceration, was assessed at the first endoscopy performed after the introduction of IFX within a mean delay of 24 ± 16 months. Clinical activity was rated by the referring physician judgment as remission, moderate, or severe disease. Radiologic activity was defined by the presence of radiologic signs of inflammation described in the report of CT scan or MRI.
Results: IFX as maintenance therapy was given to 153 patients between 2007 and 2010 for a mean duration follow-up of 44 ± 22 months. Among those 153 patients, 76 (50%) received IFX alone and 62 (40%) combination therapy with AZA (the 15 remaining patients received IFX with methotrexate or corticosteroids and were not included in the analysis). Demographic and clinical characteristics between patients receiving IFX alone or in combination with AZA were similar. Three to 6 months after IFX introduction, patients with combination therapy had less severe disease and more remission compared to patients with IFX alone (0% and 73% vs. 9% and 59%, p=0.023). After 6 months, patients with combination therapy had also less radiologic signs of inflammation (37%, n=10/27 vs. 66%, n=29/44, p=0.018). Patients with combination therapy presented more MH (75%, 24/32 vs. 48%, n=20/42, p=0.017) and had fewer hospitalizations and major abdominal surgeries compared to those with IFX alone (13% vs. 25%, p=0.075 and 1% vs. 12%, p=0.021). Modifications and withdrawal of IFX were similar in the two groups although patients with combination therapy presented fewer IFX withdrawal for allergy (0%, n=0/16 vs. 38%, n=9/24, p=0.006).
Conclusions: Combination therapy improved long-term outcome in CD patients and decreased withdrawal of IFX for allergy compared to IFX therapy alone. This study highlights the utility of combination therapy with IFX and AZA for the treatment of CD patients in clinical practice.

DOP056

Long-term outcomes of top-down versus step-up treatment in newly diagnosed Crohn's disease: final data

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Background: Early combined immunosuppression ('top-down' (TD)) is more effective than conventional management ('step-up' (SU)) for induction of remission and reduction of steroid use in patients with recently diagnosed with Crohn's disease (CD). However, it remains unknown whether short-term benefits are sustained long-term and if the natural history of CD can be altered. Therefore, we aimed to investigate the long-term effects of TD (induction IFX and maintenance azathioprine (AZA)) vs. conventional SU treatment in CD.
Methods: Long-term follow-up data was retrospectively collected from patients who participated in a randomized controlled trial evaluating TD vs. SU in patients with newly diagnosed CD[1]. For 16 semesters following the original 2-year trial, the following data was abstracted from patients' medical records: clinical disease activity by global assessment, flares, medication use, CD-related hospitalization, surgery and the occurrence of new fistulas. Colonoscopy reports were scored as one of the following: Normal (0), aphthous ulcers (1), small ulcers (2) or large/deep ulcers (3).
Comparisons were done by intention-to-treat analysis. Time to event data was evaluated using the Kaplan-Meier and log-rank test. Proportions were compared using Fisher's exact test.

Results: 119 patients (SU n=60) were included in the analysis. At the start of follow-up, 81.8% (60.0% AZA, 21.8% methotrexate) vs. 66.0% (50.9% AZA, 11.3% methotrexate) of patients used an immunomodulator, and 20.0% vs. 15.1% received IFX in TD and SU, respectively. The number of semesters in clinical remission did not differ between TD and SU (67.3% vs. 68.0%; p=0.82). However, patients in the TD group had fewer semesters with a flare (13.3% vs. 19.9%; p<0.01), and longer flare-free survival (median 9 vs. 5 semesters; p=0.02). Mean time to first hospitalization was 13.9 vs. 12.6 semesters (p=0.23), mean time to first new fistula was 15.1 vs. 14.3 semesters (p=0.21) and mean time to CD-related surgery was 15.1 vs. 14.2; p=0.25) for TD and SU, respectively. A total of 164 endoscopy reports of 78 patients (SU n=39) were scored. 20.5% of TD and 38.5% of SU patients had at least one endoscopy with large ulcers (p=0.14). 64.1% of TD and 56.4% of SU patients had at least one endoscopy with no ulceration (p=0.64).

Conclusions: Top-down treatment resulted in a reduction of flares and a longer flare-free survival compared to step-up treatment in newly diagnosed CD. These results may advocate the use of TD treatment algorithms. However, TD treatment did not result in differences in rates of remission, surgery, hospitalization or endoscopic disease activity, although a trend towards a better endoscopic outcome in the TD group was observed.

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DOP057
Evolution of the Lémann Index (LI) during the course of Crohn's disease (CD)

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Background: Stricturing or penetrating lesions develop over time in most patients with CD leading eventually to surgical resection. The Lémann Index (LI) measures the digestive damage (DD). The aim of this study was to describe the evolution of LI in an incipient cohort of CD patients and to search for predictors of DD.

Methods: We studied 221 patients (114 M, 107 F, median age 24 yr [19-33]) diagnosed with CD between 2004 and 2011, followed up prospectively in our center, and who had 2 or 3 serial determinations of LI. Abdominal CT scan (n=204), abdominal MRI (n=332), and pelvic MRI (n=56) were re-read by a couple gastroenterologist and radiologist. LI was then calculated taking into account clinical and endoscopic data and radiological re-assessment. The cut-off of LI >2.0, corresponding to the 75th percentile value of pre-operative LI in patients led to surgery, was assigned to identify patients with a substantial DD. In addition we analysed intervals between 2 evaluations. Factors associated with DD and progression of LI during one interval were searched for using univariate analyis and logistic regression.

Results: Median LI (IQR) was 2.3 (1.2-3.9) at first evaluation, 3.9 (1.6-9.8) 2-5 yr after diagnosis, and 8.3 (1-12.3) at 5-10 yr. LI increased significantly (p< 0.0001) at 2-5 yr and 5-10 yr compared to its initial value and from 2-5 yr to 5-10 yr. Last value of LI after 73 months (51-96) was >2.0 in 138 patients (63%). These patients did not differ from those without DD regarding demographic data and characteristics of CD collected at diagnosis, however their earliest LI was significantly increased. During follow-up 90 patients eventually required intestinal resection. Among 313 intervals between 2 evaluations, LI increased during 161 intervals (51%), remained unchanged during 59 intervals (19%), and decreased during 93 intervals (30%). In addition to intestinal resection, the percentage of time with clinically active disease was associated with increase of LI (p<0.001). Elevated CRP and treatment with immunomodulators or anti-TNF had no significant effect. However the increase of LI was mild in the 57 patients who received anti-TNF more than 80% of time (from 3.5 [1.6-7.2] to 4.1 [0.6-10.3]) and significantly reduced compared to those not on anti-TNF (n=204: from 2.9 [1.2-8.3] to 4.8 [1.0-10.8]) (p<0.01).

Conclusions: DD measured by LI increases significantly during the first years following diagnosis of CD. More than half the patients experience a substantial DD after 2-10 yr. Factors associated with DD are elevated LI at first evaluation, then duration of clinical activity and intestinal resection. These results underline the importance of achieving prolonged clinical remission for preventing DD.

DOP058
Long-term outcome of infliximab treatment in patients with Crohn's disease: a hospital-based cohort study from Korea

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Background: Until now, no large-scale studies have evaluated the long-term outcome of infliximab (IFX) in non-Caucasian patients with Crohn's disease (CD). The aim of this observational study was to assess the long-term outcome of IFX in patients with CD from a Korean single center.

Methods: We retrospectively analyzed 545 Korean CD patients who received scheduled IFX treatment at the Asan Medical Center. The primary analysis looked at the proportion of patients with clinical response at the end of follow-up. The definition of clinical response was maintaining IFX treatment without major abdominal surgery and dose intensification.

Results: Between February 2002 and November 2014, a total of 10,079 IFX infusions were administered to 545 consecutive patients with CD over a median of 31 months (interquartile range 14-54). At the end of follow-up, 296 of the 545 patients (54.3%) were still receiving IFX without major abdominal surgery and dose intensification. Sixty-seven patients (12.3%) underwent major abdominal surgery during the course of IFX treatment and an increase of IFX dose to 10 mg/kg became necessary in 75 patients (13.8%). IFX treatment was stopped in 107 patients (19.6%) because of loss of response (48 patients, 8.8%), side effects (29 patients, 5.3%), and patient's preference or problems with reimbursement (30 patients, 5.5%). The cumulative survival of maintaining IFX treatment without major abdominal surgery and dose intensification was 88.9% at 1 year, 75.9% at 2 years, 67.8% at 3 years and 48.1% at 5 years. Multivariate regression analysis identified that the younger age at diagnosis (< 40 years,

p = 0.007) and the short disease duration (< 3 years, p = 0.027) as independent positive predictors of a better response to IFX treatment.
Conclusions: In this large real-life cohort of Korean patients with CD, the long-term efficacy of IFX seems to be similar to that of previously published Western reports. The younger age at diagnosis and the short disease duration are predictors of a better response to IFX treatment.
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Potential competing interests: Suk-Kyun Yang has received a research grant from Janssen Korea Ltd., but this grant is not related to the topic of the current study. The remaining authors also have no competing interests.

DOP059
Clinical predictive parameters for severe Crohn's disease in real-life: Results from EPIC, a nation-wide prospective observational study

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Background: The clinical course of Crohn's disease (CD) is highly variable and requires a personalised therapeutic approach according to individual risks. Recognising a subgroup of CD patients at risk of severe disease and the need for early intervention necessitating immunosuppression (IS) is important.
The EPIC study (Early Predictive parameters of Immunosuppressive therapy in Crohn's disease) in Germany intends to identify individual clinical parameters in recently diagnosed CD patients predicted to have a severe disease course.
Methods: EPIC is an ongoing prospective, real-life, observational multicentre study in patients with a recent diagnosis of CD (≤ 6 months). Enrolled patients were naïve to conventional IS (thiopurines, methotrexate, calcineurin inhibitors), anti-TNF agents (adalimumab, infliximab, golimumab) and vedolizumab. Patient and disease characteristics at baseline (BL) were documented and correlated with the progression to a severe disease course within 2 years from BL. Group 1 comprises patients necessitating IS/anti-TNF therapy or being hospitalised, while Group 2 comprises patients without disease progression as defined by these characteristics. Univariate influence of different prognostic factors (younger age, anaemia, arthritis, glucocorticoids) was analysed in 303 patients using logistic regression analysis. To identify independent predictors, a multivariate regression analysis was performed.
Results: To date, 151 patients in Group 1 (49.8%; mean duration from BL, 6.6 months) were compared to 152 patients in Group 2 (50.2%). In Group 2, 39 patients (25.7%) completed the study after 2 years, while 113 (74.3%) patients in Group 2 are still observed. At BL, 57.1% of patients in Group 1 and 37.2% of patients in Group 2 received glucocorticoids (P=0.001). A significantly higher occurrence of anaemia (P<0.001) and elevated CRP (P=0.008) were detected at BL in patients with subsequent severe disease (Group 1) compared with patients without severe disease (Group 2). Among extraintestinal manifestations, only the presence of arthritis was significantly different between groups (Group 1: 11.3% vs Group 2: 3.3%; P=0.01). The prognostic factors predictive of severe disease are reported after multivariate analysis (Table; n=274).
Conclusions: This analysis of the EPIC study shows that younger age, anaemia, arthritis and the need for glucocorticoid therapy at BL were identified as independent clinical parameters in early CD patients predicting severe disease in a real-life observational setting.

Risk Factor	Odds Ratio	95%CI	P Value
Younger age	1.03	1.00–1.05	0.018
Anaemia	2.42	1.40–4.19	0.002
Arthritis	3.53	1.17–10.7	0.026
Glucocorticoids	1.83	1.10–3.03	0.020

DOP060
Long-term outcome of IBD patients with primary non-response to anti-TNF therapy

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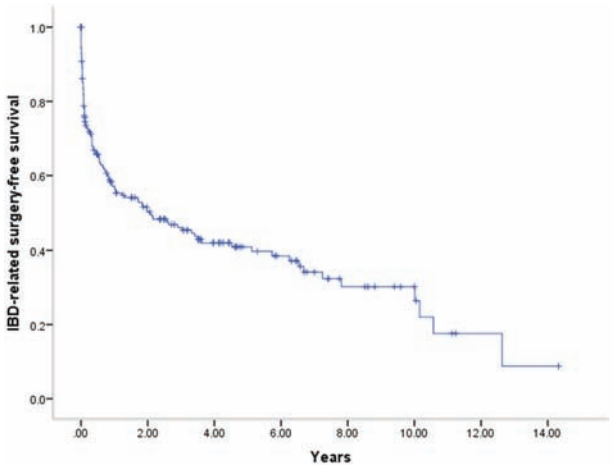
Background: Primary non-response (PNR) to tumour necrosis factor (TNF) antagonists occurs in 10-30% of inflammatory bowel disease (IBD) patients depending on the definitions used. Long-term outcome of these patients is unknown. Therefore, we studied the long-term outcome of IBD patients with PNR to anti-TNF therapy and searched for predictors of IBD-related surgery in these patients.
Methods: This was a retrospective, multi-center study including all PNR patients from three European referral centers. PNR to anti-TNF therapy was defined as a lack of improvement after the induction phase of objectively assessed signs of active inflammation at baseline. PNR was defined on clinical (physician global assessment), biological (CRP>5mg/mL) and/or endoscopic (no endoscopic improvement) criteria. Clinical benefit for patients who continued on medical biological therapy after PNR was defined as clinical remission without the need for drug discontinuation for loss of response or adverse event.
Results: A total of 198 IBD patients were identified [Crohn's disease (CD, n=75) ulcerative colitis (UC, n=123)]. PNR was either following infliximab (n=140) or adalimumab (n=58). After a median follow-up of 3.1 (IQR 1-5.8) years, 37 patients (18.7%) switched to another anti-TNF agent, 30 (15.2%) changed to a non-TNF biological agent (70% to vedolizumab), and 10 (5.1%) patients had both strategies. At last follow-up, 114 (58%) patients underwent IBD-related surgery (Figure). Univariate (Log-Rank) analysis identified several factors which were associated with surgery (Table). Multiple COX regression analysis retained only acute severe UC [p=0.001, HR: 5.4 (95%CI: 2-15)] and low albumin at baseline [p=0.05, HR: 2.6 (95%CI: 1-6.5)] as independent predictors of surgery. There was no significant difference in clinical benefit between patients who switched to another anti-TNF agent and those who switched to another dug class (31 vs 40%, p=

Associated factors *(cut-off derived from ROC analysis)	HR	95% CI	p (Log-Rank)
Age at diagnosis < 22 years*	1.6	1.1–2.4	0.017
Age at start of anti-TNF therapy < 32 years*	1.7	1.1–2.4	0.007
Disease duration from diagnosis to start of anti-TNF therapy < 3 years*	2	1.4–3	< 0.001
Albumin at baseline < 40 g/L*	3.3	1.8–6	< 0.001
CRP at baseline > 5 mg/L*	3.2	1.6–6.5	< 0.001
Acute severe colitis for patients with UC	3	1.8–5.3	< 0.001
Active smoking at start of anti-TNF therapy	1.7	0.9–2.8	0.053



0.657). Vedolizumab initiation was associated with reduced need for surgery in IBD patients compared to those who switched to another anti-TNF agent [12/19 (63%) and 16/37 (43%), respectively, p=0.259].

Conclusions: Our results indicate that about half of IBD patients with PNR to anti-TNF will undergo surgery. Switching to another drug class such as vedolizumab may be more effective than switching to another anti-TNF agent in these patients.

DOP061
Prospective,Observational Study of the Therapeutic Management of Mild to Moderate Ulcerative Colitis (Observatoire Prospectif, longiTudinal dans la prise en charge de la rectocolite héMorragiqUe légère à Modérée, OPTIMUM): follow-up at 2 years

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Background: The OPTIMUM observational study was set up in France in 2011. The purpose of this study is to describe the progression and Methods of therapeutic management of mild to moderate ulcerative colitis (UC) and to assess remission rate and duration as well as the predictive factors for relapse.

Methods: This observational study included patients aged 18 years and above experiencing a mild to moderate UC flare-up. The patient's data were recorded in an electronic CRF during consultations conducted as part of regular monitoring. At each visit, a questionnaire regarding treatment compliance was completed by the patient (the Modified Morisky Adherence Scale: MMAS-8) and the activity was assessed by ulcerative colitis clinical score (UCCS). From June 2011 to June 2012, 812 patients (51% female, average age of 45 ± 15 years) were included in the observational study by 130 gastroenterologists.

A follow-up period of three years is planned. A descriptive analysis of the data at two years is presented here. It was agreed that an annual visit would be defined by an interval of ± 100 days.

Results: In August 2014, the one-year and the two-year visit data were available for 559 (69%) and 393 (48%) of the patients, respectively. Ninety patients (11%) stopped the study prematurely; this was primarily due to a colectomy for 10 patients, a change in diagnosis for 4 patients, 1 death related to malignant thymoma and 28 cases lost to follow-up. According to the UCCS, 437 patients (78%) were in remission (score of 0 to 2) during the first year and 317 (81%) at two years. UC treatment was on-going in 474 patients (85%) at 1 year and in 327 patients (83%) at 2 years (Table 1).

Conclusions: After two year follow-up of the OPTIMUM cohort, oral 5-ASAs remain the most commonly prescribed treatment. The relapse rate was around 30% each year and about 80% of patients were in remission at 1 and 2 years. Poor compliance was associated with a higher risk of relapse

DOP062
Environmental risk factors in pediatric IBD according to the hygiene hypothesis: A case-control study

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Table 1: UC treatment at each Visit

TREATMENTS	5-ASA	Corticosteroïd	Immunosuppressant	Anti TNF ***
1 year n(%)	359 (76)	86 (18)	81 (17)	21 (4)
2 years n(%)	253 (77)	46 (14)	59 (18)	20 (6)

Background: Inflammatory Bowel diseases (IBD) are chronic, relapsing, intestinal disorders whose pathogenesis is still unknown, being the result of multifactorial agents contribution. Even if the importance of genetic predisposition has been strongly demonstrated, the primary role of environmental influence on IBD onset has been recently stressed. We investigated the impact of the emerging "Hygiene Hypothesis" (HH) in a cohort of pediatric IBD patients, in order to find a correlation between the exposure to specific environmental factors and the risk to develop both Crohn's disease (CD) and Ulcerative Colitis (UC).
Methods: A total of 698 subjects aged between 1 and 18 years, were enrolled between January and June 2014. Among these 264 were IBD patients, 230 were IBD healthy siblings and 204 were age- and sex- matched healthy controls (HC). All patients underwent a multiitem questionnaire including five different groups of potential environmental IBD risk factors: family history of IBD, perinatal period, home amenities and domestic hygiene, childhood diseases and vaccinations, infant and child diet.
Results: A positive family history of IBD was one of the strongest risk factor for developing both CD and UC (p<0.001). A lower gestational age was found to be more frequent in controls than in IBD (p=0.006), whereas a less frequent recurrence of hospitalization during the first month of life was more frequent in IBD (p=0.017), confirming that exposure to infections early in life could be protective towards IBD onset. According to the hygiene hypothesis, protective associations were found for an higher number of siblings (p<0.001), bed sharing (p=0.005), pet owing (p<0.001), and a positive family history for intestinal parasitosis (p< 0.001) and H.Pylori infection (p=0.003). Instead smoke family habit was more frequently found in CD group (p=0.08) but not in UC. Breastfeeding, with a duration > of 3 months was a risk factor for IBD (p=0.001) as well as gluten introduction in child's diet before the 6 th month of age (p<0.001), both recurring more frequently in IBD than in healthy controls. In contrast, the adherence to Mediterranean diet (p<0.001) was considered protective being less followed by IBD patients compared to controls. The MMAS-8 questionnaire was completed by 370 patients (78%) and 213 patients (65%) at one year and two years, respectively. Compliance was good (score = 8) in 104 patients (28%) at one year and 83 patients (39%) at two years. At least one relapse of UC over the year was reported in 183 patients (33%) at one year and in 119 patients (30%) at two years. Patients with poor compliance have an increased risk of recurrence OR 1.8 (95% IC [1.23-2.62]). Colorectal cancer or dysplasia was reported in three patients. At least one adverse event was reported in 20 patients (3%) and 4 were recorded as serious AEs
Conclusions: Our work confirms that environmental factors are closely linked to IBD onset and that HH can partly explain the rise of IBD in developed countries. However, prospective studies are necessary to validate these Results, in order to offer both a better disease care for patients, already suffering from IBD, and possible interventions for IBD prevention in genetically predisposed individuals.

DOP063
What is stricturing Crohn's Disease: Comparison of clinical outcome between radiological and endoscopic stricture?

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Background: Stricturing Crohn's disease (CD) was defined according to Montreal Classification as "occurrence of constant luminal narrowing with prestenotic dilatation or obstructive signs/symptoms without presence of penetrating disease." However, the definition of the 'stricture' is not uniformly across studies including radiological and endoscpic stricutre. The aim of our study was to compare the clinical outcome between radiological and endoscopic stricture in patients with CD.
Methods: This was a retrospective study. All conseuctive established CD patients with endoscopic strictures (defined as persistent severe luminal narrowing by inability to pass the scope) and radiological stricutres (defined as lumen narrowing with proximal lumen dilation on CT enterography) between 2004 and 2012 were enrolled. The primary outcome was surgery. Cox regression analysis was used to evaluate risk factors associated with surgery.
Results: Between 2004 and 2012, 86 CD patients with endoscopic stricture and 48 patients with radiological stricture enrolled the final analysis. More patients with radiological stricture had bowel obstruction symptoms (77.1%, 37/48) than those with endoscopic stricture (45.3%, 39/86) (p=0.001). Significant correlation existed between radiological stricture and bowel obstruction symptoms (r=0.565, P=0.001), whereas there was no correlation between endoscopic stricture and obstruction symptoms (r=0.228, P=0.120). During follow-up, more patients with radiological stricture (58.3%, 28/48) underwent stricutre-related surgery than those with endoscopic stricture(38.4%, 33/86)(P=0.001) . Cox regression analysis showed that CD patients with radiological stricture carried high risk of subsequent surgery than those with endoscopic stricture (P=0.001).
Conclusions: Clinical outcome was different between radiological and endoscopic stricture in patients with CD. Radiological stricture correlated more significantly with bowel obstruction symptoms and subsequent surgery than endoscopic stricture. Stricturing Crohn's disease (CD) defined according to Montreal Classification should be more specified and uniform in future.

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Digital Oral Presentations

DOP Session 8 – Predicting remission & relapse

DOP064
Predictors of disease relapse of patients with Crohn's disease in Deep Remission: Who and when can withdraw thiopurine maintenance therapy?

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Background: Few data are available on the disease course after cessation of thiopurine (TP) therapy for Crohn's disease (CD) with deep remission (DR). aimed to evaluate clinical outcomes and factors associated with relapse in CD patients with DR.

Methods: 109 CD patients in DR (clinical and endoscopic remission) who withdrawal TP were included. Prognostic factors of relapse were investigated through a proportional hazards model.

Results: After a median follow- period of 46 months (interquartile range, 27.5-67.6 months), 50(45.87%) patients had endoscopic relapse and 41 (37.61%) patients had clinical flare, 18(16.51%) patients underwent surgery, and 25(22.94%) patients received hospitalization. The cumulative probabilities of disease flare (P=0.48), endoscopic recurrence (P=0.67), CD- related bowel surgery (P=0.62), and hospitalization (P=0.72) at 5 years did not differ between patients maintaining TP and who withdrew TP.

Independent risk factors predictive of flare were prior bowel complication (HR, 1.74; 95%CI 1.02-2.96), perianal disease at CD diagnosis (HR, 2.24; 95%CI,1.06-4.72) and a CRP > 3mg/L (HR 4.05, 95% CI 1.98-8.27) by multivariate analysis. A scoring system based on age, CRP, disease duration and presence of bowel complications was developed to predict the outcome in CD patients with DR. In selective CD patients without defined risk factors, up to 70% remained in clinical remission during the 60-month follow- after the cessation of TP therapy. Importantly, 78% of these patients sustained endoscopic remission, 93.3% were free of bowel surgery.

Conclusions: Long-term outcomes of CD patients with DR did not differ between maintaining TP and TP cessation group. Therapy de-escalation maybe reasonably considered in selective patients.

DOP065
The predictive factor for relapse of ulcerative colitis in patients with endoscopic mucosal healing

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Background: Endoscopic mucosal healing has been proposed as the therapeutic goal in the treatment of patients with ulcerative colitis (UC). Despite achieving endoscopic mucosal healing, however, relapse of UC was occurred. Therefore, to validate risk factors of UC relapse is useful for therapeutic strategy in maintenance of remission and mucosal healing. The aim of this study is to evaluate the predictive factor for relapse of UC in patients with endoscopic mucosal healing.

Methods: From April 2010 to October 2014, 287 patients with UC who had been treated at Kitano hospital were analyzed, retrospectively. Clinical and endoscopic activities were evaluated with Lighter index and Mayo score, respectively. Endoscopic mucosal healing was defined as Mayo score of less than one. The relapse of UC was defined as any recurrence of symptoms of UC. Cumulative relapse rate after achieving mucosal healing was evaluated and we analyzed the difference of patient's characteristics between relapse group and non-relapse group.

Results: Of 287 UC patients, total 83 patients (28.9%) could achieve endoscopic mucosal healing. In 19 of 83 patients with endoscopic mucosal healing (22.9%), the relapse of UC was found. The median time at relapse of UC was 1.2 years after achieving mucosal healing. Based on Kaplan-Meier analysis, the cumulative relapse rate at 1, 3 and 5 years after achieving mucosal healing were 13.8%, 33.2% and 41.5%, respectively. The cumulative relapse rate of Mayo-1 group tends to be high compared to that of Mayo-0 group (27.4% (Mayo-0) and 50.0% (Mayo-1) at 5 years, respectively), although there was no significant difference of cumulative relapse rate between Mayo-0 and Mayo-1 group. Moreover, there was no significant difference of patient's characteristics, such as age at diagnosis, duration of disease, extent of disease and medical history, between relapse and non-relapse group.

Conclusions: Our data suggest that Mayo-1 might be a predictive factor for relapse of UC in patients with endoscopic mucosal healing. Therefore, we should definitely differentiate Mayo-0 from Mayo-1 for assessment of the endoscopic mucosal healing in the future clinical trial.

DOP066
Impaired mucosal permeability underlies ongoing irritable bowel syndrome-like symptoms, in patients with inflammatory bowel disease who have achieved mucosal healing

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Background: Patients with inflammatory bowel disease (IBD) with mucosal healing (MH) who continue to have ongoing symptoms, may be suffering from possible irritable bowel syndrome overlap. Impairments in small intestinal permeability have been demonstrated by confocal laser endomicroscopy (CLE) in patients with IBD and IBS, but the exact cause of ongoing symptoms with healed mucosa is unknown. This study examines small intestinal permeability via CLE (EC-3870FK, Pentax) in IBD patients who have complete mucosal healing.

Methods: Patients with IBD were prospectively recruited from Bankstown-Lidcombe Hospital for CLE. Images were obtained with fluorescein sodium as an intravenous contrast from the terminal ileum. Only patients with MH were included for analysis, defined in Crohn's Disease (CD) as no endoscopic disease and in Ulcerative colitis (UC) as endoscopic Mayo score of 0 or 1. All patients had histology to demonstrate no active disease. Blinded post procedure interpretation of images were performed with previously demonstrated CLE features of fluorescein leak, cell junction enhancement and cell drop out. Calculation of a confocal leak score (CLS), allowed quantification of the degree of small intestinal permeability. Patients were assessed to be symptomatic in CD based on their Crohn's Disease Activity Index >150 and in UC with a partial mayo >2. Symptoms of diarrhoeal motions/day and abdominal pain were collected. 20 healthy controls also underwent CLE for assessment of normal range.

Results: 80 consecutive IBD CLE cases were performed, of whom 42 had MH (62% F, 22 CD, 20 UC). 34 cases were asymptomatic and 8 symptomatic. There were no differences in baseline characteristics of median images/case, age, disease duration, C-reactive protein, erythrocyte sedimentary rate, smoking status, and non-steroidal anti-inflammatory use in the two groups (p>0.05). Median CLS for asymptomatic IBD and symptomatic IBD were 7.9 and 19.0 respectively (p=0.001). Median CLS in controls was 5.94. CLS in asymptomatic and symptomatic groups were 8.4 and 17.7 respectively in CD (p=0.019), and 6.8 and 22.3 respectively in UC (p=0.039). Within the IBD cohort, diarrhoea correlated with symptoms (r=0.75, p=< 0.001) and CLS (r=0.43, p=0.004) but abdominal pain did not correlate to either (p >0.05). On linear regression correcting for medication use, each increase of one diarrhoeal motion/day correlated with an increase in CLS of 2.14 (p=0.005). This translates to an increase of 1 diarrhoeal motion/day for each 11 point increase in CLS (B coefficient=0.089, p=0.004).

Conclusions: Increased permeability may be responsible for ongoing symptoms in IBD patients who have achieved mucosal healing, and in symptomatic patients was best explained by the symptom of diarrhea.

DOP067
Faecal calprotectin measurements by IBD patients themselves at home are feasible and provide reliable Results compared to the standard lab method.

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Background: Faecal calprotectin (FC) is a reliable biomarker for assessing disease activity in IBD patients. Current detection Methods, however, are time-consuming and patients wait up until 14 days for the result, limiting the use in clinical decision making. CalproSmart ™ is a test for FC performed by the patients themselves in their own home with a result in minutes. The aim of this study was to compare CalproSmart in the hands of patients with the gold standard; enzyme-linked immunosorbent assay (ELISA) in the lab.

Methods: As part of an eHealth trial, consecutive patients in remission or with mild-moderate active disease measured their FC levels monthly using CalproSmart. From the same stool, patients also send in a sample to the lab where ELISA is used for detection of FC CalproSmart consists of an extraction container with prefilled extraction buffer and a dosing tip and a lateral flow cassette containing antibodies against calprotectin at a control line and a test line. Using a designated smartphone app, the patient takes a picture and the ratio between the staining intensity of the two lines is calculated. The procedure takes about 25 minutes.

Correlation between ELISA and CalproSmart was calculated as well as sensitivity, specificity, negative and positive predictive values (NPV, PPV) with a pre-defined cut-off of 200 mg/kg FC as per protocol of the eHealth trial. We assessed the sample-to-sample and the sample-within-sample reproducibility of the CalproSmart test.

Results: In total 221 patients were included into the study (115 UC, 106 CD, median age 49, range 20-85 years, 60 % females). 894 faecal samples were analysed by ELISA, while 638 tests were performed at home by patients using CalproSmart. In total 1078 FC Results were eligible for Spearman's rank correlation analysis, resulting in rho = 0.685, p < 0.0001).

The coefficient of variability for the within-sample reproducibility of CalproSmart was 4.42% (mean±SD:276 ± 13, range 110-600 µg/g). The coefficient of variability for the sample-to-sample reproducibility was 10.90% (mean±SD: 292 ± 34 µg/g, range 0-600 µg/g). With a cut-off of FC at 200 µg/g to predict relapse, the sensitivity, specificity, NPP and PPV were 0.88, 0.76, 0.53 and 0.96 respectively.

Conclusions: For the first time, patients themselves are able to measure their FC levels with immediate response. CalproSmart shows strong positive relationship with the gold standard. The coefficients of variability are acceptably low and with a cut-off at 200 µg/g, the sensitivity and PPV are high. The tool allows for fast and reliable assessment of gut inflammation by the patient themselves, thereby constituting a valuable addition to clinical decision making by physicians and patients.

DOP068

DOP068 has been converted to a hard copy poster presentation upon author's request – please refer to p. S237 (P319a)

DOP069
A retrospective non-interventional European database analysis assessing adherence and persistence of mild to moderate IBD treatments

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"UC Symptoms.Prevalence and Impact on QoL"

UC SYMPTOMS	Patients suffering the previous year (%)	Most disturbing symptoms for patients (%)*
Diarrhea	60%	72%
Abdominal pain and/or stinging	48%	47%
Flatulencies (gases)	55%	44%
Rectal Bleeding	57%	57%
Urgency of defecation	60%	74%
Incontinence	25%	32%
Joint pain (wrists, feet, knees etc)	39%	34%
Fatigue or tiredness	53%	52%
I haven't had any of these symptoms during the last year	9%	-

*Each patient was requested to mark the two most disturbing symptoms

Background: The PODIUM study (Dignass2009) and MOTUS study (Flourié,B.2011) proved the benefit of once daily (qd) mesalazine dosing vs twice daily (bd) dosing. Yet, the effect of real world dosing regimens on adherence and persistence is vital to ensure the most efficient regime is reached for patient and payer; reducing costs, hospitalisations and disease flares (Kane SV 2006). A multi country study was conducted to establish whether or not patients taking high strength mesalazines with a low posology show better adherence and persistence than patients taking lower strength mesalazines with a high posology burden. Also, whether or not a connection exists between these cohorts regarding IBD flare symptoms.

Methods: A retrospective non-interventional database analysis across France and the UK; from May 2011 to May 2014 was conducted. Patients were studied as a whole group for adherence (medication possession ratio - MPR) and persistence in line with the distinct strength sets below:

A: Low strength:<=(less than or equal to) 500mg

B: Medium strength:<=1g

C: Medium (High) strength:< =1.5g

D: High strength: > (greater than)1.5g

For this study IBD flare is defined as:

An increase in average dose per day of oral mesalazines by 50% or more (mg/day)

OR Co-prescribing of a steroid or topical/enema mesalazine

Case control study (rates of IBD flare):

Patients in all four cohorts were naïve for all oral mesalazine drugs in the previous 6 months to the index date; they were 'stable' on treatment for at least 6 months. IBD flares were measured within the next 6 months.

Results: The joint dataset yields n=32,607. Sex distribution is equal (females=0.50, males=0.50). Mean age was 54.8 (SD 18.1; range 18 - 103).

Daily intake of a single mesalazine dose has a direct link with better adherence over regimens greater than 2 per day (single dose mesalazine mean adherence =0.86). Patients taking one mesalazine to reach a daily dose of 2g (2000mg) display mean adherence of 0.88 (88%), patients taking two 1g doses to reach a daily dose of 2g show mean adherence of 0.77 (77%); significantly lower than the single dose cohort.

Intake of one high dose mesalazine leads to better persistence vs multiple lower dose mesalazines. Also, patients taking one mesalazine dose of >1.5g daily show better persistence at 642 days. This result is significant when compared to categories C<=1.5g and B< =1g.

Via a matched patient pair analysis of 2,464. Patients from the >1.5g cohort display much lower levels of IBD flare when compared to patients from the <=1.5g and <=1g cohorts (p=0.015 and p<0.001 respectively).

Conclusions: We conclude that a daily intake of a single unit high dose mesalazine Results in better treatment adherence and persistence, with associated lower levels of disease flare.

DOP070

Perception of the impact of Ulcerative Colitis in the quality of life of patients from Spain - UC-life survey

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Background: Objectives. To describe the burden and impact of ulcerative colitis (UC) symptoms on the quality of life (QoL) as perceived by patients followed in hospital clinics from Spain.

Methods: UC-LIFE was a survey to UC patients. Each of the 39 participating hospital gastroenterologists handed the survey to 15 consecutive UC patients >18 years. Patients completed the survey at home and returned it by post-mail. Patients were asked to report symptoms suffered the previous year, to score which 2 symptoms worsen their quality of life (QoL) and sleep most and to describe the overall impact on life.

Results: 585 patients received the survey and 436 returned it (response rate: 75%). Mean age was 46 years (SD: 13), 53% were men. The median duration of UC was 8 years (IQR: 4-15). Twenty-four percent of patients considered that UC was frequently or always an obstacle for living a normal life, whilst 55% reported this to happen sometimes, and only 21% considered UC was never an obstacle. UC symptoms affected the quality of sleep either always or frequently in 21% of patients, 55% stated that this happened sometimes and 24% never. The most prevalent symptoms during the previous year were diarrhea, urgency and rectal bleeding (reported by ~60% of patients), followed by flatulencies and fatigue (about 55%, table)

When patients were asked to point out which 2 symptoms worsened their QoL, they most frequently mentioned urgency of defecation (74%) diarrhea (72%), rectal bleeding (57%) and fatigue (52%) (table)

Conclusions: UC patients reported to have their QoL and quality of sleep frequently affected by UC symptoms, and considered urgency of defecation and diarrhea as the most disturbing symptoms. All patients came from hospital clinics and the sample was non-randomized; thus the Results must be interpreted in this context.

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DOP071

Endoscopic detection of small bowel adenocarcinoma and dysplasia in patients with jejuno-ileal Crohn's disease: prospective study in a cohort of high risk patients (DYDJI Study)

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Background: Endoscopic screening for colorectal dysplasia/adenocarcinoma is recommended in longstanding colonic Crohn's disease (CD). There is also an increased risk of small bowel (SB) adenocarcinoma associated with longstanding small bowel CD. However, benefits of an endoscopic screening for SB adenocarcinoma had never been studied. The aim of our study was to evaluate feasibility and performance of endoscopic detection of SB dysplasia in CD in a cohort of high risk patients.

Methods: A multicenter exploratory open study has been conducted in a prospective cohort of SB CD. Included patients had SB lesions for more than 10 years and a SB cross-sectional imaging within the last 24 months. All included patients have given informed consent. Depending on CD location, SB endoscopy was performed by oral and/or anal route, including chromo-endoscopy with indigo carmine multiple random biopsies (4 every 20 cm segments investigated) and targeted biopsies on suspected lesions (including strictures). Dilation of stricture was only performed in patients with obstructive intestinal symptoms. Procedure was considered as complete if all SB lesions identified were explored and biopsied after chromo-endoscopy. Patients were follow-up one year after inclusion.

Results: From February 2010 to December 2013, 101 patients (39 females, mean age 47.7 ± 13.6 years) have been included in 10 centers. Median CD and SB lesions durations were respectively 19 [range: 13.8-26.9] years and 15.7 years [13-25.4]. Twenty-nine patients had obstructive symptoms at inclusion. Endoscopic route was oral in 7 patients (mean SB investigated: 40 cm), anal in 90 (25.5 cm) and both in 4 (40 cm). Endoscopic procedure was not complete in 41 cases (39%) due to SB stricture (n=31), poor preparation (n=3), technical failure (n=2), other (n=5). No complication was observed. Indeterminate dysplasia was found on SB biopsies (random =1, targeted=1) in two patients: one with a symptomatic stricture has been operated finding a SB undifferentiated carcinoma (T4N0), one had neither dysplasia nor adenocarcinoma at the end of follow-up. During the follow-up period, 6 other patients had surgery for SB symptomatic strictures, finding two additional cases of SB adenocarcinoma (T3N0M0 and T4N0M1, respectively).

Conclusions: In a cohort of 101 CD patients with high risk for SB adenocarcinoma, prevalence of dysplasia or adenocarcinoma was 4%. Endoscopic screening was feasible in 61% of cases and allowed detection of SBA in only 1/3 of cases. SB endoscopy cannot be recommended in this situation. SB resection has to be considered in CD patients harboring longstanding and symptomatic stricture due to the risk of associated adenocarcinoma.

DOP072
Differentiating neoplastic and non neoplastic raised lesions (polyps and pseudopolyps) in long-standing ulcerative colitis: Results from a prospective systematic study using virtual chromoendoscopy with FICE and the Kudo classification.

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Background: The colonic mucosal pit pattern is an aid to the differential diagnosis of colonic polyps in the general population. We analyzed the accuracy of the Kudo classification of pit patterns as evaluated by virtual chromoendoscopy with Fuji Intelligent Color Enhancement (FICE), in the differentiation of neoplastic and non-neoplastic raised lesions in long-standing ulcerative colitis (UC).

Methods: A prospective study was performed on consecutive UC patients with raised colonic lesions found during surveillance colonoscopy. Targeted biopsies of all raised lesions as well as polipectomy of lesions suspected for neoplasia were performed. The Kudo classification of surface pit-patterns (I-II = round/stellar, not suspicious for neoplasia, III-V = tubular/gyrus-like/irregular, suspicious; 0 = unclassifiable) as well as any other endoscopic feature (incl. disease activity) were used to predict the histology by FICE. We determined the accuracy (ACC), sensitivity (SE), specificity (SP), positive (PPV) and negative (NPV) predictive value of FICE in correlating diagnosis with histology.

Table 1:

Surface patterns	Number of lesions (N, %)	Dysplasia (N, %)
0 (unclassifiable)	31 (15%)	0 (0%)
Kudo I alone	98 (48%)	0 (0%)
Kudo II alone	42 (20%)	2 (5%)
Kudo III-l alone	26 (13%)	14 (54%)
Kudo III-s alone	0 (0%)	0
Kudo IV alone	6 (3%)	5 (83%)
Kudo V alone	2 (1%)	2 (100%)
Mixed, Kudo I and II	140 (68%)	2 (1.4%)
Mixed, Kudo III-V	34 (17%)	21 (62%)

Table 2:

Histotype	Pit-pattern					
	0	I	II	III-L	IV	V
Low-grade dysplasia (n=20)	0	0	2 (10%)	14 (70%)	4 (20%)	0
High-grade dysplasia (n=1)	0	0	0	0	1 (100%)	0
Adenocarcinoma (n=2)	0	0	0	0	0	2 (100%)
Hyperplastic polyps (n=18)	0	6 (33%)	10 (56%)	1 (6%)	1 (6%)	0
Inflammatory polyps/pseudopolyps (n=164)	31 (19%)	92 (56%)	30 (18%)	0	11 (7%)	0

Results: A total of 205 lesions (mean size 8, range 2-30 mm) were analysed from 59 patients (mean age 56 years). 23 lesions (11%) were found to be neoplastic (20 low-grade dysplasias, 1 high-grade dysplasia, 2 adenocarcinomas); non neoplastic lesions were hyperplasic (n=18; 9%) or inflammatory polyps/pseudopolyps (n=164; 80%). Tables 1 and 2 show the correlation between surface patterns and histology. 15% of lesions were unclassified according to Kudo. Discordance between Kudo and histology was significantly associated to markers of disease activity, such as Mayo subscore, inflammatory polyps and fibrin cap, as well as to pit-pattern heterogeneity ($p<0.05$ each). The ACC, SE, SP, PPV and NPV of FICE using the conventional Kudo classification were 78%, 91%, 76%, 32% and 99%, respectively. The performance of FICE significantly improved after the addition of specific endoscopic features (such as fibrin cap) as a marker of inflammatory activity in a new, modified Kudo classification (93%, 91%, 93%, 62% and 99%, respectively).

Conclusions: FICE can help to predict the histology of raised lesions in UC and to guide sampling lesions, but artefacts due to concomitant flogosis can decrease its accuracy. New classifications of pit patterns in the setting of IBD are required.

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Digital Oral Presentations

DOP Session 9 – Basic science in IBD

DOP073
Regularities of expression of membrane-associated and cytoplasmic pattern recognition receptors, as well as transcriptional regulation of T-helper cells by lymphocytes in experimental ileitis and conduct of the simvastatin and aril-1

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Background: The pathogenesis of inflammatory bowel disease is complex and multifactorial. Studies have led to the current concept that the T helper cells are components of the adaptive immune response whereas Toll-like receptors, NOD-like-receptors, RIG-I-like receptors represent key mediators of innate host defense in the intestine, and they are involved in maintaining mucosal as well as commensal homeostasis.

We studied the possibility of simvastatin and antagonist of receptors of interleukin-1 for correction of experimental ileitis in rats with a focus on the expression studies of Toll-like receptor 2, Toll-like receptor 4, NOD2, RIG-I and transcription factors T-bet, GATA-3, RORgt and Foxp3 with lymphocytes of small intestine.

Methods: Experiments were carried out on male Wistar rats aged 5-7 months. The immunopositive lymphocytes were determined using a direct and indirect immunofluorescence technique with using a monoclonal rat antibody.

Results: The study of serial sections of ileum showed that the development of acute and chronic ileitis was accompanied with one-directed tendency on increasing of total number of TLR2+ lymphocytes and decreasing of total number of TLR4+ and Foxp3+ lymphocytes in lymphoid structures of ileum. The administrations of Simvastatin and ARIL-1 in experimental animals during the development of experimental pathology was accompanied by decrease of RORgt+- and T-bet+ lymphocytes, and increasing of total number of Foxp3+ lymphocytes.

Conclusions: Simvastatin and antagonist of receptors of interleukin-1 seemed to be beneficial in indomethacin-induced rat ileitis model through modulate pattern recognition receptors expression on lymphocytes and balance between different T-helper cell subsets of small intestine.

DOP074
Thrombospondin 1 modulates monocyte properties to suppress intestinal mucosal inflammation

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Background: Monocytes (Mo) play an important role in the pathogenesis of intestinal mucosal inflammation. This study aims to investigate into the mechanism whereby the intestinal epithelial cell (IEC)-derived thrombospondin 1 (TSP1) modulates Mo properties and regulates intestinal inflammatory responses.

Methods: The production of TSP1 by IEC was evaluated by quantitative real-time PCR and Western blotting. The properties of Mos were analyzed by flow cytometry. A mouse model of colitis was established to assess the role of epithelium-derived TSP1 induced by C. butyricum in the suppression of intestinal inflammation.

Results: The Results demonstrated that mouse IECs expressed TSP1, which was markedly upregulated by butyrate or feeding with C. butyricum. Coculture the butyrate-primed IECs and Mos or exposure of Mos to TSP1 in the culture induced expression of transforming growth factor (TGF)-b in Mos. These TGF-b+ Mos had tolerogenic properties that could promote generation of inducible regulatory T cells. Importatnly, adoptive transfer with TSP1-primed Mos, or feeding C. butyricum could prevent experimental colitis in mice.

Conclusions: C. butyricum induces IECs to produce TSP1 and induces generation of TGF-β+ Mos, which further suppress experimental colitis in mice. The Results implicate that administration of C. butyricum or butyrate may have the potential to ameliorate chronic intestinal inflammation through inducing immune suppressive Mos.

DOP075
Persistent dysregulated colonic mucosal gene expression in ulcerative colitis patients with endoscopic healing after infliximab or vedolizumab therapy

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Background: Mucosal healing on endoscopy is considered the treatment goal in inflammatory bowel diseases, including ulcerative colitis (UC). However, endoscopic healing is no cure and relapses are still observed in the majority of patients when treatment is discontinued in these patients. As the triggers for recurrence of inflammation are unknown, we studied if mucosal gene expression profiling could identify pathways important in relapse. We, therefore, compared colonic mucosal gene expression profiles of UC patients achieving endoscopic mucosal healing induced by infliximab (IFX) or vedolizumab (VDZ) therapy to these of healthy controls.

Methods: Colonic biopsies from 23 UC patients before and W4-6 after first IFX, from 44 UC patients before and W6, W12 and W52 after VDZ (GEMINI I and LTS), and from 12 non-IBD healthy controls were studied. Endoscopic mucosal healing was assessed at

the same time points as the biopsies. Total RNA from biopsies was analyzed for whole genome gene expression via Affymetrix Human Gene 1.0 ST arrays (false discovery rate< 5% and >2-fold).

Results: In VDZ healers, there were no significant gene probe sets different at W6 and only 5 (down: IDO1, REG3A, KLK6, SAA2 and up: PCK1) at W12 when compared to W0. As many as 593 (462 down/131 up) gene probe sets were significantly different in VDZ healers at W52 vs. W0. The majority of the observed changes at W52 by VDZ encoded genes that were involved in immune cell trafficking, cellular movement and inflammatory response, and overlapped (63%) with the probe sets identified in IFX healers at W4-6 vs. W0 [481 (388 down/93 up) significant probe sets] probe sets. After therapy at each of the studied time points, many gene probe sets remained significantly dysregulated in the IFX and VDZ healers when compared with controls, and again a great overlap was seen between IFX and VDZ of these persistent dysregulated genes (eg. up: IL1B, TIMP1, CCL20, DEFA5/A6, PI3, AREG, PTGS2, C2, SERPINB5, FAM5C and down: AQP8, MT1H/M).

Conclusions: This study demonstrates that VDZ and IFX restore, although incompletely, the colonic expression of many immune-related genes in UC patients achieving endoscopic healing with VDZ at W52 and with IFX at W4-6. Persistent abnormalities in gene expression remain after therapy in healers and may explain why mucosal lesions recur if patients do not receive maintenance therapy. Furthermore, the significant overlap in persistent dysregulated genes between VDZ and IFX healers suggests that unidentified triggers of inflammation are incompletely blocked by these biologic agents.

DOP076
Impact of western diet on short-chain fatty acids production and host susceptibility to intestinal inflammation in a context of Crohn's Disease

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Background: Recent advances have shown that abnormal inflammatory response observed in Crohn's disease (CD) involves interplay between intestinal microbiota, host genetic and environmental factors. The escalating consumption of fat and sugar in Western countries parallels an increased incidence of CD during the latter 20th century.

Methods: We analyzed the impact of a High-Fat/High-Sugar (HF/HS) diet in mice on gut micro-inflammation, selection of E. coli population, concentration of short-chain fatty acids (SCFAs) and expression of their free fatty acid-receptors such as G-protein-coupled receptor 43 (GPR43). Fecal lipocalin-2 (Lcn-2) was measured by ELISA to detect low-grade inflammation during the course of treatment, E. coli populations associated to colonic and ileal mucosa were quantified, production of SCFAs by microbiota were measured by gas chromatography in fecal samples. GPR43 receptor was visualized by confocal microscopy after immunostaining of colonic mucosa tissues. Mice were treated with an agonist of GPR43 receptor to evaluate its potential protective effect on gut inflammation. The severity of DSS-induced colitis was evaluated by disease activity index (DAI) measurement, histological score and cytokine release.

Results: HF/HS diet increased Lcn-2 level in stools from 5 weeks until 18 weeks of treatment, showing that HF/HS diet creates a specific inflammatory environment in the gut. Interestingly, abnormal proportions of E. coli bacteria were recovered from colonic and ileal mucosa of mice under HF/HS diet, compared to mice under conventional diet. SCFAs concentrations were significantly decreased in fecal samples from mice under HF/HS diet compared to mice fed a conventional diet. In addition, HF/HS diet led to an exacerbation of gut inflammation following DSS-induced colitis, with an increase of DAI, histological score and release of pro-inflammatory cytokines. Western diet led to dysbiosis with an overgrowth of pro-inflammatory E. coli bacteria and a decrease in protective SCFAs producing bacteria. GPR43 receptor expression was reduced in mice treated with an HF/HS diet compared to mice under a conventional diet. Mice treated with an agonist of GPR43 showed a decrease of DAI, Lcn-2 level and cytokine production.

Conclusions: Western diet creates a low-grade inflammation in the gut with a decrease of protective SCFAs producing bacteria, leading to overcolonization by E. coli opportunistic pathogen bacteria which could aggravate the inflammatory process resulting in chronic inflammation. Moreover, regulation of GPR43 receptor expression could be used as a new strategy to treat patients with abnormal colonization of E. coli by intestinal microbiota modulation.

DOP077
Involvement of type VI secretion systems in virulence of adherent-invasive Escherichia coli isolated from patients with Crohn's disease

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Background: Crohn's Disease (CD) is a chronic inflammatory bowel disease characterized by an abnormal expression of CarcinoEmbryonic Antigen related Cell Adhesion Molecule 6 (CEACAM6) at the apical surface of the ileal epithelium and ileal lesions of CD patients are colonized by pathogenic Adherent Invasive Escherichia Coli (AIEC). AIEC adhere to ileal enterocytes through CEACAM6 by the type 1 pili FimH adhesin. Pathoadaptative mutations in FimH improve AIEC ability to adhere to intestinal epithelial cells. AIEC reference strain LF82, isolated from ileal mucosa of CD patients, also harbored genetic elements that may be involved in virulence, in particular several pathogenicity islands. Two of them encode for a type VI secretion system (T6SS).

Methods: To investigate their role in bacterial virulence, these islands were totally deleted and the mutant phenotype was characterized in vitro using intestinal epithelial cells, macrophages. The ability of AIEC LF82 and type VI secretion system mutants to colonize and induce gut inflammation was evaluated in vivo using CEABAC10 transgenic mice expressing human CEACAM6.

Results: Deletion of pathogenicity island encoded T6SS (deltaT6SS-1; deltaT6SS-2 and double deltaT6SS 1+2) did not alter either morphological aspects (pili, flagella) or growth of AIEC LF82 bacteria in Luria Broth (LB). However, these mutants show a drastic motility reduction compared to LF82 wild type, in particular LF82-deltaT6SS-1 and double LF82-deltaT6SS1+2. The loss of these systems leads to decrease of AIEC LF82 ability to adhere to and to invade intestinal epithelial T84 cells. Interestingly, double mutant

shows better survival in THP1 human macrophages. A study of the behavior of these mutants in murine model has shown that LF82-deltaT6SS-2 mutant were able to persist in the gut of CEABAC10 transgenic mice and to induce mucosal inflammation.
Conclusions: These Results indicate that the T6SS play a role in the virulence of AIEC strains, improving adhesion and invasion capacity and limiting survival in macrophages. In vivo, these systems are essential in the process and the maintenance of infection by the AIEC strains. It is now important to determine the conditions to activate the expression these systems in order to identify, by a proteomic approach, secreted proteins by this system. This could provide new bacterial targets for controlling the virulence of AIEC strains.

DOP078
Abnormal gut homing and activation profile of blood and colonic dendritic cells in paediatric Crohn's disease normalises in response to nutritional therapy.

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Background: Crohn's disease (CD) presenting in childhood differs from disease presenting in adults, with unique characteristics of phenotype, severity and progression. Exclusive enteral nutrition (EN) is particularly effective in childhood CD and comparable to steroids. Human intestinal dendritic cells (DC) maintain immune homeostasis in health but can trigger an abnormal immune response in inflammatory bowel disease. Despite the well-defined role of dendritic cells in adult CD, dendritic cell properties in children with CD are unknown. Here, we have characterised blood and colonic dendritic cell properties in paediatric CD (before and after EN treatment) and have compared them with those of adult CD.
Methods: Blood and distal colonic samples were collected from treatment-naïve CD patients (18 children and10 adults) and healthy controls (HC, 8 children and 8 adults). Peripheral blood mononuclear cells (PBMC) and lamina propria mononuclear cells (LPMC) were obtained by Ficoll gradient centrifugation and "walkout" protocol respectively. DC were identified within LPMC and PBMC by flow cytometry as HLA-DR+lineage – (CD3 – CD14 – CD16 – CD19 – CD34 –) cells and divided between myeloid (mDC, CD11c+) and putative plasmacytoid(pDC, CD11c-). Expression of homing markers [β 7(gut), CLA (skin)], pattern recognition receptors(TLR2 & 4) and activation markers (CD40 & 86) were studied in each DC subset.
Results: Blood dendritic cell (mDC and pDC) numbers from treatment-naïve CD children were higher (compared with healthy children) and displayed an abnormal phenotype with higher expression of activation markers (CD40, CD86), pattern recognition receptors (TLR2, TLR4) and increased gut-homing profile (β 7+CLA-) suggesting dendritic cell infiltrates at the target tissues. Indeed, dendritic cell numbers in the colon of paediatric CD patients were also increased (compared with healthy children) and their properties resembled those of circulating dendritic cells with higher expression of CD40, CD86, and TLR2, TLR4 and β 7+CLA-. Despite the differences in clinical phenotype of paediatric and adult CD, there were however no differences in the phenotype of blood or tissue dendritic cells from paediatric CD when compared with adults. Following EN, 75% of the children entered remission with blood dendritic cells from these patients (but not the non-responding ones) displaying a restored phenotype [CD40,CD86, TLR2, TLR4 and β 7+CLA-] resembling that of healthy children.
Conclusions: Blood and tissue dendritic cells from paediatric CD patients display an abnormal phenotype which normalises following EN. Further work will give more insight into the pathogenesis of paediatric CD and the mechanism of action of nutritional therapies in these patients.

DOP079
Pro-inflammatory effect of volcanic ash (v.ash) in a colitis model - is the v. ash or some of its components linked with the IBD epidemiology?

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Background: It is widely accepted a role for environmental factors in the IBD pathogenesis. Urban pollutants were associated with hospitalization rates and early IBD debut. Intestinal exposure to particulate matter (PM) has proinflammatory effect (instilled in mice) inducing permeability and TNFα. Volcanic pollution, implicated in varied health impairments, was not studied in IBD. Increase PM remained after Iceland eruptions by ash resuspension(Thorsteinsson T,2012). High IBD incidences were reported from Iceland (volcanic) Faroe Islands, N.Zealand. During devastating Peyehue (Patagonian volcano,2011) eruptions, PM increase by ash-carrying winds were detected in Buenos Aires (Argentina), as well refractoriness in Hospitalized IBD of a reference centre. Hypothesis: volcanic ash (V.ASH) may be pro-inflammatory in IBD. **Aim:** to study the effect of V.ASH (from Patagonia) in a colitis mouse model
Methods: BALB/c mice received drinking water with or without V.Ash for 14 days. On day 7 different inflammatory stimuli were intrarectally administered: TNBS, Flagellin (FliC) or ethanol (EtOH) as vehicle control. On day 14 mice were sacrificed and the colon studied (weight, length, histology, ZO-1 immunofluorescence, gene expression of IL1 β, IL6, TNFα, Ccl20, IFN γ, Tbet, IL17A, RORγt by qPCR
Results: We found a marked weight loss in mice receiving drinking water+ash vs mice with only drinking water or EtOH. Colon of mice receiving ash showed a greater **ratio weight/length EtOH/EtOH+ash** 28.4 ± 4.4 vs 31.3 ± 2.4.0 **TNBS/TNBS+ash** 28.3 ± 0.1 vs 33.7 ± 4.2, **FliC/FliC+ash** 24.7 ± 4.01 vs 31.5 ± 5.9). **Histological activity index: EtOH/EtOH+ash**: 1 vs 3 (p<0.001), **TNBS/TNBS+ash** 3.2 ± 0.3 vs 4.3 ± 0.6 (p<0.05), **FliC/FliC+ash** 2.3 ± 0.6 vs 4 (p<0.001). Mice receiving ash showed increased hemorragia, oedema, cellular infiltration of colonic wall vs controls, and also significant increased expression of Ccl20, TNFα, IFNγ, Tbet and IL-17A (Values as mean Fold Increase±SD) as follow: **Ccl20 = TNBS/TNBS+ash** (14.45 ± 3.7 vs 34.04 ± 6.7 p<0.01), **FliC/FliC+ash** (23.3 ± 4.2 vs 75.1 ± 12.1 p<0.001); **TNFα = TNBS/TNBS+ash** (2.0 ± 0.49 vs 6.3 ± 0-83 p<0.05), **FliC/FliC+ash** (2.6 ± 1.35 vs 7.48 ± 3.8 p<0.01);

IFNγ = TNBS/TNBS+ash (6.07 ± 4,55 vs 31.58 ± 1.95 p<0.001), **FliC/FliC+ash** (16.51 ± 5.27 vs 26.33 ± 4.53); **Tbet = TNBS/TNBS+ash** (3.45 ± 1.30 vs 15.82 ± 3.9 p<0.001), **FliC/FliC+ash** (5.87 ± 0,81 vs 12.71 ± 0.93,p<0.05); **IL-17A = TNBS/TNBS+ash** (0.87 ± 0.27 vs 7.423 ± 6.712), **FliC/FliC+ash** (1.69 ± 0.32 vs 6.08 ± 3.83 p<0.05). Mice receiving ash+TNBS showed colonic ZO-1 decrease

Conclusions: Oral V.ASH given to mice treated with intrarectal TNBS or FliC induced colonic proinflammatory effect,
perhaps favoured for an impaired barrier function. Maybe V.ASH (some of its compounds?) could influence geographic/ temporal IBD epidemiology trends

DOP080
iNKT cells contribute to Ulcerative Colitis through a Th1/Th17 immune response

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Background: Ulcerative Colitis (UC) and Crohn's Disease (CD) are the two major forms of Inflammatory Bowel Diseases (IBD) in humans. While a deregulated Th1/Th17 adaptive immune response has been linked with CD pathogenesis, UC-related inflammation has been classically associated with an atypical Th2 response mediated by IL13-producing NKT cells. However, the failure of clinical trials aimed at the blockade of IL13 in UC patients and recent ex-vivo studies on UC specimens have questioned the involvement of IL13 in the pathogenesis of UC.

Methods: By the use of a translational approach involving both surgical specimens from UC patients and murine models of colitis, we aimed to phenotypically and functionally characterize (i)NKT cell populations in UC and in experimental intestinal inflammation. To this end, we took advantage of a novel transgenic mouse model (CXCR6 GFP/+) as a powerful tool to track (i)NKT cells in vivo in experimental colitis, such as that induced by oral DSS and intrarectal TNBS administration, respectively. Moreover, the involvement of microbiota- and self-derived lipid antigens in triggering the (i)NKT inflammatory response in the intestine was assessed.

Results: Flow cytometry on isolated lamina propria mononuclear cells and confocal microscopy analyses confirmed that (i)NKT cell populations were enriched in the inflamed colon of both human UC and in murine experimental colitis. Intestinal (i)NKT cells predominantly released IFNgamma, IL17 and IL22. The Th1/Th17 molecular signature of infiltrating (i)NKT cells was confirmed at both RNA and at protein level. By ex vivo antigen presentation assays, we found that intestinal (i)NKT cells were able to respond to both self and bacterial antigens during the course of colonic inflammation.

Conclusions: We established a murine model that easily provides the possibility to investigate the role of (i)NKT cells infiltrating the inflamed colon during the course of intestinal inflammation. We speculate that this population may contribute to the pathogenesis of experimental and human colitis by the release of Th1 and Th17 cytokines. These Results contribute to shed light regarding the role of (i)NKT cells in intestinal inflammation.

DOP081
Soft ROCK inhibition prevents intestinal fibrosis in a murine colitis model

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Background: Intestinal fibrosis is a common complication of Crohn's disease. Fibrotic strictures are the most important indication for surgery and current therapies are unable to prevent their development. Rho kinase (ROCK) is a key mediator in TGFß-induced activation of myofibroblasts and a promising anti-fibrotic drug target. However, systemic ROCK inhibition causes significant cardiovascular (CV) side effects. Thus, we investigated the effects of AMA0825, a ROCK inhibitor with Localized Activity (referred to as "soft"), on the development of intestinal fibrosis.

Methods: CV effects of AMA0825 were assessed in spontaneous hypertensive rats (SHR). Disease activity, intestinal fibrosis and inflammation were evaluated in chronic DSS-induced colitis. Effects on the production of fibrotic and inflammatory mediators were measured in human intestinal fibroblasts (HIF), HT29 colonic epithelial cells and THP1 macrophages. mRNA and protein expression was analyzed by qPCR, Luminex bead assay and immunocytochemistry.

Results: In SHR, AMA0825 had no CV effects at 10 mg/kg p.o. Daily treatment of mice with AMA0825 (3 mg/kg p.o.) reduced colonic weight/length ratio (p=0.03) and bacterial translocation to the liver (p=0.02), while no signs of toxicity were noticed. Trichrome-positive fibrotic tissue was reduced in the muscularis mucosae, mucosa and submucosa compared to placebo (p=0.003). Lower colonic protein levels of pro-fibrotic cytokines IL6, IL13 and TGFβ1-2 were observed, and DSS-induced production of matrix metalloproteinase (MMP) 2,3 and 9, and to a lesser extent 8 and 12, was prevented in treated mice. Interestingly, transcription of COL1A1 and ACTA2 was profoundly reduced, suggesting decreased activation of myofibroblasts.

Inflammatory cell infiltration and myeloperoxidase activity was unaffected by AMA0825 treatment, however, local levels of pro-inflammatory CXCL2, KC, IFNγ , TNFα and MCP1 were significantly reduced.

In HIFs, AMA0825 dose-dependently inhibited TGFβ1-induced phosphorylation of myosin light chain (a marker of ROCK activity), formation of actin stress fibers and expression of COL1A1 and ACTA2. TGFβ1-induced production of IL6, TGFβ1 and MMP2,3 and 12 was also abrogated, whereas TNF, IL8 and MCP1 were not induced by TGFβ1. AMA0825 did not affect IL8 secretion from TNF-stimulated HT29 cells or LPS-challenged THP1 cells either. Since these cell types largely contribute to inflammation in DSS-colitis, AMA0825 may not exert a direct anti-inflammatory effect.

Conclusions: Inhibition of ROCK by oral administration of AMA0825 in mice is safe and profoundly diminishes development of intestinal fibrosis by suppressing pro-fibrotic expression profiles. These effects are mainly due to direct inhibition of myofibroblast formation and activation.

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Digital Oral Presentations

DOP Session 10 – The genome and microbiome

DOP082
Genome-wide association identifies multiple collagenous colitis susceptibility loci

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Background: Microscopic colitis (MC) accounts nowadays for 10-13% of the cases investigated for chronic, non-bloody diarrhea. The etiology of MC remains unknown. As in Inflammatory Bowel Disease (IBD) different components contribute to the pathogenesis of MC such as environmental factors, a genetic predisposition and an aberrant immune response. The HLA associations and the higher occurrence of immune-mediated diseases in patients with collagenous colitis (CC) strongly suggest a role for auto-immunity. The nature of the adaptive local immune responses in the mucosa of CC is still unknown. A decreased amount of CD4+ lymphocytes in the lamina propria has been described. No genome-wide association or fine mapping studies of CC have been conducted. Accordingly we carried out an unbiased genome-wide association study of CC with the aim of identifying genetic loci that are closely associated with CC.
Methods: We extracted DNA from ~450 CC formalin-Fixed, paraffin-embedded tissue (FFPE) of patients with histologically confirmed CC. DNA samples that passed the quality control (N=295) were genotyped using the Illumina Immunochip array. Existing Immunochip genotyping data on IBD-free individuals (N=1,228) provided by the NIDDK IBD Genetics Consortium were obtained to explore unique pathways associated with CC.
Results: Ten loci passed the study-wise statistical significance for association with CC after accounting for the number of independent tests. Among them there were loci previously reported to be associated with that map to chromosomes 5 (IL7R), 6 (PTPRK), 9 (TNFSF15), 17q12 (IKZF, ORMDL3), and 17q12 (ATP6V0A1, STAT3). The most significant association signal we observed genome-wide in CC was near HLA-DQA1, a majot histocompatibilty complex class II implicating CD4+ T cells in CC pathogenesis. Numerous additional SNPs within the MHC region have been significantly associated with CC. A significant association was also identified for CTL4, a marker of the T-regulator cells (Treg), CD44 and ICOS.
Conclusions: These preliminary findings support the hypothesis that CC has a genetic component that involves pathways which potentially overlap with those of IBD as well as other pathways that are unique and further support the important role of CD4+ T-cells in CC pathogenesis.

DOP083
Comparison of Disease Phenotype in 35,128 European and 4,686 non-European IBD Cohort of the IIBDGC

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Background: IBD is relatively common in the West and is increasing in non-Western countries. Comparative data on clinical phenotype of IBD between European and non-European populations are scarce. We have recently characterised the genetic architecture of IBD in European and non-European populations through the International IBD Genetics Consortium (IIBDGC) cohorts. We now describe the detailed distribution of clinical sub-phenotypes across these populations.
Methods: Detailed sub-phenotpye data were collected on standardised proforma after retrospective case-note review by trained physicians or assistants at each site. Patient demographics and subphenotypes were compared between patients of European (n=35,128) versus non-European descent (East Asian, Indian, Iranian; n=4,868).
Results: IBD cases had a lower prevalence of a family history of IBD (5.6% vs.28.3%; $p=4.78X10^{-85}$) in non-European than Europeans.
Crohn's disease (CD): Whilst the age at diagnosis of CD was similar

	Crohn's Disease		Ulcerative Colitis	
	CEU	Non CEU	CEU	Non-CEU
Age of diagnosis	28.39 (±14.16)	27.58 (±12.19)	34.10(±15.78)	35.76(±13.69)
Gender, male	8467 (45.1%)	1325 (67.1%)	7870 (52.1%)	1319 (50.4%)
Smoking				
Never	8737 (57.3%)	376 (77.8%)	7174 (59.8%)	2102 (87.0%)
Ex	2359 (15.5%)	49 (10.1%)	3448 (28.7%)	47 (1.9%)
Current	4159 (27.3%)	58 (12.0%)	1382 (11.5%)	267 (11.1%)
FH of IBD	4438 (28.3%)	88 (5.6%)	2763 (21.8%)	151 (6.2%)
Location				
L1 (ileal)	4,916 (29.6%)	498 (34.8%)		
L2 (colonic)	3,921 (23.6%)	269 (18.8%)		
L3 (ileocolonic)	7,778 (46.8%)	665 (46.4%)		
Behaviour				
B1 (inflammatory)	7,478 (46.4%)	408 (29.9%)		
B2 (stricturing)	4,453 (27.6%)	587 (43.0%)		
B3 (penetrating)	4,174 (25.9%)	393 (28.8%)		
Perianal	4,516 (27.8%	663 (42.1%)		
UC location				
E1 (proctitis)			1,726 (12.9%)	285 (14.2%)
E2 (left-sided)			5,097 (38.2%)	1,033 (51.6%)
E3 (extensive)			6.526 (48.9%)	686 (34.2%)
Surgery	8,656 (52.8%)	728 (48.1%)	2,385 (18.5%	100 (4.1%)

across populations (19,290 European CD, 1,991 non-European CD), there was a striking male predominance (67.1% vs.45.1%; p=7.09X10^{-78}) in non-Europeans. In CD, there were more active smokers in Europeans than non-Europeans. CD location was broadly similar. While stricturing (43% vs.27.6%; p=2.73X10^{-33}) and perianal diseases (42.1% vs.27.8%; p=5.35X10-33) were more prevalent in non-Europeans than Europeans, surgical rates for CD were numerically lower in non-Europeans (48.1% vs.52.8%; p=5.42X10^{-4}). **Ulcerative colitis (UC):** There were very few non-European ex-smokers with UC compared with European patients (1.9% vs.28.7%). Extensive colitis (34.2% vs.48.8%; p=1.52X10^{-34}) and colectomy for UC (4.1% vs.18.5%; p=1.22X10^{-69}) were also less common in non-Europeans. In multi-variable analysis, independent factors for colectomy in UC were extensive colitis (OR 10.35; 95% CI, 7.85-13.64), European origin (OR 4.71; 95% CI, 3.72-5.96) and ex-smoking (OR 1.2; 95% CI, 1.08-1.36).

Conclusions: In the largest dataset comparing IBD sub-phenotype in European and non-European patients, there are several striking demographic differences in non-Europeans (male predominance in CD; less ex-smokers developing UC) which may yield clues to the role of environmental factors in disease etiology. Major disease sub-phenotypes (location, behavior and surgery) are broadly similar. CD phenotype appears to be as severe, if not more severe, in Asia than in the West. This may relate to delayed diagnosis or late presentation or real differences due to underlying genetic and microbial factors.

DOP084
Interpreting genetic variants in IBD as quantative immune traits by the assessment of cytokine profiles

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Background: In the most recent genome-wide association studies (GWAS) in IBD, published by Jostins et al, 2012, 163 genetic variances (single nucleotide polymorphisms; SNPs) are linked to IBD. They describe that, across all IBD-correlated loci, 'regulation of cytokine production' is the most significantly enriched Gene Ontology term, specifically regulation of IFN-g, IL12, TNFa and IL10. The effect of regulatory variants in the DNA can best be studied in both unstimulated 'steady-state' cells as well as in stimulated cells, to assess the interaction of genetic predisposition and exposure to environmental factors. Currently, we aim to assess the functional implication of IBD-related SNPs by analyzing cytokine expression in unstimulated and stimulated peripheral blood of IBD patients.

Methods: Whole blood of 40 CD patients has been stimulated with aCD3/aCD28 antibodies and LPS to mimic the adaptive resp. innate immune response. 28 cytokines were measured by a multiplex cytokine assay. Genotyping was performed by a customized GWAS chip (Immunochip) including all IBD-related SNPs.

Results: Cytokine levels are differently expressed when patients are stratified for IBD-associated risk alleles, both in a cis- and trans-eQTL fashion. For this abstract we focused on analyzing SNPs associated with TNFSF members, hereby providing the SNP in the TNFSF15/TL1A gene as an example. Carriers of the G risk allele (RA) for this SNP are significantly less able to upregulate the anti-inflammatory IL10 following a 24-hour LPS stimulus (fold change + standard deviation (FC + s.d.); AA 57.6 + 40.6; AG 48.0 + 20.6; GG 27.3 + 31.43; P=0.026). Interestingly, also upregulation of the pro-inflammatory TNFa is hindered in these RA carriers, both at 4 hours (FC + s.d.; AA 255.2 + 188.8; AG 122.3 + 99.1; GG 9.0 + 7.5; P=0.01) and at 24 hours (FC + s.d.; AA 441.4 + 0; AG 213.1 + 105.6; GG 20.13 + 6.1; P<0.0001).

Conclusions: The concept of our study approach provides insight into specific immunological processes underlying the complex nature of IBD. We mimicked the human immune response by performing whole blood stimulation assays in vitro. By risk allele stratification of patients we can identify subgroups with differently expressed cytokines. However, further research should also focus on single cell studies in order to find subsets of cells responsible for this altered cytokine expression caused by the regulatory variation. Despite reported inter-individual variation in the innate immune reactivity, we did find significant patterns of genetic variance correlating to a modified immunological response. Larger sample sizes would strengthen these Results, and contribute to the development of patient-specific therapies based on genetic profiling.

DOP085
A candidate gene study of rare monogenic disorders with IBD-like phenotype identified rare variants in XIAP gene in a cohort of early-onset IBD patients

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Background: Chronic granulomatous disease, glycogen storage disease Ib, Chediak-Higashi syndrome, Hermansky-Pudlak syndrome, leukocyte adhesion deficiency, congenital, cyclic and autoimmune neutropenias, Wiskott-Aldrich syndrome, IPEX syndrome, IL10 deficiency and XIAP deficit are all rare monogenic primary immunodeficiencies (PID). These disorders are characterized by a defective innate or adaptive immune response and demonstrate chronic intestinal inflammation reminiscent of inflammatory bowel disease (IBD). We aimed to investigate whether the causative genes identified so far

for these monogenic disorders may harbor low frequency and rare variants contributing to inherited predisposition to IBD.

Methods: We analyzed 23 selected candidate genes underlying ten monogenic diseases in IBD patients, for the presence of (i) low frequency variants by association analysis using meta-data corresponding to genotypes of ~17,000 Crohn disease (CD) case / control individuals obtained from the International IBD Genetics Consortium (IIBDGC) and imputed with 1,000 Genomes Project reference panels, testing for the presence of CD-associated variants in 1Mb loci centered on the selected candidate genes, (ii) rare variants by means of high-throughput resequencing (HTS) of 4800 individuals (2400 early-onset and adult-onset CD/ 2400 controls) and (iii) integrating the Results of the association analysis with functional information (eQTL) generated in nine tissue types relevant in IBD pathogenesis.

Results: We identified rare missense coding variants in XIAP gene conferring susceptibility in early-onset CD patients, but not in adult-onset CD patients. None of the XIAP mutation carriers demonstrate the full expression of PID X-linked lymphoproliferative disease type 2 (XLP2). No significative Results was found for the other candidate genes. Increasing further more the sample size of the current cohort may reveal additional rare variants in XIAP or in other candidate genes.

Conclusions: We examined 23 coding genes underlying monogenic disorders characterized by IBD-like intestinal inflammation and could identify rare missense variants in the XIAP gene in early-onset CD. XIAP gene underlies the PID X-linked lymphoproliferative disease type 2 (XLP2) and encodes for a molecule that belongs to the family of inhibitor of apoptosis proteins (IEPs). XIAP activate also the NfKB via an indirect interaction with the NOD2-interacting protein RIP2. This study emphasizes the need to perform gene testing for XIAP deficit in patients with early-onset CD.

DOP086
Enteric micriobiota alterations in patients with a normal ileal pouch may be predictive of pouchitis

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Background: Pouchitis is a common complication in patients with ulcerative colitis undergoing proctocolectomy with ileal pouch-anal anastomosis (pouch surgery). Since inflammation occurs in a previously normal small bowel, it may be considered as a model for the development of Crohn's disease. Our aim was to examine whether patients with a normal pouch have microbial stool characteristics that can predict pouch inflammation.

Methods: Patients undergoing pouch surgery were prospectively recruited. Normal pouch was defined as pouchitis disease activity index (PDAI) ≤ 6 or according to physician's global assessment if no endoscopy within 30 days of stool sample. Fecal samples were used for microbiota analysis by 16S rRNA gene pyrosequencing and for measuring fecal calprotectin (FC) level. Patients with pouchitis or a history of antibiotic treatment 3 months prior to stool sampling were excluded. Disease activity was assessed at two time points (T1 & T2) during the longitudinal follow up. Patients were classified into one of two groups:

Normal pouch at T1 and at T2 (T2-normal); normal pouch at T1 and pouchitis at T2 (T2-active).

Results: A total of 20 patients were recruited (age: 47.7 ± 14.9 years, male: 11, pouch age [time from pouch surgery/ ileostomy closure] 97 ± 98 months) and followed up for a median of 10.2 months (range 4.5-31). Pouch patients with a normal pouch at baseline had comparable microbial diversities whether active disease developed at T2 or not [Shannon diversity index (DI) T2-normal=4.09 (n=13), T2-active=4.07 (n=7)]. However, diversities of both groups decreased during follow up to 2.93 and 2.33, respectively.

A hypothesis-free analysis for differences among genera at baseline did not reveal differences between the two groups of patients at T1. However, a targeted approach comparing taxa reported to be decreased in pouchitis, revealed that some of these taxa were decreased before pouchitis developed in the T2-active vs the T2-normal patients. Specifically, Ruminococcus (Lachnospiraceae family- 2.3% vs 4.3%, P<0.01), and Coprococcus (1.8% vs 4%, P<0.05) were decreased in patients who developed pouchitis at T2, while Faecalibacterium (1.8% vs 3.7%) and Megamonas (Veillonellaceae family, 0.12% vs 1.16%) only trended to be decreased.

Interestingly, FC levels at baseline were significantly higher in patients who developed pouchitis (T2-normal =100 ± 102 vs T2-active =349 ± 209 mg/kg, P<0.01).

Conclusions: Changes in the microbiota of patients with a normal pouch precede pouchitis. These alterations may result from subclinical inflammation reflected by increased FC levels. Altogether this may suggest that changes in the microbiota contribute to the development of intestinal inflammation and may be predictors of pouchitis.

DOP087
Intestinal microbial signature in patients with primary sclerosing cholangitis

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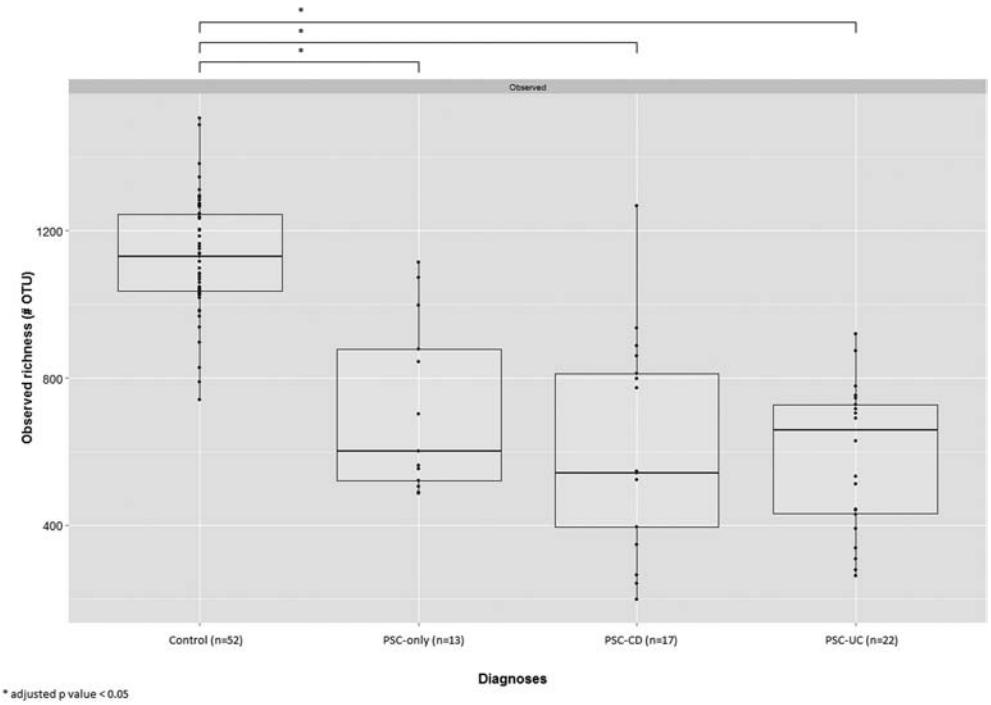
Background: Primary sclerosing cholangitis (PSC) is a cholestatic liver disorder very frequently associated with inflammatory bowel diseases (IBD). The intestinal microbiota seems to be essential in PSC as bacterial translocation is thought to play an important role in the pathogenesis of the disease. Given the association with IBD and the fact that patients with IBD have a well-documented intestinal dysbiosis, we hypothesized that dysbiosis would also play a role in PSC.

Methods: Faecal samples from 52 PSC patients and 52 age, sex and BMI matched healthy controls were collected. Within the PSC cohort, 39 patients had concomitant IBD (17 Crohn's



"Figure 1: Observed microbiota richness"

disease (CD) and 22 ulcerative colitis (UC)). After bacterial DNA extraction, 16S rDNA paired-end sequencing was performed using Illumina MiSeq sequencer. Successfully combined reads were quality-filtered (30 QS over 90% of read length) and chimeric sequences filtered out (UCHIME). Sequencing depth was downsized to 10000 reads/sample by random selection. Reads were clustered at 97% sequence similarity for species-level de novo OTU picking (USEARCH). The Ribosomal Database Project classifier was used for taxonomic assignment. Statistical analyses were performed with R package phyloseq, using non-parametric Mann-Whitney U and Kruskal-Wallis tests, with multiple testing correction (FDR).

Results: The overall microbiota diversity was significantly decreased in PSC patients compared to healthy controls ($p<0.0001$). This reduction was observed in each subgroup of PSC patients (PSC only, PSC+CD, PSC+UC) versus healthy controls (adjusted $p<0.0001$) (Figure 1).

At genus level, five genera were consistently more abundant in PSC patients compared to healthy controls (adjusted $p<0.02$): Enterococcus, Fusobacterium, Lactobacillus, Veillonela and Morganella. PSC patients with IBD versus controls showed differences in the abundance of an additional 33 genera (adjusted $p<0.05$) including Faecalibacterium, Roseburia, Blautia and Butyricicoccus.

Conclusions: The intestinal microbiota of PSC patients is clearly different from that of healthy controls, even in the absence of intestinal inflammation such as IBD. A unique microbial signature of five genera is observed in PSC patients, irrespective of the presence of IBD. In PSC patients with concomitant IBD, a dysbiosis involving previously described IBD-related genera is also observed in addition to the PSC specific microbial signature. Our data support the hypothesis that the intestinal microbiota plays an important role in the pathogenesis of this chronic cholestatic liver disease.

DOP088
Changes in faecal microbiota in UC patients after Faecal Microbiota Transplantation

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Background: A disturbed gut microbiota is assumed to play a crucial role in the chronic inflammation in ulcerative colitis (UC). A radical way to interfere with the intestinal microbiota is faecal microbiota transplantation (FMT) using faeces from a healthy donor. The aim of our study was to study signature changes upon FMT in UC patients who did and did not respond to FMT.

Methods: Faecal samples from 37 patients who participated in the TURN trial and samples from corresponding donors were used for microbiota profiling. In this trial, active UC patients were 1:1 randomised to duodenal infusion of FMT derived from donor faeces (FMT-D) or patients' own faeces (FMT-P) after bowel lavage. Twelve patients (FMT-D: 7/17 patients, FMT-P: 5/20) achieved remission ('responders') at week 12 and 25 did not ('non-responders'). Composition and diversity of the microbiota from donors and recipients were compared and contrasted phylogenetic microarray analysis of 16S rRNA amplions by means of the Human Intestinal Tract Chip.

Results: Twelve weeks after treatment fecal microbiota diversity increased significantly in all responders (n=12), (fig.1). In the FMT-D group the similarity index of recipients to their respective donors had significantly increased at week 12 in responders, whilst this was not seen in the non-responders (fig. 2). Moreover, at 12 weeks the similarity to corresponding donors was significantly higher in responders versus non-responders. The differences at week 12 between responders and non-responders

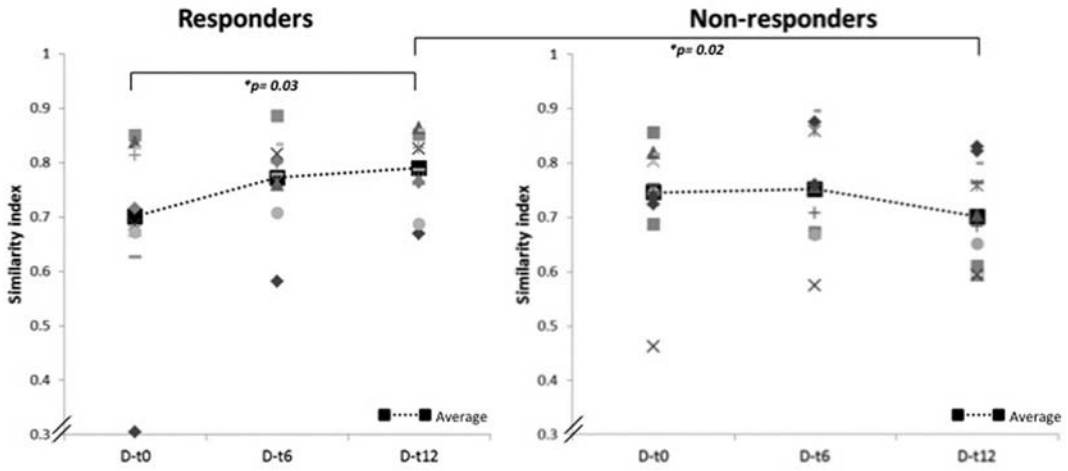

Figure 1 "Diversity grouped by treatment and response to therapy at week 0, 6 and 12 weeks after FMT."

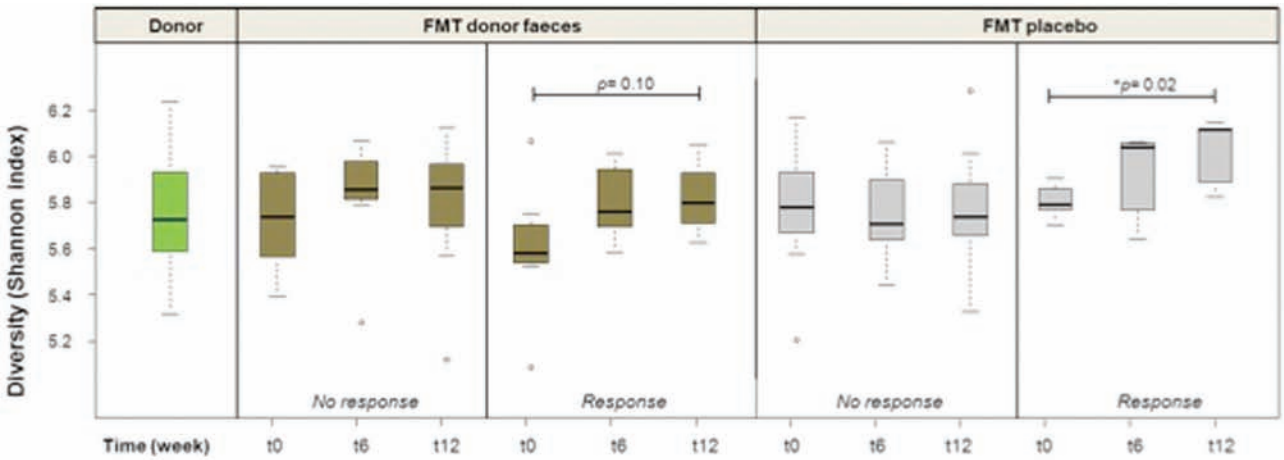

Figure 2 "Similarity in FMT donor group with donor faces"

were exclusively explained by a 2-4 fold increase in abundance of Clostridium cluster XIVa members in responders (p<0.01, FDR<0.20), while at t=0 there were no differences between responders and non-responders.

Figure 1. Diversity grouped by treatment and response to therapy at week 0, 6 and 12 weeks after FMT.

Figure 2. Pearson correlation between individual samples and their donors in the FMT-D group. Three responders and 2 non-responders received donor faeces from two successive donors.

Conclusions: In UC patients who respond after FMT the disturbed microbiota diversity and lack of potentially beneficial Clostridium clusters are restored.

DOP089
Comparative genome analysis of Crohn's Disease-associated adherent, invasive Escherichia coli fails to detect a common molecular property

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Background: Adherent-invasive E. coli (AIEC) are a leading candidate bacterial trigger for Crohn's disease (CD). The AIEC phenotype is based on a strain's ability (i) to adhere to and invade epithelial cells (ECs), and (ii) to survive and replicate within macrophages. No defining molecular features have been identified for AIEC and phenotypic testing is the only way to identify them. The aim of this study was to identify a common molecular property of the AIEC phenotype.

Methods: The whole genomes of 41 B2 phylogroup E. coli strains, isolated from 19 patients with inflammatory bowel disease (IBD [14 with CD, 5 with ulcerative colitis]), and 17 without IBD, were sequenced using the Illumina HiSeq 2000 platform. Adherence/invasion assays were conducted using I-407 ECs and survival/replication assays using THP-1 macrophages. The genomes were assembled in

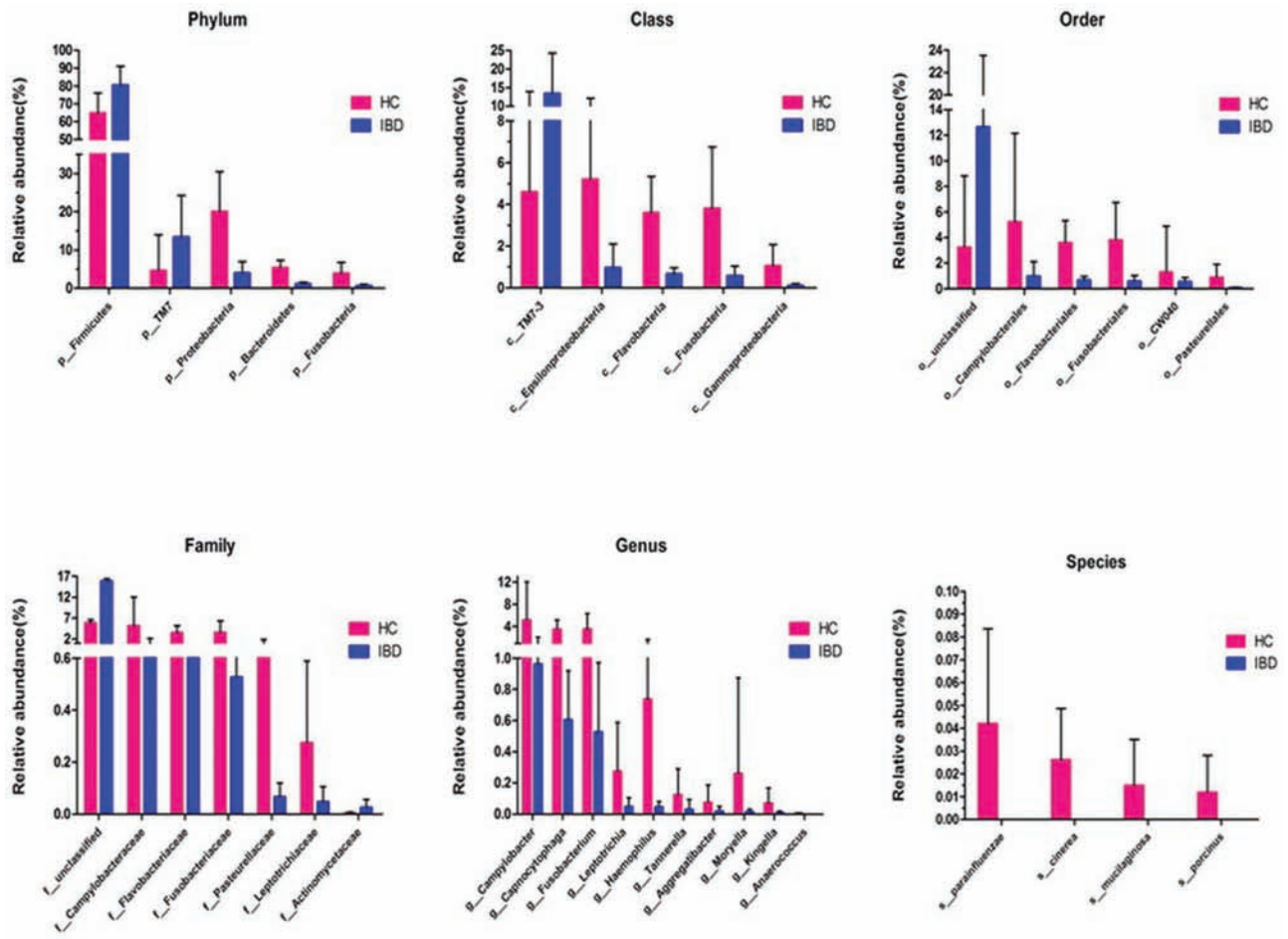
CLC workbench and annotated in Genoscope. Protein cluster analysis was conducted using CD-HIT. The resulting matrices were analysed in R to determine genes unique/more frequent in AIEC strains compared to non-AIEC strains. The Harvest software suite was used to detect SNPs and generate core-genome phylogenies.

Results: 12/41 strains displayed the AIEC phenotype (5 CD, 2 UC, 5 non-IBD). The AIEC strains were scattered throughout the phylogenetic tree and we did not identify a gene in common to all, or the majority of, AIEC isolates despite restricting the analysis to B2 phylogroup strains. For patients 12 and 55, we isolated two strains that were highly similar (same sequence type), differing by just 127 and 341 genes, respectively. One strain from each patient displayed the AIEC phenotype, the other did not. None of the genes, or SNPs, observed in the AIEC strain was observed in all, or the majority of, other AIEC strains.

Conclusions: Comparative genomic analysis of AIEC and non-AIEC strains failed to detect a molecular property exclusive to the AIEC phenotype. Our Results indicate that multiple sets of genes, and/or regulatory differences, contribute to the AIEC phenotype.

Details of clinical manifestations of IBD patients. *Disease activity were evaluated by Mayo score in UC and CDAI in CD.

	Gender	Age	Subtype	Duration	Montreal classification	Activity*	Severity	Extraintestinal manifestations	Current therapy
Patient 1	M	62	UC	2y	E2	7	Moderate	Oral ulcer and skin	Oral 5-ASA
Patient 2	M	56	UC	11y	E2	8	Moderate	No	5-ASA: oral +suppository
Patient 3	F	29	UC	3y	E3	12	Severe	Arthralgia	5-ASA: oral+enema
Patient 4	F	54	UC	2m	E3	3	Mild	No	Oral 5-ASA
Patient 5	M	35	CD	8y	A2L2B2	224	Moderate	Oral ulcer	AZA
Patient 6	F	54	UC	12y	E1	4	Mild	No	5-ASA suppository



"Taxa differing significantly between the salivary microbiota of the healthy control (HC) and inflammatory bowel disease (IBD) groups at the phylum, class, order, family, genus, and species levels."

DOP090
Dysbiosis of oral microbiome in adult Chinese patients with active Inflammatory Bowel Diseases

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Background: The imbalance of altered gastrointestinal(GI) flora and host's immune system is believed to be the main cause of IBD.The diversity of salivary microbiota in healthy human is similar to that of gut microbiota,however,oral flora in patients with systemic diseases such as IBD was seldom investigated.As entrance of GI tract,oral cavity may somehow reflect the relationship of host's immune system and mucosal microbiota adhered to the GI tract.In fact,oral cavity is one of the most commonly involved extraintestinal organs in IBD patients.Given the ease and repeatability of direct sampling of the oral cavity,study of oral microbiome is of particular importance for this special disease with the characteristic of repeated relapse.The purpose of this study is to compare the oral microbiome in active Chinese IBD adults with healthy controls,and then to study the change of oral microbiota in IBD patients using 16S rRNA gene pyrosequencing.

Methods: Unstimulated saliva was collected from six patients with active IBD and ten healthy adults respectively.Bacterial DNA from saliva samples was extracted and purified,the v3-v4 hypervariable regions of bacterial 16S rRNA were amplified via PCR,and then pyrosequencing of the PCR products were performed on MiSeq sequencing platform .

Results: Overall diversity of oral microbial communities associated with IBD had a decreasing tend in despite of no significance.Given relative abundance of phylum level,the difference of bacterial compositions between healthy and IBD groups was significant,including Bacteroidetes,Proteobacteria,Fusobacteria with significant decrease in IBD and TM7,Firmicutes with increase.Analysis at the species level showed that Haemophilus parainfluenzae,Neisseria cinerea,Rothia mucilaginosa,and Streptococcus porcinus were significantly reduced in IBD group in comparison with healthy control.

Conclusions: Our data showed significant differences of salivary microbiota compositions in active IBD patients and healthy adults,and suggested that the oral microbiome was uniquely altered in patients with active IBD.It can be postulated that the dysbiosis of oral microbiota may participate in the development of IBD,and may be partially responsible for the relapse of the disease.Furthermore, oral microbiota may reflect the development of gut microbiota to some extent,particularly in IBD.

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Poster presentations

Poster presentations

Basic science

P001
Chronic exposure to LPS but not MDP induces goblet cell development in human colonic enteroids

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Background: Inflammatory Bowel Disease (IBD) is thought to be the result of an aberrant response of the intestinal immune system to the commensal microbiota in a genetically susceptible host. It is generally felt that disruption of the intestinal barrier contributes to the development of IBD. However, development of the intestinal barrier is dependent upon the commensal bacterial, although whether this is a result of direct interaction between the commensal bacterial and the epithelium or mediated by intestinal immune system is unknown. Here we have used primary cultures of human colonic intestinal epithelium (enteroids), to investigate the effect of microbial stimuli on the development of the intestinal epithelium via the modulation of intestinal stem cells, independent of immune input.
Methods: Enteroids were grown from crypts isolated from the transverse colon of healthy individuals and transferred to Matrigel and growth media for 15 days in the presence and absence of lipopolysaccharide (LPS, 20 ng ml-1), a TLR 4 agonist, or muramyl dipeptide (MDP, 20 ng ml-1), a NOD 2 agonist. Enteroid structure was assessed by light and transmission electron microscopy and gene expression by microarray, qPCR, Western blotting and immunohistochemistry (IHC).
Results: At 15 days the enteroids consisted primarily of columnar epithelial cells resembling colonocytes with little evidence of goblet cells, which normally make up 15-20% of the colonic epithelium. Inclusion of LPS or MDP in the growth medium resulted in increased expression of transcript of genes associated with cell cycle, growth and differentiation. However, LPS also induced increased expression of genes associated with goblet cells (MUC2, TFF3, KLF4, Clca1, Zg16, Mpgc60, microtubule-associated protein and resistin-like beta protein) and this was associated with an increase in the number of goblet cells to 18.5 ± 5% ($P<0.05$, ANOVA with Dunnets test) of the total cells compared with 2%±2.1% in the MDP treated cells and 1.5 ± 1.4% in the untreated controls. Western blot confirmed an increased expression of MUC2, while IHC confirmed an increase in the number of MUC2 and TFF3 positive cells following treatment with LPS, suggesting a lineage change towards goblet cell development.
Conclusions: These data indicate that components of the commensal microbiota differentially induce changes in gene expression in intestinal epithelial cells independent of input from intestinal immune cells. This suggests a direct cross-talk between the intestinal stem cells and the microbiota occurs, which differs dependent on the receptor involved, and will influence epithelial homeostasis and barrier properties in the intestinal epithelium. Disruption of this cross talk may contribute to the development of IBD.

P002
Genetic deletion of tissue inhibitor of metalloproteinase-1/TIMP-1 attenuates DSS-induced inflammation and fibrosis in a mouse model of colitis.

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Background: Tissue remodeling and fibrosis are hallmarks of inflammatory bowel diseases (IBD). An increased level of tissue inhibitor of metalloproteinase-1 (TIMP-1) has been reported in fibrotic strictures in Crohn's disease (CD). The aim of this study was to investigate the effect of TIMP-1 deficiency in an acute and chronic mouse model of inflammatory colitis.
Methods: Colitis was induced in 8-10 week old female B6.129S4-Timp1^{tm1Pds}/J knock-out (KO) mice and C57BL/6J control mice. Acute colitis was induced by oral administration of 3% dextran sodium sulphate (DSS) for 7 days followed by 2 days of regular water. Chronic colitis was induced by 3 cycles of 1 week of exposure to 1.75-2.0% DSS followed by a recovery phase of 2 weeks. Systemic inflammation, colonic inflammation and fibrosis were assessed by macroscopic parameters, histopathology analysis and tissue collagen levels. Gelatinase levels were determined with gelatin zymography and gene expression differences were assessed with Affymetrix Mouse Gene 1.0 ST arrays (false discovery rate < 5% and >2-fold).
Results: In comparison with control mice, DSS administration to TIMP-1 KO mice resulted in significantly less weight loss ($p<0.001$ [acute] and $p=0.006$ [chronic]) and less systemic inflammation ($p<0.001$ [acute] and $p=0.031$ [chronic]). After chronic DSS administration, TIMP-1 KO mice had reduced colonic inflammation (macroscopic damage: $p<0.001$, histological inflammation: $p=0.016$) and lower tissue collagen levels compared to control mice ($p=0.003$). ProMMP-9 levels were higher in controls with chronic colitis

(p=0.050), whereas proMMP-2 (p=0.002) and activated MMP-2 (p=0.040) levels were higher in controls with acute colitis compared to TIMP-1 KO mice. Comparison of gene expression levels after acute DSS administration showed that TIMP-1 KO mice had an upregulation of *Ido1* (Fold change [FC]=15, p=0.010), *Gal3st3* (FC=8.8, p=0.010), *Xpnpep2* (FC=7.5, p=0.002) and downregulation of *Mmp-2* (FC=3.3, p=0.020), *Mmp-9* (FC=3.1, p=0.030), *Cldn1* (FC=3, p=0.040) compared to control mice. Young TIMP-1 KO mice (10-12 weeks) *versus* older animals (19-21 weeks) showed significantly increased expression of *Reg3g* (FC=16, p=0.03), *Reg3b* (FC=12.6, p=0.040) and *Ido1* (FC=3.5, p=0.008), whereas the expression levels of *Mir200b* (FC=2.2, p=0.009), *Ctse* (FC=1.3, p=0.030) and *Wnt2b* (FC=1.1, p=0.002) were decreased.

Conclusions: TIMP-1 deficiency leads to upregulation of anti-bacterial and innate immunity genes, resulting in an attenuated development of acute colitis. In a chronic setting of inflammation, TIMP-1 KO mice have less remodeling and fibrosis. Unraveling the role of TIMP-1 in extracellular matrix remodeling will be necessary to understand the biology of intestinal wound healing and fibrosis in IBD.

P003
Anti-fibrotic Effects of Pirfenidone in Gut-derived Fibroblasts from Patients with Active Crohn's Disease

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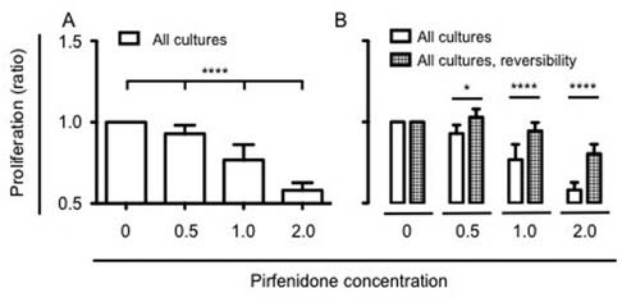
Background: Crohn's disease (CD) patients suffering from complications of intestinal fibrosis and stricture formation often require repeated surgical resection. However, the high recurrence rate associated with resection necessitates the exploration of new therapeutic approaches. Pirfenidone (Esbriet®, Pirespa®) (PFD), an anti-fibrotic and anti-inflammatory drug approved in Europe for the treatment of idiopathic pulmonary fibrosis, may be able to inhibit the proliferation and matrix formation of gut-derived fibroblasts from CD patients and may be a candidate drug for prevention of stricture formation in CD.

Methods: Fibroblasts were isolated from endoscopic biopsies from macroscopically inflamed (n=8) and non-inflamed (n=5) colonic mucosa or from surgical specimens from strictured ileal mucosa (n=2). As a control fibroblast population we used a fibroblast cell line derived from human neonatal foreskin (strain BJ; ATCC no. CRL-2522). The fibroblasts were cultured with increasing concentrations of PFD and we studied the impact on fibroblast proliferation, collagen synthesis and production of MMP-3 and TIMP-1.

Results: PFD inhibited the proliferation of gut-derived fibroblasts in a dose-dependent way (Figure 1.A) (P<0.0001). PFD was added in the following concentrations: 0.5 mg/ml, 1.0 mg/ml, and 2.0 mg/ml. The relative inhibitory effect of PFD was 0.93 (IQR 0.91-0.98); 0.77 (IQR 0.72-0.86); and 0.58 (IQR 0.49-0.63) respectively. Importantly, the inhibitory effect of PFD on fibroblast proliferation was reversible in vitro (Figure 1.B).

PFD, in the same amounts as above, significantly inhibited collagen synthesis and the production of both MMP-3 and TIMP-1 dose-dependently (all P<0.0001). For MMP-3 the median relative inhibition was 0.81 (IQR 0.67–0.94); 0.71 (IQR 0.61–0.83); and 0.62 (IQR 0.52–0.67) respectively (Figure 2.A). For TIMP-1 the median relative inhibitory effect was 1.11 (IQR 0.92-0.1.20); 0.97 (IQR 0.87–1.16); and 0.72 (IQR 0.61–0.82) respectively (Figure 2.B).

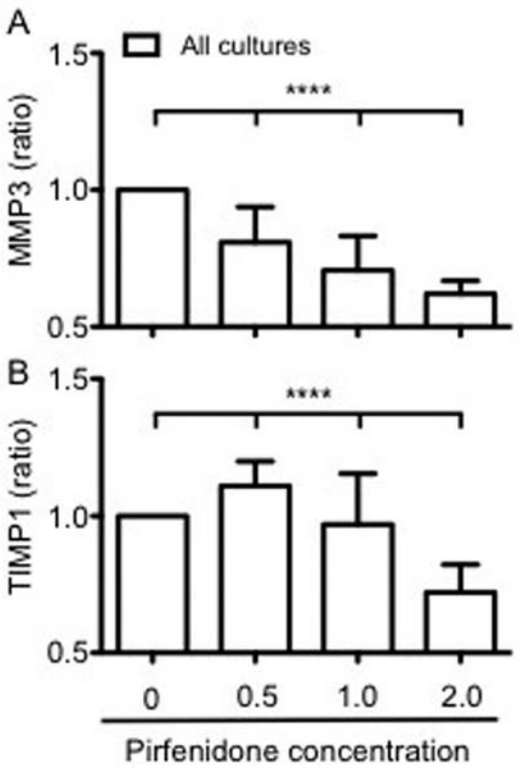
Conclusions: PFD inhibits the proliferation and secretion of collagen, MMP-3 and TIMP-1 in fibroblasts from CD patients. Our observations of the impact of PFD on fibroblast proliferation support the use of PFD in the treatment of stricturing CD.



"Figure 1: Suppression of fibroblast proliferation. A) The fibroblast proliferation decreased after treatment with PFD dose-dependently. B) The suppression was reversible for all conc. of PFD."

P004
Activation of the GCN2/eIF2alpha/ATF4 signaling pathway triggers autophagy response to infection with Crohn's disease-associated adherent-invasive Escherichia coli

A. Bretin[1], J. Carrière[1], G. Dalmasso[1], N. Barnich[1], A. Bergougnoux[1], A.-C. Maurin[1], A. Bruhat[2], H. Nguyen*[3]



"Figure 2: Suppression of fibroblast production of MMP-3 and TIMP-1. Fibroblast production of A) MMP-3 and B) TIMP-1 decreased after treatment with pirfenidone in a dose-dependent manner."

[1]UMR 1071 Inserm/Université d'Auvergne; USC-INRA 2018, Microbes, Intestine, Inflammation et Susceptibility of the host, Clermont-Ferrand, France, [2]INRA, Human Nutrition Unit (UNH), Theix, France, [3]University of Auvergne, UMR 1071/Inserm, Clermont-Ferrand, France

Background: A high prevalence of the adherent-invasive E. coli (AIEC) in the intestinal mucosa of Crohn's disease patients has been shown. We previously showed that upon AIEC infection, autophagy is induced in host cells to restrain AIEC intracellular replication. The mechanism underlying such autophagy induction, however, remains largely unknown. Here, we investigated the role of the GCN2/eIF2α/ATF4 pathway in autophagy response to AIEC infection.

Methods: Autophagic activity was assessed by Western blot and immunofluorescent labelling of LC3. Intracellular bacterial number was determined by bacterial invasion assay and confocal microscopy. Binding of ATF4 to autophagy gene promoters was assessed by Chromatin immunoprecipitation (ChIP) assay. Wild type (WT) and GCN2 knockout (KO) mice were infected with an AIEC reference strain LF82 by gavage.

Results: Infection of human intestinal epithelial T84 cells with the AIEC LF82 strain activated the GCN2/eIF2α/ATF4 pathway as shown by increased phospho-GCN2 and phospho-eIF2α levels, enhanced ATF4 protein expression, and upregulated mRNA expression levels of ATF4 target genes. To explore the role of this pathway in host responses to AIEC infection, we used GCN2-deficient mouse embryonic fibroblasts (GCN2-/- MEF). GCN2 depletion suppressed eIF2α activation and inhibited the increase in ATF4 protein level induced by LF82 infection. mRNA expression levels of the autophagy genes p62, MAP1lc3, Beclin1, atg3 and atg7 were significantly increased in WT MEF upon LF82 infection, and this was blocked in GCN2-/- MEF. ChIP assay showed that GCN2 depletion inhibited the LF82-induced binding of ATF4 to the promoters of these autophagy genes. Consequently, autophagy induction upon LF82 infection was suppressed in GCN2-/- MEF, leading to increased LF82 intracellular replication and elevated pro-inflammatory cytokine production, compared to WT MEF. In vivo study consistently showed that LF82 infection activated the GCN2/eIF2α/ATF4 pathway in enterocytes from WT mice, but not GCN2 KO mice. In response to AIEC infection, autophagy was induced in WT mouse-derived enterocytes, and this was not observed in KO mice. LF82 persistence in the gut was increased in KO mice, leading to aggravated intestinal inflammation, compared to that in WT mice. Depletion of GCN2 did not affect susceptibility of mice to DSS-induced colitis, indicating that the effects obtained were not a consequence of inflammation and were specific for AIEC infection.

Conclusions: The GCN2/eIF2α/ATF4 pathway is activated in host cells during AIEC infection, which is served as a defense mechanism to induce a functional autophagy to control AIEC intracellular replication.

P005
Characterization of human colonic and ileal dendritic cells in health and Crohn's disease

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Background: Human intestinal dendritic cells (DC) maintain a balance between tolerance to nutrients/commensals and immunogenicity against pathogens. Changes in intestinal DC properties are found in inflammatory bowel diseases including Crohn's disease (CD). Most studies, however, do not consider DC compartmentalization through the human gut. Here we studied whether DC subsets and phenotype change through the human gut in healthy controls (HC) and CD patients.

Methods: Paired biopsies from human proximal colon and the terminal ileum (TI) were obtained from HC and CD patients. DC were identified following collagenase digestion where DC phenotype were assessed by flow cytometry. Antigen presenting cells (CD45+HLA-DRhigh) were identified within single viable cells. Discrimination between DC and Mφ was subsequently performed based on lineage marker expression (CD3,CD14,CD16,CD19,CD34) and side scatter properties of the cells identifying DC as CD45+HLA-DR+lineage-complexitylow. DC were further distinguished from Mφ as CD64- with CCR7 up-regulation following overnight culture.

Results: In all samples, intestinal DC were myeloid (mDC, CD11c+) and were further divided into different subsets based on CD103 and SIRPα expression. CD103-SIRPα+ and CD103+SIRPα+ were type 1 immature mDC (CD1c+CD141-ILT3+) while CD103+SIRPα- were type 2 mature mDC (CD1c-CD141+ILT3-). CCR2 was expressed in all CD103-SIRPα+ DC, with expression being variable on CD103+SIRPα+ and absent on CD103+SIRPα- DC.

In HC, total DC numbers were higher in the proximal colon compared with the TI with no differences in the CD103/SIRPα DC subset composition between compartments. However, the TI from HC carried higher numbers of CCR2+DC and CD11cdimCD1c-DC.

In CD patients compared with healthy controls, DC numbers were higher in both the colon and the TI and displayed a specific reduction of CD103+SIRPα+ DC in both tissues. CCR2 expression on ileal and colonic DC did not differ between HC and CD. In CD, however, the proportion of ileal CD11cdimCD1c- DC was lower in CD patients than in HC, an effect that was not seen in the proximal colon. Finally, TLR2 and TLR4 expression were higher in both the colon and TI from CD patients, compared with the healthy matched tissue, due to a specific up-regulation of CD11c+CD1c+DC.

Conclusions: DC subsets and phenotype change through the length of the human gastrointestinal tract and display different tissue-specific alteration in CD patients. Tissue compartmentalization is, therefore, likely to affect the Results of studies addressing the immune system of the human gut, both in health and disease.

P006
Intestinal alkaline phosphatase ameliorates experimental colitis via TLR4-dependent pathway

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Background: Intestinal alkaline phosphatase (IAP) is an intestinal brush border enzyme, and the expression of epithelial IAP was reduced in patients with inflammatory bowel disease (IBD). IAP has a protective effect on colonic inflammation possibly due to dephosphorylation of lipopolysaccharide (LPS), but the precise mechanism on colitis has not been clarified. The aim of the present study was to evaluate whether the effect of IAP was mediated via LPS/Toll-like receptor 4 (TLR4)/NF-κB pathway.

Methods: Peritoneal macrophages from wild-type (WT) and TLR4-/- mice were pretreated with IAP, and stimulated with LPS. The secretion

of pro-inflammatory cytokines was measured by ELISA. The effect of IAP on NF-κB signaling was evaluated by Western blot and Electrophoretic mobility shift assay (EMSA). Immunofluorescence was performed to confirm the effect of IAP in WT and TLR4-/- macrophages. For in vivo study, dextran sulfate sodium (DSS) was given for 7 days in WT and TLR4-/- mice, and IAP was administered by oral gavage as preventive or therapeutic models. The effect of IAP on colitis was evaluated by disease activity score and histology, and NF-κB activity in colitis tissue was assessed by phosphorylated IκB-α and p65 immunohistochemistry.

Results: The secretion of TNF-α and IL-6 was significantly inhibited by IAP in the LPS-stimulated WT macrophages, whereas the effect of IAP was much decreased in the LPS-stimulated TLR4-/- macrophages. In the WT macrophages, the IκB-α phosphorylation and NF-κB DNA binding activity were inhibited by IAP. However, the inhibition of NF-κB signaling by IAP was attenuated in the TLR4-/- macrophages. The immunofluorescence staining confirmed that the inhibitory effect of IAP on p65 nuclear translocation in the LPS-stimulated WT macrophages, but not in the TLR4-/- macrophages. In the preventive and therapeutic models of WT mice, oral administration of IAP significantly reduced loss of body weight, disease activity score and histologic grade of colitis. However, the protective effect of IAP was attenuated in the both models of TLR4-/- mice. The inhibitory effect of IAP on p65 and phosphorylated IκB-α expressions was also found in the WT colitis tissue, but the effect was decreased in the TLR4-/- colitis.

Conclusions: These Results revealed that IAP has a protective effect on experimental colitis mainly via TLR4-dependent pathway. The consideration of TLR4 expression or polymorphisms could be useful when administrating exogenous IAP in patients with IBD.

P007
Disruption of phosphatidylcholine paracellular movement to intestinal mucus predisposes to Ulcerative Colitis

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Background: Phosphatidylcholine (PC) in intestinal mucus forms a hydrophobic barrier against colonic microbiota. Ulcerative colitis (UC) is a common inflammatory bowel disease characterized by bloody diarrhea and pain, with a defective mucosal barrier being the most likely underlying cause and for which symptomatic anti-inflammatory therapy is often unsuccessful. Here we propose that our observation of an intrinsic low mucus PC content is a key pathogenic feature of UC, which may result from the disruption of PC translocation into mucus.

Methods: The mechanism of luminal PC secretion was investigated in CaCo2 human intestinal tumor cells grown for 21 days in Transwell tissue culture dishes until apical/basolateral polarization and establishment of tight junctions (TJ. For functional in vivo studies genetic mouse models with ulcerative colitis were employed (intestinal deletion of kindlin 1 and 2). Biopsy samples of patients with UC, Crohn's disease and controls were examined in regard to luminal PC Transport.

Results: This study demonstrates for the first time that phospholipids containing choline but no other head groups translocate by a novel paracellular transport pathway across lateral tight junctions (TJ) to the apical mucus compartment. This translocation is stimulated by apical bicarbonate secretion mediated by cystic fibrosis transmembrane conductance regulator. The apical accumulation of negative charge drives PCs from TJ to the mucus side where PC is trapped to membrane-localized mucin 3. This concept of PC transport across TJ was confirmed in mice with TJ defects caused by intestinal deletion of kindlin 1 and 2: luminal PC secretion in these mice was reduced by 70 %, with the consequent low mucus PC concentration producing an UC phenotype that was mitigated by oral PC supplementation. When biopsies of UC and Crohn's disease patients and normal controls were compared, a disturbed TJ barrier with expanded crypt diameters was detected and paracellular luminal PC movement was suppressed only in UC patients.

Conclusions: Thus, a low PC concentration resulting from disrupted paracellular PC translocation into mucus and the consequent loss of hydrophobic protection by intestinal mucosa is a pathogenic mechanism in the development of UC. Topical PC supplementation delivered by delayed-release oral PC preparations can re-establish the hydrophobic barrier and could serve as an innovative treatment for UC.

P008
IL-34 antibody ameliorates experimental Colitis by alternating IL-12p40 expression in macrophages

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Background: Previously, we reported the involvement of IL-34 in the pathophysiology of Crohn's disease. However, the effect of IL-34 antibody on colonic inflammation remains unclear.Therefore, the aim of this study is to examine the possibility of IL-34 as a therapeutic target cytokine using the murine colitis model.

Methods: 1) Gene expression of IL-34 was evaluated in acute colitis of C57BL/6 mice with dextran sulfate sodium (DSS). To induce colitis in C57BL/6 mice, 3% DSS was provided ad libitum up to 5 days. On day 5, they were switched to normal drinking water. Mice were sacrificed on day 7. 2) To evaluate the possibility of IL-34 as a therapeutic target, the therapeutic effect of intraperitoneal administration of IL-34 antibody (R&D Systems, Inc., Minneapolis, MN) was studied using DSS-induced colitis model. Treatment with intraperitoneal administration of anti-IL-34 antibody (10μ g/body) was performed from day 0 to day4, and mice were sacrificed at day 7. After sacrifice, colon length was evaluated and the severity of inflammation of colon was scored using a histological index. 3) To evaluate the effect of IL-34 on the function of macrophages, gene expressions of inflammatory cytokine were evaluated using peritoneal macrophages derived from C57BL/6 mice. Peritoneal macrophages were incubated with IL-34 (25ng/ml) for 24 hours followed by stimulation with LPS (1μ g/ml) for 24 hours. After stimulation with LPS, gene expressions (TNF- α , IL-6, IL-12p40) were evaluated with real-time polymerase chain reaction (PCR).

Results: 1) Gene expression of IL-34 in colonic tissue of mice with DSS-induced colitis was significantly higher than that in control mice. 2) In DSS-induced colitis model, colon length of IL-34 antibody group was significantly longer than that of control group. Histological score of IL-34 antibody group was significantly lower than that of control group. Moreover, gene expression of TNF- α and IL-12p40 in colon of IL-34 antibody group was lower than that

of control group. 3) After stimulation with LPS, gene expression of IL-12p40 in IL-34 pretreated peritoneal macrophages was significantly higher than that without pretreatment of IL-34, despite there was no difference of gene expression of TNF- α and IL-6.
Conclusions: Our data suggested that IL-34 antibody ameliorated DSS-colitis by alternating IL-12p40 expression in macrophages.

P009
Stimulation of Toll-Like Receptor 7 normalises colonic epithelial barrier function during colitis in mice

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Background: Intestinal inflammation is associated with dysregulated mucosal immune responses and an altered epithelial barrier function (EBF). Stimulators of innate immunity, including Toll-like receptor 7 (TLR7) agonists, have anti-inflammatory activity, with beneficial effects in IBD. We assessed if TLR7 participates in EBF modulation during states of intestinal inflammation.
Methods: Colitis was induced in CD1 male mice (dextran sodium sulfate, DSS; 5 % in water for 5 days). At day 7 (acute colitis), the effects of the acute TLR7 stimulation with Imiquimod (IMQ) on colonic epithelial permeability to macromolecules (4 kDa fluorescein isothiocyanate-dextran, FD4) was assessed in vivo (passage of FD4 administered intracolonicaly to blood and urine) and in vitro (apical-to-basolateral flux FD4 in a Ussing chamber system).
Results: During DSS-induced colitis, passage of FD4 to blood and urine in in vivo conditions was increased by 18- and 26-fold, respectively (P<0.05 vs. non-inflamed controls; Table 1). Acute treatment with IMQ (300 µg/mouse, intracolonic, 1 h before testing permeability) attenuated the passage of FD4, indicating a partial restoration of EBF (Table 1). Preliminary observations show similar effects during the repeated treatment with IMQ (3 consecutive days).
In colonic sheets from DSS-treated animals the in vitro (Ussing chamber) flux of FD4 was increased by 2-fold vs. non-inflamed tissues (P<0.05; Table 2). In these conditions, apical and basolateral addition of IMQ (300 µg) restored the epithelial permeability to FD4 to basal levels. In non-inflamed tissues, apical or basolateral addition of IMQ reduced the flux of FD4 by 44% and 41%, respectively (Table 2).
Conclusions: Stimulation of TLR7 leads to an improvement of epithelial barrier function, observed mainly in inflammatory states. TLR7-mediated innate immune responses might regulate EBF with a defensive function, preventing the passage of luminal factors and, therefore, reducing antigens exposure and the development of exacerbated immune responses and intestinal inflammation.

P010
The Gut Microbiome-Immune System Interaction as an Aetiological Factor for Fistulising Perianal Crohn's Disease

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Background: An interaction between genetic, microbiological and immunological factors drives Crohn's disease. Bacterial infection probably initiates idiopathic anal fistulas but does not maintain them. Dendritic cells (DC) express Toll-Like receptors (TLR), which are pattern recognition receptors that are activated by bacterial ligands. We compared the expression of TLRs and microbiota profiles of CD and idiopathic fistulas.
Methods: Biopsies were taken from Crohn's and idiopathic fistulas at surgery. DC were identified as HLA-DR-positive and lineage-negative, and characterized by flow cytometry using fresh samples. The expression of TLR2 and 4 was determined. Immunohistochemical techniques determined the expression of TLR2, TLR4 and TLR9 on paraffin-imbedded biopsies. DNA was extracted from frozen samples and bacterial 16S rRNA genes were sequenced using a MiSeq sequencer.
Results: TLR2 and 4 were expressed on DC from both Crohn's and idiopathic perianal fistulas using flow cytomtery. There was no significant difference in TLR2 (p=0.27) or TLR4 (p=0.45) expression on CD and idiopathic fistulas. Immunohistochemistry showed equal expression of TLR2 (p=0.42) and TLR4 (p=0.11) on lymphocytes. TLR9 expression was significantly higher in CD fistulas (p=0.01).
Microbiota were classified as common and abundant, infrequent, and rare. The total number of operational taxonomic units (OTUs)

Table 1 Flux of FD4 assessed in vivo (data are mean±sem, n=4–6; *: P<0.05 vs. vehicle-vehicle)

	Vehicle-Vehicle	Vehicle-IMQ	DSS-Vehicle	DSS-IMQ
FD4 in serum (µg/mL)	1.22 ± 0.24	1.71 ± 0.18	22.02 ± 12.65	8.73 ± 4.16
FD4 in urine (µg/mL)	5.96 ± 0.91	12.03 ± 2.78	155.80 ± 60.15 *	85.97 ± 35.46

Table 2 Flux of FD4 assessed in vitro (Ussing chamber) (data are mean±sem, n=5–10; *: p<0.05 vs Vehicle-vehicle. #: p<0.05 vs. DSS-vehicle)

	Apical-to-basolateral flux of FD4 (% in 60 min)			
	Vehicle-Vehicle	Vehicle-IMQ	DSS-Vehicle	DSS-IMQ
Basolateral addition of vehicle/IMQ	0.00156 ± 0.0005	0.00093 ± 0.0004	0.00314 ± 0.0008 *	0.00240 ± 0.00087
Apical addition of vehicle/IMQ	0.00182 ± 0.0005	0.00102 ± 0.0002	0.00408 ± 0.0010 *	0.00190 ± 0.0005 #

observed and the number of species identified in Crohn's fistulas was significantly higher than idiopathic (p=0.02). The most abundant species in the Crohn's group were Bradyrhizobium pachyrhizi followed by Pseudomonas azotoformans and Prevotella oris.
Conclusions: Bacterial products and the local immune response to them are present in perianal fistula tracts. Fistula persistence may be driven by bacterial products rather than live bacteria. This could provide therapeutic treatment targets for Crohn's anal fistulas.

P011
Analysis of Innate-like Lymphocyte Subsets in Ulcerative Colitis

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Background: Ulcerative colitis (UC) is a chronic relapsing and remitting inflammatory disorder of the large intestine. Recent studies have found that the failure of the immune tolerance towards the enteric bacteria or auto-antigens is one major pathogenic mechanism for the immune disorder in UC, but other aetiologic factors are yet to be identified. Innate-like lymphocytes are members of the lymphoid lineage that have emerging roles in mediating immune responses and regulating tissue homeostasis pertained to inflammatory bowel diseases (IBD) including Crohn's disease and UC. This study was to investigate the role of innate-like lymphocyte subsets in patients with UC.
Methods: A total of 36 UC patients and 34 age and gender matched healthy subjects were included in this study. Peripheral blood mononuclear cells (PBMC) were purified, and innate-like lymphocytes (MAIT cells, γδT cells, NK cells, iNKT cells, B-1 cells) were analysed by FACS LSR Fortessa with Flowjo software. Additionally, the production of cytokines including interleukin (IL)-17, IL-6, tumour necrosis factor (TNF)-α and interferon (IFN)-γ from each cell subsets, and activation markers were analysed by FACS. MAIT cells were identified as CD3+γδTCR-Vα7.2TCR+CD16 high cells, γδT cells as CD3+ γδTCR+ cells, iNKT cells as CD1d/PBS-57tetramer+CD3+cells, NK cells as CD3-CD56+cells, and B-1cells as CD19+CD20+CD27+CD43+cells.
Results: In patients with UC, the frequency of MAIT cells and NK cells in the peripheral blood was significantly reduced as compared with healthy controls. The frequency of other innate-like lymphocytes such as γδT cells, iNKT cells, B-1cells showed no significant differences between patients and healthy individuals. The frequency of MAIT cells did not reflect the disease activity in UC patients, however there was a correlation between the activation marker for MAIT cells and the disease activity (measured by Mayo score). Further, MAIT cells from UC patients secreted more IL-17 than ells from healthy controls.
Conclusions: This study demonstrated that the activation marker expression for MAIT cells reflected UC disease activity. Mucosal associated invariant T (MAIT) cells are known as an innate-like lymphocyte phenotype, which exists in the mucosal tissue. The emergence of peripheral MAIT cells depends on the presence of commensal gut flora. Accordingly, MAIT cells could be involved in the pathogenesis of UC, and this study may suggest that the activation marker for MAIT cells may be a new biomarker for UC.

P012
Efficacy, toxicity and positive psychological effects drive IBD patient preferences on steroid use

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Background: Corticosteroids induce remission or response in 85% of patients with active inflammatory bowel disease (IBD). However, corticosteroids have significant toxicity [1] and it has been suggested that their early use may be associated with poor long-term outcomes. We aimed to determine the patient, IBD and steroid-experience factors that shaped patient perspectives on the use of corticosteroids.
Methods: An on-line questionnaire examined patient demographic, IBD, comorbidity and drug therapy data, including patient experiences of corticosteroid use. The primary outcome was whether patients would take corticosteroids again for IBD. Patients were recruited through Christchurch Hospital IBD clinics, CCNZ and associated patient support groups. Patients were ineligible if they were aged less than 18 years or had never received corticosteroids.
Results: Four hundred and fifty-three participants completed the questionnaire and had their data analysed. Baseline demographic, disease and co-morbidity data are shown in Table 1.

Three hundred and twenty-two out of 585 (71.1%) of respondents would use corticosteroids again for the treatment of IBD. In

"Table 1 Baseline characteristics of study population"

	Crohn's disease (321)	Ulcerative colitis (115)	Indeterminate colitis (17)	Inflammatory Bowel Disease (453)
Female Sex (%)	212 (66)	74 (64)	11 (65)	297 (66)
Mean Age (years) (SD)	39 (13)	44 (16)	37 (15)	40 (14)
Currently in a relationship (%)	204 (64)	75 (65)	10 (59)	289 (64)
Post High School Education (%)	147 (46)	62 (54)	14 (82)	223(49)
NZ European Ethnicity (%)	311 (97)	98 (85)	14 (82)	423 (93)
Years since Diagnosis (SD)	11 ± 9	12 ± 11	8 ± 9	10.97 ± 9.30
Previous Surgery for IBD (%)	162 (50)	17 (15)	3 (18)	182 (40)
Mean current HBI (SD)	5.26 ± 3.85	-	-	-
Mean current SCCAI (SD)	-	3.98 ± 3.37	4 ± 3.32	-
Ever hospitalised for IBD (%)	269 (84)	66 (57)	12 (71)	347 (77)
IV Hydrocortisone ever (%)	176 (55)	48 (42)	6 (35)	230 (51)
Immunomodulator use ever (%)	280 (87)	80 (70)	10 (59)	370 (82)
Biological use ever (%)	151 (47)	19 (16)	5 (29)	175 (39)
Depression (ever) (%)	107 (33)	33 (29)	8 (47)	148 (33)
Anxiety (ever) (%)	76 (24)	18 (16)	6 (35)	100 (22)
Current smoking (%)	36 (11)	3 (3)	1 (6)	40 (9)

a multivariate model, previous moderate-complete steroid efficacy (odds ratio (OR) 6.4 [95% confidence intervals (95%CI) 3.6–11.4]), steroid toxicity (OR 0.09 [0.04–0.25]) and positive steroid side effects (e.g., elevated mood or energy; OR 3.3 [95%CI 1.9–5.9]) were associated with patients being prepared to take steroids again for IBD.

Conclusions: While steroids remain a mainstay for the induction of remission of IBD, these data suggest that preferences for steroid use are not only driven by previous experience of steroid efficacy and toxicity, but also positive side effects associated with steroid use.

There is little recognition that some patients may experience mild pleasant side effects from steroids which might encourage prolonged steroid use. However, positive psychological effects may lead to steroid-seeking behavior in a sub-group of IBD patients. Therefore, clinicians should enquire about positive side effects of steroids and monitor those patients who experience them closely.

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P013
Characterization of enterochromaffin cells in pouchitis after proctocolectomy with ileal pouch-anal anastomosis for ulcerative colitis

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Background: Serotonin-producing enterochromaffin (EC) cells are the prevalent neuroendocrine cell type in the gut. EC cells are characterised by the expression of the pan-neuroendocrine marker chromogranin A (CgA). Several immune-mediated gastrointestinal disorders, including inflammatory bowel disease (IBD), are associated with EC cell hyperplasia. We here characterised EC cells in patients with pouchitis after proctocolectomy with ileal pouch-anal anastomosis for ulcerative colitis (UC).

Methods: Serial sections from 17 patients affected by pouchitis and from ileum of 13 IBD patients (5 Crohn's ileitis and 8 UC backwash ileitis) and 11 control subjects were processed for the immunohistochemical detection of CgA and serotonin. Mucosal tryptophan hydroxylase (TpH)-1 and serotonin-selective reuptake transporter (SERT) transcripts were measured by quantitative RT-PCR.

Results: We observed an increase in CgA-positive cells in both patients affected by pouchitis and those with IBD ileitis compared to control subjects, with no difference between pouchitis and IBD ileitis. No change was found for EC cells amongst pouchitis and the other two groups, whereas IBD patients with ileitis have higher EC cells than control subjects. Moreover, we detected an increase in CgA-positive and serotonin-negative cells, calculated by subtracting the number of CgA-positive cells from the number of EC cells, in pouchitis in comparison to IBD ileitis and control subjects. Raised transcripts of mucosal TpH-1, but not SERT, were found in IBD ileitis in comparison to control subjects, without significant difference amongst pouchitis and the other two groups.

Conclusions: We show hyperplasia of neuroendocrine cells in the mucosa of both pouchitis patients and those with IBD ileitis. EC cells and TpH-1 transcripts are increased in the mucosa of IBD patients with ileitis, but not in pouchitis patients. Hyperplasia of neuroendocrine cells seems to be due to other cell types in pouchitis. Further studies are underway to ascertain what is the cell type/s causing neuroendocrine cell hyperplasia in pouchitis.

P014
Selective Janus Kinase 1 inhibitor targets monocytes and tissue macrophages during DSS colitis

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Background: Non-selective Janus Kinase inhibitors have shown efficacy in treatment of inflammatory bowel diseases. Janus Kinase 1 inhibitors (JAK1i) interfere with cytokine signaling which is important in both adaptive and innate immune responses. The aim of this study was to investigate the ability of JAK1i to protect mice from an acute Dextran Sulphate Sodium (DSS) colitis, or to ameliorate a chronic DSS colitis. In addition, cellular targets of JAK1i were examined in vitro and in vivo. JAK1i is a selective JAK1 inhibitor (formerly known as GLPG0555) in-licensed by GSK from Galapagos.

Methods: To assess the effect of JAK1i on inflammatory responses, murine bone marrow derived macrophages (BMDM) were stimulated with LPS 100ng/mL and IFNγ 10ng/mL (n=6) of which 3 mice were stimulated in presence of JAK1i. Next, a microarray experiment (Illumina Mouse WG-6 v2) was performed. Genes downregulated by JAK1i were validated in vitro by qPCR. In DSS experiments C57/Bl6 mice (8-12 weeks) were given 2% DSS in drinking water, combined with oral gavage of JAK1i as indicated in figure 1. Clinical and histological inflammation scoring were performed.

Results: In the microarray experiment, JAK1i (1000nM) downregulated 47 LPS/IFNγ-induced genes and upregulated 37 genes (10-300 log2 fold in comparison to LPS/IFNγ treated BMDM). JAK1i left 88 genes unaffected. JAK1i in vitro showed a downregulation of indoleamin 2,3-dioxygenase (IDO1), kynureninase (KYNU) and

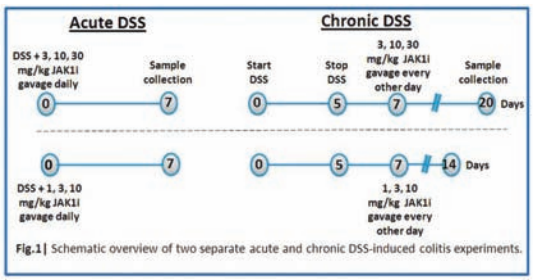

Fig.1| Schematic overview of two separate acute and chronic DSS-induced colitis experiments.

"Figure

lymphocyte antigen 6 complex (Ly6a) in comparison to BMDM treated with LPS/IFNγ alone (resp. p = 0.018, 0.002, 0.001). Next, mice were treated with JAK1i in acute DSS colitis. Treatment with 1, 3, 10 and 30 mg/kg JAK1i did not protect mice from weight loss in comparison to DSS treated animals (all p =1). In contrast, JAK1i worsened clinical disease scores in acute and chronic DSS. Colon samples treated with JAK1i showed a decreased expression of IDO1 and KYNU in comparison to DSS treated colon samples, replicating the effects seen in vitro. In chronic DSS, mice treated with 3 mg/kg JAK1i showed a faster weight recovery at day 14 than mice treated with DSS, 10 mg/kg and 30 mg/kg JAK1i. At repetition, weight of mice treated with 3 or 10 mg/kg JAK1i did not ameliorate in comparison to DSS treated mice at day 14 (both p = 1).

Conclusions: In vivo, JAK1i did not reduce colitis symptoms and mucosal inflammation in acute and chronic DSS colitis. In vitro, JAK1i affects mediators of the tryptophan catabolism in IFNγ/LPS triggered BMDM, which might attribute to compromised bacterial clearance in this colitis model.

P015
Exploring the barrier; RNA sequencing of laser microdissected epithelium from IBD patients

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Background: Studies of the gene expression in IBD colon samples have contributed greatly to the current understanding of IBD pathophysiology. However, all these studies have been performed on full thickness pinch biopsies. Here, the differential expression is dominated by the contribution of inflammatory cells infiltrating the lamina propria. In this study we present an RNA expression sequencing done on laser capture microdissected (LCM) epithelium from ulcerative colitis (UC) and normal control (N) pinch biopsy specimens. By isolating the gene expression to the epithelial monolayer (EM), we identify epithelial processes important in IBD pathophysiology without needing to take contribution from infiltrating inflammatory cells into consideration.

Methods: Pinch biopsies from colonic mucosa of six UC patients and N subjects were collected as previously described[1]. An area corresponding to approx. 10 000 cells was isolated from cryosections of each sample using CellCut Plus LCM microscope. RNA was isolated using RNeasy Plus Micro kit, followed by sequencing using the TruSeq RNA Access kit (Illumina, CA, USA). Reads were aligned to the human genome using Tophat2 and sample quality control was performed using RSeQC. A gene count matrix was built using featureCounts from aligned reads and UCSC gene annotations revised through cufflinks assembly. Differential gene expression analysis was performed using Limma-Voom within the edgeR Bioconductor package.

Results: The analysis resulted in > 4000 differentially expressed (DE) genes between UC and N samples. The resulting list of DE genes agreed with previously published Results from analysis of full thickness pinch biopsies[1]. Genes previously identified as highly expressed in the epithelium of UC colon are also found to be DE between the LCM samples[2]. Enrichment of epithelial cells appears to have been successful. E.g., IL8, a chemokine produced by macrophages infiltrating the lamina propria in IBD, showed in whole biopsies the 3rd highest fold change and a p value <0.001 in the contrast UC vs. N. The present study showed IL8 as the 283rd gene (p value = 0.08) sorted for fold change.

Conclusions: The colon epithelial monolayer has an important role in maintaining homeostasis. A leading hypothesis regarding IBD initiation is that it is result of a loss of epithelial integrity and a breakdown in homeostasis. In this study, LCM of the epithelial monolayer from colonic pinch biopsies followed by expression profiling has been demonstrated to be feasible, resulting in biologically interpretable data. This opens for a targeted interpretation of the role of the epithelial monolayer in IBD pathophysiology.

References:

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P016
Adipokines link childhood Crohn's disease and the gut immune system.

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Background: Crohn's disease (CrD) is an inflammatory bowel disease characterised by dysregulated mucosal immunity underscored by increased numbers of mature dendritic antigen-presenting cells (DC)¬¬. An early symptom of CrD is increased abdominal fat, providing a source of adipokines including leptin (pro-inflammatory) and adiponectin (anti-inflammatory). Exclusive enteral nutrition (EN) containing TGF-beta and medium-chain-triglycerides, induces remission and leads to mucosal healing in active paediatric CrD. We hypothesised that effects of EN involve immunomodulatory actions of lipids and adipokines. Our aims were therefore to investigate adipokines and lipid contents of DC in paediatric CrD before and after EN treatment.

Methods: Methods: Eight CrD children (median = 13, age 9 - 15), with PCDAI at diagnosis (median = 55, range 25 - 65), were treated with EN for 6 weeks. Blood samples were collected before and after therapy. DC were identified in peripheral blood mononuclear cells from paediatric CrD patients as a cell population positive for HLA-DR and negative for CD3, CD14, CD16, CD19, CD34 and CD56 by flow cytometry. Lipid content, maturation status, leptin, leptin receptor, adiponectin and the adiponectin receptor R2 of DC were determined.

Results: Results: Treatment with EN induced clinical remission in all patients (PCDAI < or = 10) and improved nutritional status defined by weight gain. Leptin expression was significantly decreased in DC after EN treatment by 17% (p<0.03) and there was a trend towards a decrease in its receptor. In contrast, the expression of adiponectin and its receptor significantly increased in DC post-EN by 68% and 40% (p<0.007 and p<0.03) respectively.

ILT3 expression, a surface receptor which is highly expressed on immature DC and renders them "tolerogenic", was significantly increased on DC post-EN by 55% ($p<0.03$). There were no significant differences in total lipid content of DC before and after treatment.

Conclusions: Conclusion: Beneficial actions of EN in paediatric CrD may include the inhibition of DC maturation and regulating DC activity by increasing intracellular levels of the immunosuppressive adipokine, adiponectin.

P017
Long-term stimulation with cytokines acquires irreversible accumulation of NF-κB signaling in colonic epithelial cells

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Background: The patients with ulcerative colitis are at increased risk of developing colitis-associated cancer, because long-term Inflammation in colon leads to the development of carcinogenesis. The precise mechanism of the carcinogenesis in colitis-associated cancer however remains unknown. Recently, 3D primary spheroid culture of colon epithelial cells has been established in our group (Nature Medicine 2012). We therefore aimed to assess the effect of long-term stimulation with cytokines on colon epithelial cells in vitro, using 3D primary spheroid culture of colon epithelial cells.

Methods: Colonic crypts were isolated from 8-week old female mouse and were cultured by TMDU method. To mimic chronic inflammation on colon epithelial cells, the mixture of tumor necrosis factor-α(TNF-α), interleukin-1β(IL-1β), interleukin-6(IL-6), lipopolysaccharide(LPS) and flagellin was treated into primary colonic spheroids were added into medium every other day. The expression of NF-κB target genes IL-8, DUOX2 and DUOXA2 was assessed by quantitative RT-PCR. For the analysis of accumulation of NF-κB p65 in nuclei, 3-dimentional immunohistochemistry of whole spheroid was performed by stain with anti-NF-κB p65 antibody. To evaluate reactive oxygen species(ROS) in live spheroids, CellROX Deep Red Stress Reagents (Life echnologies) was added to medium for 1 day. Spheroids were visualized by confocal laser fluorescent microscopy.

Results: The treatment with TNF-α, IL-1β, IL-6, LPS and flagellin showed the significant induction of NF-κB target genes in primary colonic spheroids. Interestingly, continuous treatment with all factors resulted in the elevated expression of DUOXA2 gene. suggesting that NF-κB signaling might be accumulated by the stimulating time.

3-dimentional immunostaining analysis showed stronger accumulation of NF-κB p65 in nuclei by the longer time of the stimulation, indicating that long-term stimulation with cytokines might lead to a stronger activation of NF-κB signaling. Interestingly, amplified NF-κB signaling by long-term stimulation was still active after the removal of all cytokines, whereas NF-κB signaling induced by short-term stimulation was completely shut down by the removal of all cytokines. ROS were induced by the stimulation with all cytokines. Moreover, ROS in the spheroid with long-term stimulation was shown at 11 weeks after the removal of cytokines, suggesting that oxidative stress in the spheroid with long-term stimulation is also irreversible.

Conclusions: Long-term inflammation leads to irreversible NF-κB signaling activation in colonic epithelial cells, suggesting that "signal spiral" might be crucial for the carcinogenesis of colitis-associated cancer.

P018
Role of CCL20-CCR6 axis and MMP9 in the mucosal inflammation and fibrosis in Inflammatory Bowel Disease

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Background: Inflammatory bowel diseases (IBD) are characterized by the activation of the innate immune system. Recent data suggest the alteration of the CCL20-CCR6 axis in IBD. Faecal matrix metalloprotease 9 (MMP9) was lately described as a valuable non-invasive biomarker of the disease activity. Our aims were to investigate the pathogenetic role of the C-C Chemokine ligand 20 (CCL20), human beta defensin 2 (hBD2)-Chemokine receptor 6 (CCR6) axis in the inflamed, fibrotic and healthy areas of the mucosa of the patients suffering from UC (ulcerative colitis), CD (Crohn's disease) or IBS (irritable bowel syndrome), and to observe the MMP9 expression pattern in these samples.

Methods: 76 patients in 2 endoscopic centres were recruited. (Healthy: 29, CD: 25, UC: 14, IBS: 8) Mucosal biopsies were taken from inflamed, fibrotic and healthy area of the colon and inflamed or healthy ileum. QPCR analysis was performed to determine the CCL20 and MMP9 and hBD2 mRNA expression. Immunohistochemistry was performed from frozen colon samples of active ulcered CD or UC and inactive fibrotic CD or CU mucosal samples to analyze CCR6 receptor protein expression.

Results: In healthy patients, ileal and colonic mRNA expression of CCL20 is not significantly different; hBD2 mRNA is not detectable; MMP9 mRNA is significantly ($p=0,0018$) more expressed in ileum compared to colon. In ileal samples both CCL20 and MMP9 are significantly more expressed in inflamed CD compared to the healthy subjects. There was no change in the colonic CCL20, hBD2 or MMP9 mRNA expression in the IBS patients compared to the control group. In CD or UC significantly higher mRNA expression of CCL20 and MMP9 were observed in inflamed mucosa than in macroscopically intact areas. The CCL20 expression is more prominent in the fibrotic zones than in the active ulcers, conversely, MMP9 mRNA expression is less intense in the fibrotic zones. HBD2 expression is just detectable in certain samples from acute mucosal inflammation and fibrotic areas. Regarding to CCR6 we found unique apical expression in the cryptal mucosal enterocytes. The receptor expression is down-regulated in ulcered lesions in CD, but not in UC samples and in the fibrotic areas both in CD and UC group.

Conclusions: Our study shows that hBD2-CCL20-CCR6 axis is involved in ileal and colonic inflammation and even in the scar formation in IBD. CCL20 axis is more active in fibrotic areas, which suggests it may play a role in fibrosis process. We found that MMP9

is more expressed in the normal ileum compared to colon, while elevated MMP9 mRNA level is linked to mucosal lesions in both UC and CD. CCR6 receptor expression profile is different in both diseases. Our data highlights the differences in the immunological process in CD and UC.

P019
Determinism of enteric glial reactivity in Inflammatory Bowel Disease

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Background: In inflammatory bowel disease (IBD) patients, enteric glial cells (EGC) present some differences in the expression level of glial markers. Whether these changes are determined by the pathological environment or represent a constitutive feature of pathological EGC is unknown. The purpose of our study is (i) to determine if, ex vivo, human EGC from IBD patients present the lesions observed in vivo in healthy and non-healthy mucosal areas of Crohn's disease (CD) or ulcerative colitis (UC) patients, and (ii) to determine if an inflammatory environment can reproduce the changes observed in vivo.

Methods: Culture of human EGC from CD, UC and control patients (CONT) and biopsies of IBD patients (18 CD, 9 UC and 15 CONT) were analyzed for glial marker expression as described hereafter. Biopsies were performed by endoscopic procedures in macroscopicaly non-inflamed mucosal area (NI) and in inflamed mucosal area (I) for each patient. Culture of human or rat EGC were subjected to chronic inflammatory stress represented by TNF α and interleukin-1 β (TI; 1ng/ml) or lipopolysacharide (LPS; 0.1µg/ml) for four days. Expression of the glial markers Sox10, S100 β and glial fibrillary acid protein (GFAP) were assessed by quantitative real time PCR and Western blot analysis.

Results: Culture of human EGC from CD, UC and CONT did not present any significant changes in glial marker expression. TI treatment of EGC induced a significant over-expression of the three glial markers. LPS stimulation of EGC also induced an over-expression of Sox10 and S100 β but did not affect GFAP expression. Concerning the biopsies, the mRNA expression levels of Sox10 and S100 β were significantly elevated in I and NI areas of CD patients compared to CONT or UC.

Intermediate isoform of GFAP was significantly increased in inflamed area of CD patients compared to controls (p=0.011).

Conclusions: Our work shows that glial marker expression is determined by the pathological environment and is not a constitutive feature of EGC from CD or UC patients. Secondly, we have observed that GFAP is differentially regulated by inflammatory cytokine and endotoxin. Ex vivo, the LPS reproduces the Sox10 and S100 β expression changes observed in vivo.

P020
Quantification of the concentration of antibodies against Infliximab in human serum using a pure antibody as calibrator

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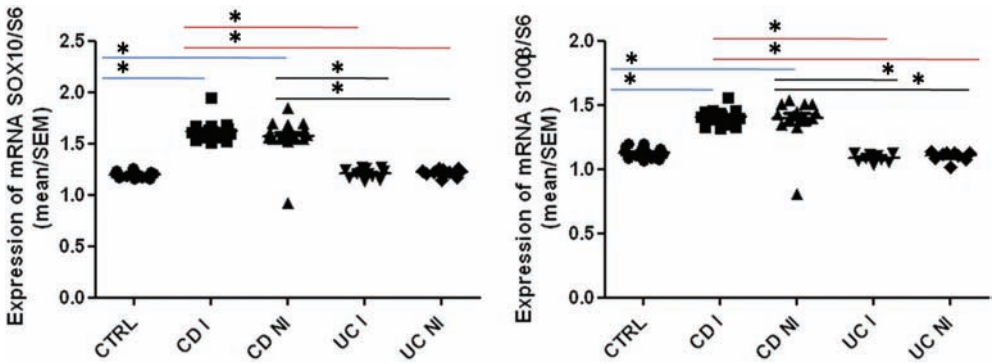
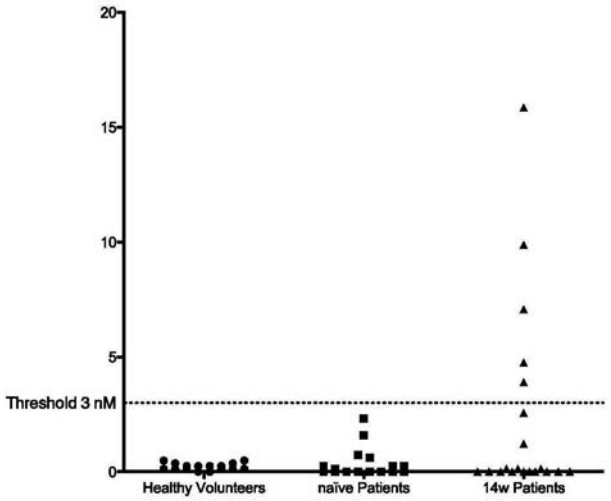
Background: The development of antidrug antibodies (ATI) has been associated with IFX failure. Several Methods have been developed for detecting ATI; homogeneous mobility shift assay (HMSA) is considered the most accurate method as it allows studying the



"Expression of mRNA of S100 and Sox 10 is significantly increased in colonic biopsies of CD patients compared to controls and UC patients"



"Figure 1: ATI levels in healthy volunteers, Crohn's disease patients naïve to anti-TNF drugs and after 14 weeks of treatment with IFX"

interaction between IFX and ATI by analysing the changes in the molecular weight of the drug. This characteristic increases the specificity of the method and avoid false-positive Results observed with ELISA based Methods. However, an optimal calibrator to quantify the concentration of ATI is lacking.

Aims: To improve the method for quantifying ATI by the use of an optimal calibrator.

Methods: Human sera from healthy volunteers (n=20) and Crohn's disease (CD) patients (n=19) were analysed. CD patients with active disease (CDAI>150) naïve to anti-TNF treatment were included. Patients received IFX 5 mg/kg at weeks 0, 2, 6 and 14. Biochemical evaluation of ATI was assessed at baseline and week 14. ATI were measured using HMSA. After incubation of human sera with IFX-alexa 488, samples were injected onto Size Exclusion Yarra 3000 HPLC column (Phenomenex, USA) to measure ATI-IFX complexes. The calibration curve in order to quantify ATI in serum was constructed by diluting a pure IgG1 anti-idiotypic anti-IFX antibody generated by HUCAL (Human Combinatorial Antibody Library) technology (Abd Serotec, Germany) in human serum. The purity of the calibrator was corroborated by electrophoresis and subsequent silver staining. The characterization of the molecular weight of the complex between the calibrator and IFX was estimated by SE-HPLC using IFX-alexa 488

Results: We observed a peak for the complex corresponding to 300 kDa as expected for 2 IgG bound. The calibrator showed a high affinity (Kd = 3.9 nM) and a high specificity for IFX. These parameters were assessed by measuring the decrease of fluorescence of 300 kDa peak in presence of unlabelled IFX for the affinity study and of adalimumab or anti-Fc for specificity study. The calibration curve in a range of concentration of 1.3-33.3 nM was linear. The limit of detection was 1.3 nM. At week 14, 26.3% of the patients (n=5) had over 3 nM of ATI concentration (Figure 1).

This concentration could be considered threshold because none of the healthy volunteers and the patients before receiving IFX had over 3 nM of ATI concentration.

Conclusions: A pure IgG1 anti-idiotypic anti-IFX antibody for the calibration curve allows accurately quantifying the concentration of ATI identified by HMSA

P021
Differential plasma microRNA expression profile in ulcerative colitis patients according to their response to corticosteroids

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Background: Corticosteroids (CS) remain the first line treatment for moderate and severe active ulcerative colitis (UC). However up to 40% of patients do not have an adequate response. We use clinical and biological variables to predict a bad response after three days of treatment, but to date we have not been able to predict response before starting therapy. MicroRNA (miR) are small non-coding RNA fragments that modulate gene expression at a post-transcriptional level, playing a critical role in many biological processes. In previous studies we found a differential miR profile in rectal mucosa of patients with UC responders and non-responders to CS. Objective: To compare the miR profile in plasma of patients with active UC responding and non-responding to CS.

Methods: Plasma samples were obtained from UC patients before CS treatment for a moderate-to-severe flare, and also from healthy controls. Patients were grouped according to clinical response (non-responder = moderate or severe activity according to Montreal's classification or need of rescue therapy at day 7; responder = mild activity or remission without rescue therapy at day 7). miR were identified on plasma samples by means of a sequencing method (Illumina kit). After the comparison between groups those miR with a fold change greater than 1.5 and adjusted p-value less than 0.05 were further studied. Potential targets of selected miR were checked in Target Human Scan and miRwalk database, and their impact on biological activity was searched in GeneCodis database.

Results: 10 healthy controls and 20 patients with UC (10 responders and 10 non responders to CS) were included. Comparison between responders and non-responders showed no significant differences. However, we found three miR with differential expression between healthy controls and non-responders (miR-1290, miR-4508, and miR-149-5p). In silico study of these miRNAs showed more than 1000 genes potentially regulated by each, mainly involved in MAPKinasa signaling pathway, regulation of cytoskeletum, calcium signaling pathway, and endocytosis.

Conclusions: The plasma miR profile obteined in the present study is not usefull to identify patients with active UC not responding to CS. However further studies integrating plasma and tissue miR profiles may help us to develop a potential biomarker of response to CS in UC.

P022
Histone deacetylases in inflammatory mucosa distinguish Crohn's disease from ulcerative colitis

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Background: Inflammatory bowel disease (IBD) creates a high burden of both patient disability and health care costs. There is a high unmet need to better understand the pathophysiology of IBD, leading the way to novel therapeutic targets. Histone deacetylation (HDAC) regulates chromatin remodeling and influences inflammatory gene transcription. Sirtuin(SIRT)1, SIRT6 and HDAC9 are members of the HDAC superfamily that exert proinflammatory properties. Interestingly, murine research suggested a critical role for HDAC9 in breaching immune homeostasis in experimental colitis. Considering the advent of a new generation of HDAC inhibitors we aimed to explore the role of HDACs in IBD.

Methods: We collected colon resection tissue from Crohn's disease (CD) patients and ulcerative colitis (UC) patients operated on for therapy refractory disease. From each patient both macroscopically inflamed and non-inflamed areas were collected, and for CD patients stenotic lesions were collected as well. For RNA isolation the lamina propria was separated from the muscularis externa, and a micro array was performed for HDAC and SIRT mRNA expression.

Results: Baseline characteristics were comparable for 15 CD (47% male) and 9 UC (66% male) patients with mean age at operation of 34 +/- 10 years in CD and 37 +/- 10 years in UC pts. Of the CD patients, 53% had ileal and 47% ileocolonic disease, of the UC patients had 44% left sided colitis and 56% pancolitis. Serum CRP levels immediately before surgery averaged 18 mg/L in both cohorts. Expression of HDAC9 was at average 3.81 fold higher in the inflamed mucosa in CD patients compared to the inflamed mucosa of UC patients (p=0.002), in the uninflamed mucosa the expression of HDAC did not differ significantly. Moreover, in the inflamed mucosa of CD patients SIRT6 was significantly upregulated in comparison to UC patients (p=0.003), whereas in the inflamed muscularis mucosa the expression of SIRT1 was higher in CD than in UC patients (p=0.04). Intriguingly, the increased levels of HDAC9, SIRT1 and SIRT6 were only present in inflamed tissue and were found to be the same compared to UC in stenotic or non-inflamed lesions.

Conclusions: Our findings show an increased expression of HDAC9 and SIRT6 in the mucosa of inflamed CD colon compared to inflamed UC colon. Therefore, histone deacetylases expression has the potential to serve as an additional marker to distinguish CD from UC in tissue biopsies. Further research is necessary to investigate the functional properties of histone deacetylation in CD pathogenesis, which could grant opportunities for therapeutical action.

P023
Dipotassium glycyrrhizate normalises the mucosal healing gene expression altered by inflammation in a murine model of colitis

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Background: Dipotassium glycyrrhizate (DPG) is a compound derived from glycyrrhizin, a glycoconjugated triterpene produced by the licorice plant, Glycyrrhiza glabra, whose anti-inflammatory properties are well-known. DPG reduce inflammation though various mechanisms, including the inhibition of the alarmin high mobility group box (HMGB)1 and the enzyme 11beta-hydroxysteroid dehydrogenase 2 (11betaHSD2). We previously demonstrated that DPG significantly reduces the DSS-induced colitis in mice, that showed a surprising recovery of body weight and large intestine length as well as an increase in histological score, the latter indicating the occurrence of a mucosal healing (MH).

The aim of the present study was to deeply investigate the effect of DPG on the expression of genes involved in the mucosal healing (MH) pathway during inflammation

Methods: C57BL/6 mice were divided into 3 experimental groups (5 mice for each group): DSS (3%)-treated mice, DSS (3%)+DPG (8mg/Kg)-treated mice and control mice. After 7 days, mice were sacrificed and the colon removed. Tissue samples were analysed by a PCR array (QIAGEN) able to evaluate 84 key genes central to the wound healing response. To identify the most altered genes, a threshold of 3.5 times was chosen. Selected genes were divided into functional groups. The expression level of the most altered genes inside each group was validated by RT-PCR

Results: DSS treatment significantly up-regulated 19 MH genes, as showed by comparing DSS-treated vs control mice. These genes were significantly down-regulated to control values by DPG treatment, as showed by comparing DSS+DPG mice vs DSS mice.

Altered genes were classified into 6 different functional groups: cytokines (IL-10, IL-1beta, IL-6), chemokines (CCL12, CCL7, CXCL1, CXCL3, CXCL5), extracellular matrix (ECM) components/collagen proteins (Col3a1, Vtn), growth factors (Csf3, Fgf2, Fgf7), remodelling enzymes (Mmp9, Timp1, Plat, Plaur, Serpine1), others (Ptgs2). Expression analysis of most altered genes within each functional group was validated by RT-PCR ($p<0.001$:IL-1beta, IL-6; $p<0.01$: CXCL3, CXCL5, Col3A1, Vtn, Fgf7; $p<0.05$: Mmp9, Serpine1).

Conclusions: We show for the first time that the use of DPG in mice with a DSS-induced colitis strongly improves the MH by modulating the expression levels of genes involved in wound healing response. Due to the total lack of side effects, we believe that DPG could represent a very innovative and useful tool for the management of human intestinal inflammation

P024
Role of Interleukin 27 (IL-27) in the Colonic Mucosa of Patients with Inflammatory Bowel Disease.

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Background: The pathogenesis of inflammatory bowel disease (IBD) is not completely understood. The chronic relapsing inflammation is thought to be the result from a pro-inflammatory microenvironment and an aberrant immune response. The interleukin 27 (IL-27) is an immune-regulatory cytokine, has both anti- and pro-inflammatory properties. As an anti-inflammatory, IL-27 seems to induce a general negative feedback program that limits T and NK-T cell activity and also mediates inflammation during chronic disease. Nevertheless, no previous studies have explored their expression in patients with IBD.

Methods: This is an observational and cross sectional study, we included a total of 30 active UC (aUC), 22 inactive UC (iUC), 20

active CD (aCD), and 20 inactive CD (iCD) patients and 30 patients as control group (without endoscopic and histological evidence of intestinal inflammation). Gene expression was measured by real time polymerase chain reaction (RT-PCR). Protein expression was detected in tissue by immunohistochemistry. The Dunn´s Test was used for all pairwise comparisons and comparisons against the control group following rank-based ANOVA

Results: The IL-27 gene expression was significantly elevated in control group versus active UC (P=0.04) and inactive UC (P=0.02). The IL-27 expression was increased in patients with active CD compared to inactive CD (P=0.03). We also found a decrease expression of IL-27 among active CD versus non-inflamed tissues. In order to determine in situ the IL-27 protein expression in intestinal tissue from IBD patients, tissues were immunostained and compared with non-inflamed tissue. The percentage of IL-27 immunoreactive cells was higher in active UC compared with CD patients and controls. The IL-27***producing cells were found mainly in mucosa, submucosa, muscularis, adventitia and perivascular inflammatory. The IL-27 was synthesized largely by epithelial cells, endothelial cells and lymphocytes.

Conclusions: The IL-27 gene expression and producing cells in active UC patients were increased compared with non-inflamed tissues and CD patients. We found different gene expression of IL-27 between UC and CD groups. This cytokine might significantly shape and differentiate inflammatory process, severity, and tolerance loss between UC and CD pathophysiology. Additional studies are required about IL-27 in the gut mucosal immune response in order to confirm the role of this cytokine in patients with IBD.

P025
Matrine induces intestinal apoptosis in dextran sulfate sodium-induced colitis

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Background: Matrine, the major alkaloid component from Sophora flavescens, has been used to treat chronic hepatitis in China. It has been reported that matrine has several pharmacological effects including regulation of immune reaction. However, the impact of matrine is unknown on intestinal apoptosis.

Methods: Intestinal epithelial cells (IEC-18) were used to determine the in vitro effect of matrine on LPS-induced apoptosis signaling. The therapeutic efficacy of matrine was assessed using dextran sulfate sodium (DSS) induced colitis model with mice. Matrine (100 or 200 mg/kg) was administered by using oral gavage. Disease activity index including weight loss, stool consistency, and stool blood and histology score was used to determine the colitis severity. Apoptosis of mouse was evaluated with Western blot and TUNEL assay.

Results: In vitro study, the expression of Bax significantly increased, Bcl-2 and Cox decreased in IEC-18 cells treated with matrine. The effect for inhibition of appoptosis, evaluated by Western blot was increased with dose of matrine. In DSS-induced acute colitis, disease activity index and histological scores were not significantly different among the mice groups according to the matrine treatment. As shown in vitro study, the expression of Bcl-2 was decreased in the matrine treatment mice. However, Bax was increased in low dose matrine (100 mg/kg) and decreased in high dose (200 mg/kg). In the same manner, cleaved Caspase-3 was increased in the mice group treated with low dose matrine. Furthermore, Tunel assay in colon tissues of matrine treated mice was not significantly different with that of matrine untreated mice.

Conclusions: Although matrine didn't have significant effect on inhibiting intestinal inflammation, matrine increased the apoptosis on LPS-induced IEC-18 cells and DSS-induced colitis through decrease of Bcl-2 and increase of Bax and cleaved Caspase-3.

P026
Relationship between histological and endoscopic activity and angiogenic and lymphangiogenic factors expression in patients with inflammatory bowel disease

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Background: Aim: To correlate the main angiogenic and lymphangiogenic factors expression in colonic mucosa biopsies with the endoscopic and histological activity in patients with inflammatory bowel disease (IBD)

Methods: Prospective study in patients with IBD that underwent a colonoscopy because of medical criteria. Samples of colonic tissue biopsies for histological analyses were obtained. In patients where activity was observed during colonoscopy, samples from affected and non-affected mucosa were also taken. Endoscopic activity was assessed by endoscopic Mayo subscore for ulcerative colitis (UC) and SES-CD for Crohn's disease (CD). Considering histological findings, patients were classified into four groups: Quiescent IBD, mild, moderate and severe lesion. VEGFA, -C, -D, -R1, -R2, -R3 and PlGF expression Results were graded as follows: (++) over 50% of the tissue cells were stained, (+) below 50%, and (-) completely negative. Ang1, Ang2 and Tie2 were assessed as the average density of five hot spots at a magnification of x40. Protein expression was determined by immunohistochemistry

Results: 82 biopsies from 58 patients with IBD (36 UC and 22 CD) were included. 64% of the patients did not have endoscopic activity, 16% had moderate, 14% mild and 6% severe activity. There were significant ($p<0.01$) differences in the mean count of Ang1 and Ang2 depending on endoscopic activity. Higher expression of Ang1 and Ang2 was found when the endoscopic activity was severe compared to inactive disease. According to histology, 60% of the patients had quiescent IBD, 20% had moderate lesions, 15% mild and 5% severe lesions. Expression of VEGFD ($p<0.05$), PlGF ($p<0.05$) and VEGFR3 ($p<0.01$), and mean count of Ang1 ($p<0.05$) and Ang2 ($p<0.01$) were also significantly different depending on the histological activity. These expressions were increased in parallel with the severity of histological lesions excepting for VEGFD, that was decreased with the severity of the activity. Positive correlations ($p<0.05$) between histological activity and expression of Ang1 ($r=0.4$), Ang2 ($r=0.5$), PlGF ($r=0.4$), VEGFC ($r=0.3$), and VEGFR3 ($r=0.3$), and negative for VEGFD ($r=-0.3$), were demonstrated. On the other hand, positive correlations ($p<0.05$) between endoscopic activity and expression of Ang1($r=0.4$), Ang2($r=0.5$), PlGF($r=0.4$), and negative for VEGFD($r=-0.3$), were found. The best area under the Receiver Operator Characteristic (ROC) curve for the diagnosis of histological activity was 0.73 for Ang1 (cut-off at 39.8: 89% sensitivity and 56% specificity)

Conclusions: The expression of VEGFA, -D, -R3, PlGF, and Ang1 and -2 in mucosal biopsies correlates with the histological activity of IBD. Ang-1 and -2 expressions in mucosal samples are markers of histological and endoscopic activity

P027
Dysregulation of T cells by N-glycosylation: a new molecular mechanism in Inflammatory Bowel Disease pathogenesis.

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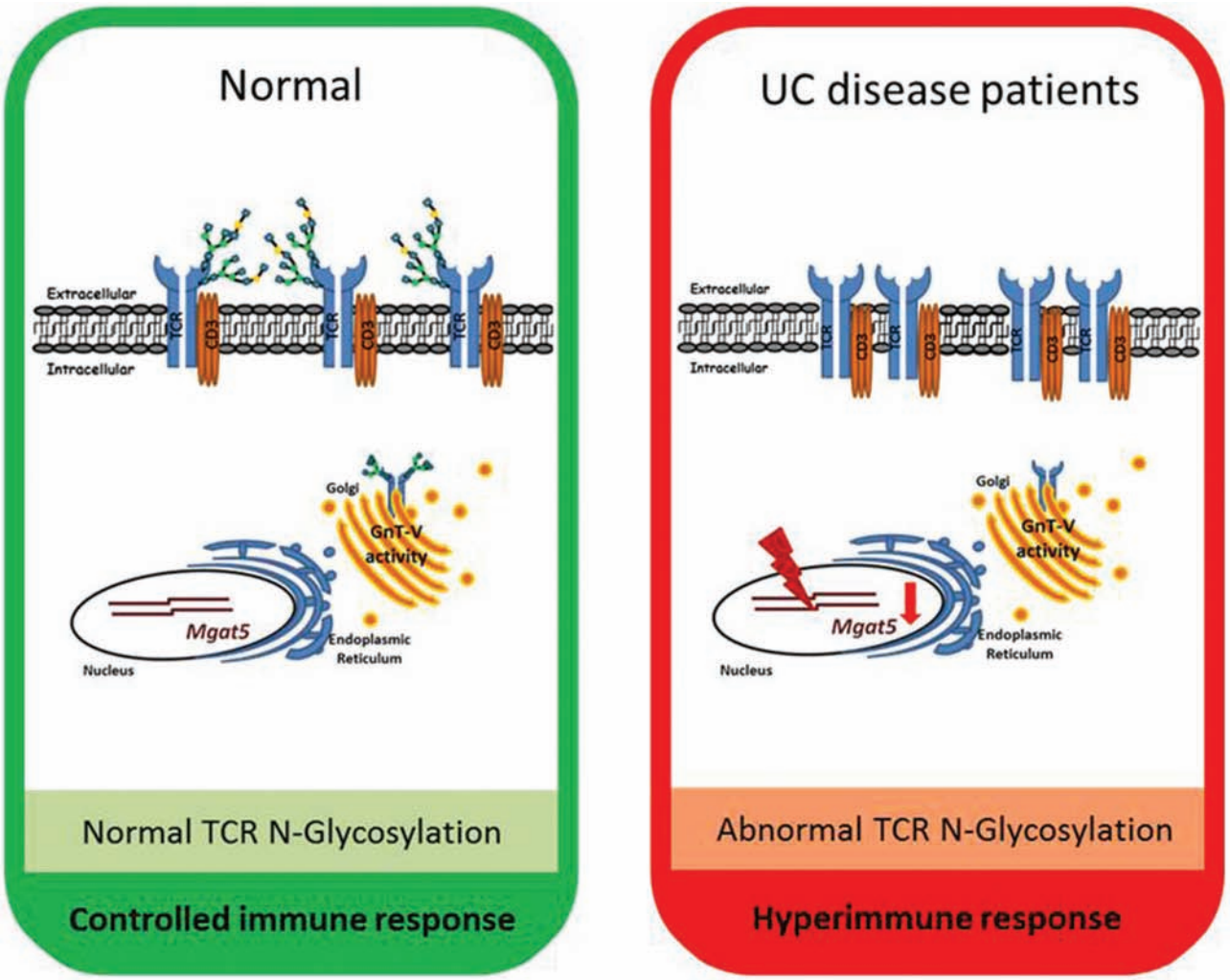
Background: Accumulating evidence suggests that IBD Results from an inappropriate inflammatory response in a genetically susceptible host, although the underlying molecular mechanism remain elusive. One of the major clinical gaps in IBD is the ability to predict the severity of flares and their response to treatment. It is therefore of paramount importance to characterize the underlying molecular mechanism of IBD pathogenesis in order to improve the development of novel biomarkers that help the determination of prognosis and also improve the patients´ therapeutic stratification.

Recent evidences support that T cell activity and function is tightly regulated by post-translational modifications through glycosylation [1] [2] [3] [4] .

In this study we address whether the (dys)regulation of N-glycosylation in T cells activity and function is a major contributory factor and an yet uncovered molecular mechanism in IBD.

Methods: The evaluation of the branched N-glycosylation levels and profile of intestinal T cell receptor (TCR) were assessed in colonic biopsies from Ulcerative Colitis (UC) patients and healthy controls. The underlying molecular mechanism was assessed using ex vivo intestinal T cells from UC patients and IBD-induced mouse models. Expression alterations of the glycosyltransferase gene MGAT5 were also evaluated [5] .

Results: Our Results showed that UC patients exhibit a dysregulation of GnT-V-mediated glycosylation of the TCR from intestinal lamina propria T cells. Patients with severe UC showed the most pronounced defect on N-glycan branching in mucosal T cells [5] .



"Tcells regulation by N-glycosylation in IBD."

This dysfunction of GnT-V-mediated T cells glycosylation was shown to affect T cell function and signaling, being associated with increased T cell proliferation; increased TH1 differentiation and hyperimmune response. We also showed that UC patients (with active disease) exhibit, in T lymphocytes, a reduced MGAT5 gene expression, which underlies the observed dysregulation of T cells N-glycosylation. This deficiency in T cells N-glycosylation accompanies disease severity.

Conclusions: Overall, this study shows a new molecular mechanism in IBD pathogenesis through T cells regulation by N-glycosylation [5], opening new windows of opportunity to further explore the potential applicability of this mechanism in predicting disease course and/or susceptibility

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P028
Role of the receptor for advanced glycation end products (RAGE) in intestinal fibrosis

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Background: Intestinal fibrosis is a common and severe complication of inflammatory bowel disease (IBD) characterized by excessive deposition of extracellular matrix components (ECM). Inflamed colonic mucosa of patients with active IBD shows a significant increase in expression of the receptor for advanced glycation end products (RAGE), a member of the immunoglobulin superfamily of cell surface receptors. Several evidences in kidney, liver and lung fibrosis show how the increased myofibroblast activation and the consequent ECM accumulation are regulated by RAGE.

Aim of this study is to investigate the involvement of RAGE i) in in vitro differentiation of human colonic fibroblasts (CCD-18 Co) and epithelial cells (HT29) into myofibroblasts and ii) in the development of the DSS-induced intestinal fibrosis in mice.

Methods: Differentiation of CCD-18 Co and HT29 into myofibroblasts was induced by 4 day of TGF-beta administration (1ng/mL and 10 ng/mL, respectively). Expression of alpha-SMA (ACTA2) gene and fibronectin (Fn-1) gene, as well as RAGE was measured by quantitative RT-PCR. Chronic colonic fibrosis was induced in C57BL/6 mice by successive 2,5% (w/v) DSS administration in drinking water for 6 weeks. After 6 weeks main parameters associated to a pro-fibrotic profile were assessed macroscopically (weight/length of the colon, edema, ulcers, adhesions, thickness, dilatation), histologically (inflammatory infiltrate, collagen deposition) and biologically (Tgf-beta1, Col1A1 and Fn-1 gene expression)

Results: TGF-beta-induced myofibroblast activation was associated to a significant increase in the ACTA2 expression (65%, p< 0.01 for CCD-18 Co and 183.8%, p< 0.001 for HT29) and mRNA Fn-1 levels (75.5%, p<0.001 in CCD-18 Co and 122%, p< 0.001, in HT29) and correlated with a significant RAGE upregulation both in CCD-18 Co and HT29 (48%, p<0.005 and 1.47%, p<0.005, respectively). RAGE-/- mice showed a significant 23.8% decrease of total macroscopic score and 49% decrease of total microscopic score compared to WT mice. mRNA Tgf-beta1 expression was significantly increased 3.4 fold by the DSS administration in WT mice colon, whereas it was unchanged in RAGE null mice compared to mice receiving only tap water. Col1A1 and Fn-1 genes were upregulated in DSS-treated WT mice (5.52 folds, p= 0.137 and 53 folds, p= 0.0016, respectively). Lack of RAGE decreased 3.17 folds (p= 0.0341) Col1A1 expression and totally prevents the Fn-1 upregulation induced by DSS treatment

Conclusions: The potential pro-fibrotic RAGE properties in IBD represent a new frontier for a better understanding of the mechanisms related to intestinal fibrosis and for the development of new therapeutic approaches.

P029
Amyloidosis in Inflammatory Bowel Disease: Preliminary Results of screening in a selected population

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Background: Amyloidosis is deposition of insoluble fibrils in extracellular space. Secondary amyloidosis(AA)is seen as a result of chronic inflammation.Amyloid fibrils are mainly deposited in kidneys, heart, spleen and liver. Kidney involvementmainly causes overt disease. Main treatment is the control of underlying disease. We have recently encountered an ulcerative colitis (UC) patient with renal amyloidosis leading to nephrotic range proteinuria.

Methods: We screened pathological specimens of 20 difficult to treat inflammatory bowel disease(IBD) patients (4 Crohn's, 16 UC)finding 2 more patients with amyloid staining in colonic biopsy specimens. We like to share our Results and provide a brief review about AA

Results: First patient is a 43 year-old male with a 7 year history of UC who did not attend to regular follow up. His albumin was 2.14 g/dl, creatinin 0.62 mg/dl, sedimentation 85 mm/hr. Daily protein excretion was found to be 6450 mg. There was a fragile concentric narrowing between 8-23 cm of colon with pseudopolyps. Pathology confirmed the presence of amyloid in a vessel wall and AA type amyloidosis was detected after typing. The patient did not respond to medical therapy both in terms of proteinuria and diarrhea and surgery was advised. After that we retrospectively screened our 20 difficult to treat IBD patients . First is a recently diagnosed 54-year old female UC patient with a 30 year history of ankylosing spondylitis(AS).Reevaluation of the specimens revealed amyloid staining. Her albumin was 4.12 but she had 330 mg/day protein excretion, significant but not in the nephrotic range. Second is a 38 year old female with pancolitis diagnosed 2.5 years ago.

Colonoscopy performed at initial diagnosis revealed multiple pseudopolyps across the whole colon suggesting the disease activity has been long going. Her serum albumin was 4.5 and again urine collection revealed 320 mg/day protein excretion.

Conclusions: Secondary amyloidosis in IBD is a rare entity mostly described for Crohn's disease .Incidence of secondary amyloidosis is reported to be < 1% in Crohn's disease and 7/10000 in UC. Predisposing factors are suppurative complications or extraintestinal manifestations.Resection of the involved bowel may be considered in selected cases. But most important is the medical treatment of the IBD.

Our 3 patients with amyloid staining suggest that uncontrolled disease activity may cause amyloid deposition in colon and possibly in kidneys. Clinical implication of amyloid positivity in IBD remains to be determined. Urinanalysis should be routinely performed in IBD patients.Serum albumin can be normal in amyloid positive patients. Also in difficult to treat patients histological specimens should be also be evaluated for amyloid staining.

P030
Analysis of the protease MT1-MMP as therapeutic target in IBD

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Background: We have recently demonstrate higher levels of the MT1-MMP by qPCR -in biopsies- and higher levels of its substrates thrombospondin-1 (TSP1) and nidogen-1 (NID1) -in serum- from patients of inflammatory bowel disease (IBD), a chronic disorder involving inflammation and angiogenesis. Our objective was analysing the functional role of MT1-MMP in the angiogenesis and damage produced in IBD.

Methods: Gene expression of MT1-MMP was detected by qPCR in biopsies, and TNF α , VEGFA, TSP1, NID1 levels were quantified by ELISA in serum from patients with active ulcerative colitis (UC) or Crohn's disease (CD). Clinical IBD activity was assessed respectively by the Mayo score for UC, and by the Harvey-Bradshaw index for CD. Endoscopic activity was determined with the Mayo subscore and the SES-CD index. MT1-MMP, TSP1 and NID1 expression and the angiogenic response were also analyzed by immunostaining (IF) in colonic sections from controls or patients affected by IBD. Besides, we used a mouse model of dextran sulphate sodium (DSS)-induced colitis to analysed the angiogenic response by IF with the specific endothelial cell markers CD31, VE cadherin, and the expression of MT1-MMP, and its substrates TSP1 and NID1 by IF of histological colon sections from either control mice or mice treated with 1% DSS (moderate colitis) or 4% DSS (severe colitis), in wild type mice. The endothelial MT1-MMP expression was also analysed in MT1-MMP$^{LacZ/+}$ mice. Finally, the in vivo functional analysis was done in mice with endothelium-specific deletion of MT1-MMP generated by (MT1-MMP$^{flox/floxx}$VECadhERT2-Cre) breeding analyzing: (i) colitis score; (ii) vascular pattern quantifying, perfusion, endothelial proliferation and colonic hypoxia (injection and stainings of isolectinB4, EdU, and Pimonidazole); and (iii) inflammatory infiltrate (IF with CD11b).

Results: MT1-MMP expression was higher in biopsies of patients with active IBD, moreover, serum levels of TSP-1 and NID1 were significantly increased in UC and CD patients with low activity. In the mouse colitis model, serum levels of TNF α*** , VEGF-A, TSP1 y NID1 and MT1-MMP expression in intestinal tissues, were increased along the progression of the mouse disease, as well as the angiogenesis in the intestinal mucosa. Our preliminary Results indicate that the absence of MT1-MMP in EC protects from IBD, through a vascular normalization (reestablishment of structure and function of blood vessels), with the consequent decrease of colonic hypoxia and inflammation.

Conclusions: These data support the potential use of TSP1 and NID1 as biomarkers in the diagnostic of pre-symptomatic or low activity IBD, aiming the endothelial MT1-MMP as a new therapeutic target for normalization of vasculature and improve the symptoms in IBD

P031
GPR84 inhibition as a novel therapeutic approach in IBD: mechanistic and translational studies

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Background: GPR84 is a GPCR activated by medium chain fatty acids, mainly expressed in white blood cells. White blood cell migration is induced by GPR84 agonists. Recently, we reported that pharmacological GPR84 inhibition reduces disease activity in experimental colitis (Dupont et al., UEGW 2014). To gain mechanistic insights, the impact of GPR84 inhibition on colon gene expression profiles was investigated in experimental colitis. In addition, translational studies were engaged, measuring GPR84 expression levels in patient samples.

Methods: In vivo efficacy of GLPG1205, a GPR84 antagonist, was evaluated in a mouse chronic DSS (dextran sodium sulphate, 3 cycles)-induced colitis model using macroscopic and histopathological scorings and gene expression analysis (Affymetrix mouse genome 430 2.0 array). Blood and intestinal samples from ulcerative colitis (UC) and Crohn's disease (CD) patients were collected (before and after first Infliximab treatment, with response to treatment defined as complete mucosal healing) as well as from healthy controls. Gene expression was analysed (Affymetrix Human Genome U133 Plus 2.0 Array, QrtPCR and immunohistochemistry (IHC)).

Results: Disease activity in a chronic DSS model was strongly reduced by GLPG1205 (10mg/kg, q.d.) and sulfasalazine (SSZ,

20 mg/kg, q.d.). Micro-array analysis of expression profiles in DSS-treated mice showed a strong negative correlation between GLPG1205 treatment and controls (R2=0.8), comparable to the impact of SSZ (R2=0.75). Comparison to human expression datasets showed an impact of GLPG1205 on several gene sets associated with IBD. Micro-array and QrtPCR data indicated an increase in GPR84 expression in inflamed UC colon and CD colon/ileum which was more pronounced in patients not responding to infliximab. Moreover IHC showed a positive GPR84 staining in mucosal inflammatory cells which was increased in active IBD mucosa and very pronounced in granuloma and pouchitis samples. Additionally, patient blood samples displayed increased GPR84 expression levels as well.

Conclusions: GLPG1205 has profound effects on experimental colitis that were confirmed at gene expression level and were comparable to SSZ. In patient biopsies, an increase in GPR84 expression was observed, reflecting infiltration of the mucosa by GPR84+ inflammatory cells. The increased GPR84 expression specifically in active disease conditions represents an advantage with regard to the safety profile of GPR84 inhibitors. As GPR84 expression is increased in circulating white blood cells of patients, GPR84 inhibition may impact disease through systemic effects as well.

P032
Pharmacokinetic Properties of RPC1063, a Selective S1P1 and S1P5 Receptor Agonist, Significantly Contribute to Efficacy in Animal Models of Inflammatory Bowel Disease

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Background: Pharmacologic activation of the sphingosine 1-phosphate 1 receptor (S1P1R) leads to immunomodulatory effects as a consequence of disruption of lymphocyte egress from secondary lymphoid organs. RPC1063, an S1P1,5R agonist, is in clinical development as an oral monotherapy for inflammatory bowel disease (IBD) and relapsing multiple sclerosis (RMS). The aim of this study was to assess RPC1063 and other novel S1P1,5R modulators with similar potencies but varying pharmacokinetic (PK) profiles for their efficacy in a TNBS model of IBD. RPC1063 was further assessed in a CD4+CD45RBhi T cell adoptive transfer model in SCID mice.

Methods: In the TNBS model, 14 compounds were assessed in 7 separate studies. Compounds were administered by orally to Sprague-Dawely (SD) rats once a day at 1 mg/kg for 7 days, with the first dose 2 hours post-TNBS instillation. Prednisolone served as a positive control. RPC1063 was further assessed at 0.1, 0.3 and 1 mg/kg. Improvements in body weight, colon shortening, weight, thickening, length:weight ratio, ulcer number and size, strictures and adhesions were quantified. Circulating lymphocytes were quantified at the end of the study. Plasma PK parameters were determined in separate studies by oral gavage in SD rats. For the adoptive transfer model, RPC1063 was administered after establishment of disease at 1.2 mg/kg PO and continued for 21 days. An anti-TNF antibody (300 µg 1x/week, IP) served as a positive control. Experimental end points included body weight change and histopathology. Statistical analysis was by Student T-test or One-way ANOVA, and correlations determined by calculating Pearson r.

Results: In the TNBS model, 3/14 compounds, including RPC1063, significantly ameliorated ($p<0.05$) all 8 disease parameters. There were significant correlations between efficacy and volume of distribution (Pearson r=0.6, P=0.027), Cmax (Pearson r=-0.6, P=0.035), and exposure (AUC; Pearson r=-0.8, P=0.001). RPC1063 significantly suppressed colitis in both disease models. Histopathological analysis in the adoptive transfer model established that RPC1063 preserved intestinal architecture and significantly reduced inflammation, gland loss, erosion and epithelial hyperplasia.

Conclusions: RPC1063 is a selective S1P1,5R agonist that demonstrates significant efficacy in two animal models of IBD. Importantly, optimal PK properties of RPC1063, including a high volume of distribution, appear requisite for maximal efficacy in models of IBD. This data supported the decision to evaluate RPC1063 in humans where it has demonstrated a strong safety and efficacy profile during the induction stage of a phase 2 ulcerative colitis clinical trial and in a phase 2 RMS clinical trial.

P033
Expression of aryl hydrocarbon receptors (AHR) in the condition of experimental acute ileitis and administrations simvastatin and antagonist of receptors in interlekin-1

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Background: The aryl hydrocarbon receptor (AhR), a transcription factor activated by a large number of environmental agents, modulates the activity of immune and no immune cells in the gut, and may represent an important link between the environment and the immune perturbations which underlie the pathogenesis of inflammatory bowel disease. We studied the possibility of simvastatin and antagonist of receptors of interleukin-1 for pharmacological correction of acute ileitis in rats with a focus on the expression intensity studies of AhR with lymphocytes of small intestine.

Methods: Experiments were carried out on male Wistar rats aged 5-7 months (body mass 260-285 g). Rats were divided into four experimental groups: group 1-control; group 2-rats with indomethacin-induced ileitis; group 3-rats given Simvastatin; group 4-rats given antagonist of receptors of interleukin-1. For induction of an acute ileitis, rats received one subcutaneous dose of indomethacin (Sigma, 15 mg/kg).The AhR immunopositive lymphocytes were determined using an indirect immunofluorescence technique with using a monoclonal rat antibody (Santa Cruz Biotechnology).

Results: We established that development of ileitis was accompanied with the change of amount of AhR + lymphocytes and the density of AhR in immunopositive cells. Drug administration during the development of experimental pathology was accompanied by changes in the expression of AhR and their density on lymphocytes.

Conclusions: These novel findings may help explain how Simvastatin and antagonist of receptors of interleukin-1 seemed to be beneficial in indomethacin-induced rat ileitis model through regulate mucosal immune responses and modulate AhR expression with lymphocytes of small intestine.

P034
The IBD-Cope: A new instrument for measuring coping in Inflammatory Bowel Disease patients

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Background: Inflammatory bowel disease (IBD) has a major impact on psychological wellbeing. Coping is the cognitive and behavioral efforts to mitigate the burden of a stressor, such as a chronic illness [1] . Coping has often been associated with disease activity and health related quality of life (HRQOL) [2] . There is no IBD specific coping instrument. A disease specific approach is likely to improve the predictive power [3] . We aimed to develop a brief, IBD-specific questionnaire (IBD-Cope) to assess coping strategies and to determine whether it has test-retest reliability and validity.

Methods: Twenty items were initially selected for the questionnaire. Participants were recruited from a database. Test-rest reliability was performed on these questions and intraclass correlation coefficients (ICC) determined the most pertinent items (ICC>0.65). Exploratory factor analysis (EFA) led to subscale determination. Sum scores of IBD-Cope subscales were tested against Brief Cope subscales and the IBD questionnaire (IBDQ). Re-validation of the IBD-Cope was performed on participants from the general outpatient setting.

Results: Table 1 shows the demographics of the recruited participants.

Test-retest reliability revealed 8/20 questions with ICC>0.65. EFA produced two components that explained 42% of the variance, and reflected "good" and "bad" coping. Good and bad coping on IBD-Cope was positively associated with adaptive (r=0.57, p<0.01) and maladaptive coping (r=0.55, p< 0.01) on Brief Cope, respectively. Re-validation of the IBD-Cope showed three items consistently grouping into both good and bad subscales (Table 2).

Bad coping in IBD-Cope is negatively correlated with IBDQ scores (r=-0.51, P< 0.01). Good coping is not significantly associated with IBDQ scores (r=-0.12, P >0.05).

Conclusions: The IBD-Cope is a concise, reliable, valid and IBD-specific questionnaire. IBD-Cope subscales are moderately correlated with adaptive and maladaptive subscales on the Brief Cope. Higher scores of bad coping on IBD-Cope are associated with lower HRQOL as measured by IBDQ. Further longitudinal studies utilizing the IBD-Cope are required to determine its accuracy for identifying IBD patients who may benefit from interventions to improve coping strategies.

Table 1 Demographics of study samples.

	Test-rest reliability sample (n=58)	Initial validation sample (n=199)	Re-validation sample (n=179)
Age	44.3 (16.5)	38.8 (12.3)	38.3 (13.0)
Male sex	15 (25.9%)	71 (35.7%)	82 (45.8%)
Diagnosis Crohn's disease	40 (69.0%)	137 (68.8%)	124 (69.3%)

Table 2 Good and bad coping strategies

Good coping	Bad coping
Have you used relaxation techniques (e.g. meditation, progressive muscle relaxation, yoga) to help you deal with your stress?	Have you laid awake worrying about your IBD or other things in your life?
Have you altered your diet in an attempt to improve your IBD?	Have you NOT taken your medication?
Have you tried to take positives out of your IBD? (e.g., it makes me a stronger person")	Have you blamed yourself for making your IBD worse?

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P035
Comparative structural, functional, nonclinical, and phase 1 similarity assessments of PF-06438179, a potential biosimilar to infliximab, and marketed reference products

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Background: PF-06438179 is being developed as a potential biosimilar to Remicade® (infliximab), which is a chimeric mouse/human monoclonal antibody that binds to the tumour necrosis factor (TNF) protein, in a stepwise approach following globally accepted regulatory guidelines. The similarity of PF-06438179 to infliximab reference products sourced from the United States (infliximab-US) and from the European Union (infliximab-EU) was assessed in structural, functional, in vivo nonclinical pharmacokinetic (PK)/tolerability and clinical PK studies.

Methods: Structural similarity was assessed using chromatographic peptide mapping. Functional similarity was assessed in vitro using an inhibition of soluble TNF-induced cell apoptosis assay. PK, tolerability and anti-drug antibody (ADA) response were evaluated in rats administered a single IV dose (0, 10 or

50 mg/kg) of PF-06438179 or infliximab-EU. In a phase 1 study (NCT01844804), 146 healthy volunteers received a single 10 mg/kg IV dose of PF-06438179 (n=49), infliximab-US (n=48), or infliximab-EU (n=49). All subjects provided informed consent. PK was evaluated over 8 weeks; safety and ADA were assessed up to 12 weeks. PK similarity in humans was considered to be demonstrated if the 90% confidence interval (CI) of the test-to-reference ratio of maximum concentration (C_{max}) and area under the concentration time curve (AUC) were within the 80.00%-125.00% bioequivalence (BE) acceptance window.

Results: Peptide mapping showed superimposable chromatographic profiles of PF-06438179, infliximab-US and infliximab-EU, demonstrating structural similarity. The dose-response curves of inhibition of cell apoptosis induced by all three study drugs were also superimposable, demonstrating functional similarity. In rats, PF-06438179 and infliximab-EU were well-tolerated. Systemic exposures (assessed by C_{max} and AUC) in dosed animals appeared similar, with mean exposure ratios of PF-06438179 relative to infliximab-EU ranging from 0.88 to 1.16. None of the rats developed detectable levels of ADA. In healthy volunteers, the three study drugs exhibited a similar PK profile, and the 90% CI for the ratios of C_{max} and AUC were within the BE acceptance window of 80.00%-125.00% for each, individual three-way comparison. Overall safety and ADA profiles were comparable among the treatment groups.

Conclusions: Comparative studies demonstrated structural, functional, and nonclinical and clinical PK profiles of PF-06438179 to be similar to infliximab-US and/or infliximab-EU. A global, comparative clinical study is ongoing to assess efficacy and safety of PF-06438179 and infliximab-EU in combination with methotrexate in subjects with active rheumatoid arthritis.

P036
Apoptotic neutrophils ameliorate intestinal inflammation - possible mechanism of granulocyte/monocyte apheresis

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Background: Granulocyte/monocyte apheresis (GMA) is used as a therapeutic option for induction therapy for inflammatory bowel diseases (IBD). An Adacolumn is an adsorptive type carrier-based medical device for GMA and its major components are cellulose acetate beads. The main concept behind the development of the Adacolumn is removal of activated leukocytes. However, the actions of the column are more than just removing leucocytes, as a type of immunomodulation has also been suggested in Results of several clinical and basic research studies. For the present study, we hypothesized that apoptosis is induced in leukocytes by reactive oxygen species (ROS) generated in the Adacolumn, and a considerable number of apoptotic leukocytes re-enter the body and contribute to the efficacy of GMA.

Methods: A rabbit GMA model was established as reported previously (Inflammation. 2002). We used a mini GMA column with a diameter of 1.5 cm and length of 10 cm, which contained 11 g of cellulose diacetate carriers. The amount of O_2^- was measured by directly counting the number of photons emitted by MCLA upon reaction with O_2^-. Neutrophils were isolated from the outflow blood during GMA and apoptosis induction of those cells was evaluated by flow cytometry. Next, we established a SCID mouse colitis model by adoptive transfer of $CD4^+$ T cells isolated from SAMP1/Yit mice, a murine model of Crohn's disease. Peritoneal exudate cells (PECs) were isolated for preparing injected apoptosis cells from a control strain AKR. Apoptosis was induced in PECs by H_2O_2 treatment and those apoptotic cells were intravenously injected to the colitis mice in the presence of co-transferred whole B cells. Seven weeks after colitis induction, the severity of colon inflammation was evaluated by weight loss, colon length, histopathology, and detection of inflammatory cytokines in colon tissues.

Results: Photon counts were gradually increased after initiation of GMA, which was not found in a sham apheresis model. Generation of O_2^- in the column was confirmed by infusion of superoxide dismutase into the column. A significant decrease in L-selectin expression on neutrophils was observed in the GMA outflow, while hypodiploid apoptotic neutrophils were also significantly increased in the outflow. To mimic apoptotic neutrophils generated during GMA therapy, apoptosis was induced in PECs by exposure to H_2O_2. Intravenously injection of H_2O_2-induced neutrophils significantly reduced the colonic inflammation as compared to the PBS injection group.

Conclusions: Apoptosis was induced in circulating neutrophils by ROS generated in the Adacolumn, which may contribute to the anti-inflammatory effect of GMA as a novel therapeutic mechanism for IBD.

P037
Patient-derived colonic epithelial cultures as a valuable tool for personalized medicine

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Background: Inflammatory bowel diseases (IBD) are caused by an aberrant immune response towards intestinal microbiota in genetically predisposed persons, most likely facilitated by intestinal epithelial defects. The intestinal epithelium has an important role in the intestinal immune response by conserving host-microbial interactions and tissue homeostasis.

The imminent introduction of new therapeutic classes for IBD patients emphasizes the need for personalized medicine for which the epithelial resistance or response to cytotoxic agents, therapeutics, dietary components, etc. may be essential.

However, a simple epithelial model with the potential for personalized determination has not been tested. Therefore we developed and validated a short term culture system for IBD patient-derived intestinal epithelial cells (IECs).

Methods: Endoscopically-derived mucosal biopsies were obtained from both inflamed and non-inflamed regions from the colon of IBD patients. Colonic crypts from biopsies were isolated through chemical and mechanical separation (adapted intestinal organoid protocol by Sato et al. [1]. Intact intestinal crypts were immediately plated in collagen-coated wells containing in-house designed medium, resulting in a monolayer of IECs. The epithelial character of the cells was confirmed by ICC for epithelial tight junction protein E-cadherin

and positive detection of cytokeratin (CK) 18 and 20 mRNA at different time points by qRT-PCR, whereas detection of fibroblast markers PDGFR and COL1A1 and COL1A2 mRNA remained negative. Inflammasome sensors NLPR3, AIM2 and IFI16 were assessed by ICC.

Results: Crypt isolation was successful in 80%. The crypts attached to the bottom of the wells overnight. After 24 hours, normal crypt architecture switched to a monolayer culture, observed as patches of densely packed cuboidal cells. We were able to culture the IECs for a maximum of 12 days before cell death and detachment appeared. As an initial validation, we could confirm the reported cytoplasmic localization for inflammasome sensors NLRP3 and AIM2, whereas IFI16 showed nuclear staining.

Conclusions: We have developed a simple ex vivo 2D IEC culture system complementary to the 3D organoid culture system. Endoscopy-derived IEC isolation will allow clinicians to evaluate patient-specific epithelial response to e.g. different or new classes of gastrointestinal therapeutics. This approach also provides a simple model for screening of drug effects at the site of the intestinal epithelium in a personalized manner. Moreover association of epithelial responses with patient-specific genetic profiles (eg. with mutations in inflammasome-related genes) may lead to further insights into disease biology of intestinal diseases such as IBD.

References:

[1] Sato, Toshiro Stange, Daniel E Ferrante, Marc Vries, Robert G J Van Es, Johan H Van den Brink, Stieneke Van Houdt, Winan J Pronk, Apollo Van Gorp, Joost Siersema, Peter D Clevers, Hans, (2011), Long-term expansion of epithelial organoids from human colon, adenoma, adenocarcinoma, and Barrett's epithelium, Gastroenterology, 1762-1772

P038
Retinoic acid primed dendritic cells induce Interferon gamma (IFN γ) and reduce FOXP3 expression on human Th9 cells

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Background: Retinoic acid (RA) produced by intestinal dendritic cells (DCs) induces gut homing molecules, α 4 β 7 and CCR9 on T cells and in presence of TGF β drives the differentiation pathway towards FOXP3+ Treg cells while inhibiting the Th17 and Th1 differentiation. Th9 is a recently identified CD4 T helper cell subset, which secretes Interleukin (IL) -9 in the presence of TGF β , and IL-4.While TGF β initiates Treg differentiation, IL-4 inhibits FOXP3 and promotes Th9 differentiation. We investigated the effect of RA primed DCs on CD4+ T cell responses with and without TGF β and IL-4 in healthy human subjects.

Methods: Monocyte (Mo) derived DCs were generated from peripheral blood samples collected from healthy human subjects by incubating CD14+ cells with GM-CSF and IL-4 in the presence and absence of RA. LPS stimulated Mo-DCs and RA-DCs were co-cultured with sorted naïve CD4+ T cells in the presence and absence of TGF β and IL-4 (Th9 conditions)) and cytokine expression of T cells were checked by flowcytometry. The data was analyzed with Graph Pad Prism 5.0 software.

Results: Characterization of RA-primed DCs showed an increased expression of CD103 while HLA-DR, CD86 and CD83 were decreased as compared to non-RA-primed DCs. These RA primed DCs, when co-cultured with naïve CD4+T cells induced elevated levels of IFN- γ and FOXP3 with reduction in IL-9 and IL-17. When naïve CD4 T cells and RA-DCs were cultured in presence of TGF- β and IL-4 , there was reduction in IL-9, however, it resulted in significantly reduced FOXP3 and elevated IFN- γ expression(as shown in figure below).

Conclusions: We report a novel role of RA in immune regulation. RA inhibits DC maturation, thereby maintaining its anti-inflammatory role. On the other hand, RA not only reduces the IL-9 production by CD4+T cells but surprisingly also reduces FOXP3 while inducing IFN γ expression suggesting a pro-inflammatory role.

P039
Role of the CARD family (CARD10, CARD11 and CARD14) in the colonic mucosa of patients with Ulcerative Colitis

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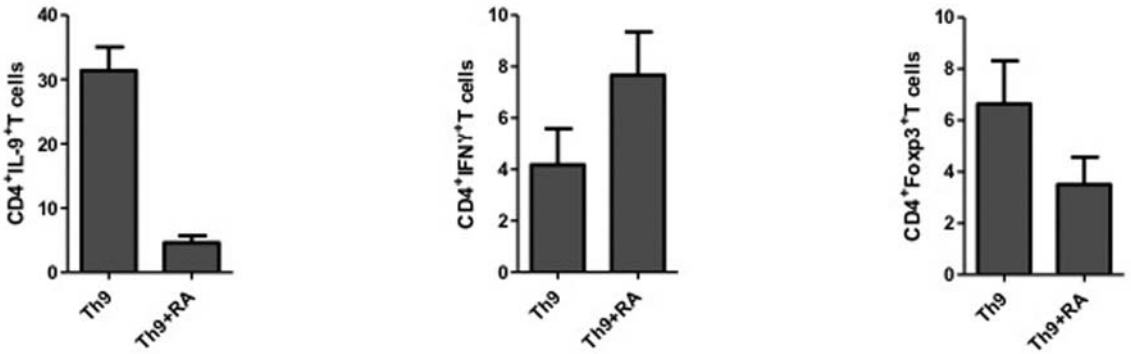
Background: Ulcerative Colitis (UC) is one of the two forms of Inflammatory Bowel Disease (IBD), whose multifactorial origin is well accepted but its etiology remains unknown. The gene NOD2 (CARD15) is the major one associated gene regarding the development of Crohn´s Disease (CD), and codifies for a cytoplasmic protein that is involved in the molecular mechanisms of CD. Other members of the CARD family include the CARD10, CARD11 and CARD14



"Naïve CD4+T cells were stimulated with Mo-DC and RA-DC in the presence of TGFb and IL-4. Percentages of (a) IL-9+ cells (b) IFNg+ cells (c) Foxp3+ cells were determined by flow cytometry. * P<0.05, *** P<0.0001"

are recently recognized genes that encode cytoplasmic proteins from the same family that play a role in the apoptotic signaling cascade and activation of Nuclear Factor kB.

Aim: To determine the expression of some members of the CARD family (CARD10, CARD11 and CARD14) in patients with UC and controls without inflammation.

Methods: A total of 183 individuals divided into 3 groups (63 patients with active UC, 60 patients with UC in remission and 60 controls without histologic inflammation). In all cases the diagnosis was confirmed by histopathology. Total ribonucleic acid (RNA) was extracted from intestinal tissue, subsequently complementary deoxyribonucleic acid (cDNA) was obtained by polymerase chain reaction (PCR). For each gene, relative quantification was made by real-time PCR. The statistical analysis was performed using SPSS version 17.0, using Kruskall Wallis non-parametric test, Spearman`s correlation, Fisher`s exact test and Odds Ratio (OR) in order to determine the strength of association. A P value < 0.05 was considered as significant.

Results: The CARD14 gene expression was significantly higher in the group with active UC compared to controls (P=0.008) and statistical trend of significance in the group of UC in remission (P=0.07). The low expression of CARD14 gene was associated with a more benign clinical course of UC, characterized by initial activity followed by long-term remission longer than 5 years (P=0.01, OR= 0.07, CI 95%: 0.007-0.70). No statistically significant differences were found in the CARD10 and CARD11 gene expression.

Conclusions: The CARD family might be involved in UC pathophysiology. The CARD14 gene expression was increased in patients with active UC and the low expression of CARD14 gene was associated with a benign clinical course characterized by long-term remission.

P040
The biosimilars of infliximab are equally well quantified in a clinically validated infliximab assay

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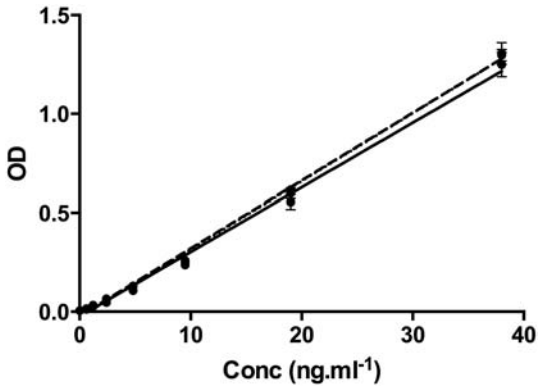
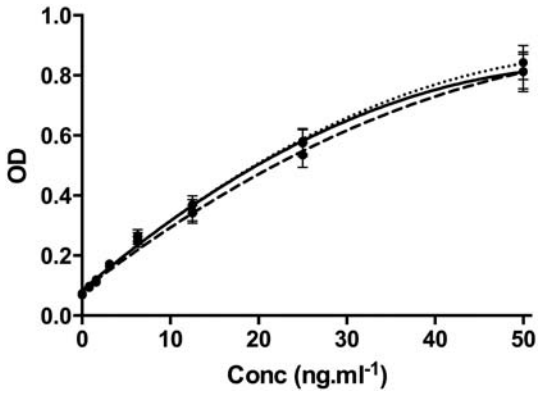
Background: A panel of 55 monoclonal antibodies towards the anti-tumour necrosis factor (anti-TNF) biological Remicade® (infliximab, IFX) was previously generated. The highly specific monoclonal antibody, MA-IFX6B7, was selected to quantify Remicade® in a clinically validated in house-developed infliximab ELISA, which was recently converted into CE-marked kits (distributed by ApDia and R-Biopharm). Recently, two biosimilars of Remicade®, Remsima® and Inflectra® were launched. We evaluated the 'cross-reactivity' of the MA-IFX panel towards these biosimilars and we evaluated the quantification of biosimilars in the infliximab ELISA.



"Figure 1 Dose-response curve of MA-IFX6B7 for reaction with Remicade® (solid line), Remsima® (dashed line) and Inflectra® (dotted line) (p >.5). Data are presented as mean ± SE (n = 24)."



"Figure 2: Dose-response curve of Remicade® (solid line), Remsima® (dashed line) and Inflectra® (dotted line) in the infliximab ELISA. Data are presented as mean ± SE (n = 6). The fitted curves show no significant differences (p >.4)."

Methods: First, the reactivity of the MA-IFX panel was tested using an ELISA in which either Remicade®, Remsima® or Inflectra® was coated on microtiter plates. Different concentrations (ranging from 0.8 ng/ml to 50.0 ng/ml) of each MA-IFX were applied and binding was detected using horseradish peroxidase (HRP)-conjugated rabbit-anti-mouse IgG. Secondly, calibration curves of Remicade®, Remsima® and Inflectra® (ranging from 0.6 ng/ml to 38.0 ng/ml) were applied in the in-house developed infliximab ELISA using TNF for capture and HRP-conjugated MA-IFX6B7 for detection. Statistical analyses were performed using mixed model analysis in SAS version 9.2. Thirdly, different concentrations of Remicade®, Remsima® and Inflectra® (ranging from 0.5 µg/ml to 12.0 µg/ml) were spiked in phosphate-buffered saline containing 1% bovine serum albumin. Samples were diluted and the recovery was calculated versus the Remicade® calibration curve.

Results: Screening each of the 55 MA-IFX revealed similar reactivities towards Remicade®, Remsima® and Inflectra®. An identical reactivity of MA-IFX6B7 towards all biologicals was statistically proven (Figure 1). No significant differences were observed between the calibration curves of the three anti-TNF biologicals in the infliximab ELISA (p >.4) (Figure 2). Spiked samples revealed recoveries of 92 ± 5%, 95 ± 6% and 95 ± 5% for Remicade®, Remsima® and Inflectra®, respectively (n=3).

Conclusions: We have demonstrated that MA-IFX6B7 raised against Remicade® exhibits an identical reactivity towards Remsima® and Inflectra®. We analytically validated that the infliximab assay, using MA-IFX6B7, is well suited for quantification of Remsima® and Inflectra®.

P041
Mesenchymal stem cells protect from acute dextran sulphate sodium-induced colitis by attenuating function of antigen presenting cells

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Background: Acute dextran sulphate sodium (DSS)-induced colitis is a well-established murine model of colitis, because of the high degree of uniformity, reproducibility and similarities to acute human colitis. DSS induces mucosal injury and inflammation which is accompanied with migration of inflammatory cells in the colon. Because of their immunomodulatory characteristics, mesenchymal stem cells (MSC) are considered as promising therapeutic agents for the therapy of immune mediated diseases. Recently published studies suggested therapeutic potential of MSC for the treatment of colitis, but the mechanisms remain unknown. The main aim of this study was to evaluate possible cellular targets of MSC in the pathology of acute colitis.

Methods: DSS (3%, molecular weight 40kDa) was dissolved in water and given to C57Bl/6 mice in place of normal drinking water (ad libitum) for 7 days. Mouse bone marrow-derived MSC (2 x 106 cells) were intravenously injected daily. Disease Activity Index (DAI: weight loss, stool consistency, visible blood in feces), was used to assess the clinical signs of colitis. The histology score of colitis was calculated as the sum of "infiltration" and "damage of epithelium" sub-scores for each mouse. The cellular make up of colon and phenotype of colon-infiltrated immune cells was determined by flow cytometry.

Results: DAI and histology score were significantly attenuated in DSS+MSC-treated mice (n=16) compared to DSS-only treated animals (n=16). This was associated with the reduced infiltration of innate immune cells in the colon, particularly antigen presenting cells (CD11c+CD11b+ inflammatory dendritic cells and F4/80+CD11b+macrophages). In addition, intravenous injection of MSC attenuate expression of major histocompatibility complex II and co-stimulatory molecules on antigen presenting cells. The percentage of protective CD3+NK1.1+ NKT cells and F480+CD206+ alternatively activated macrophages was higher in colons of DSS+MSC-treated mice compared to DSS-only treated animals. Injection of MSC did not affect infiltration and phenotype of CD45+Ly6G+CD11c- neutrophils, CD45+SinglecF+CD11c- eosinophils and FcERI+CD117+mast cells.

Conclusions: MSC attenuate function of inflammatory antigen presenting cells in colon and protect from acute DSS-induced colitis

P042
Response to corticosteroids in Ulcerative Colitis may be related to modulation of mTOR signaling pathway genes by microRNAs

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Background: Up to 40% of patients with active Ulcerative Colitis (UC) do not have an adequate response to corticosteroids (CS). Mechanisms of resistance to CS in UC are not well understood. MicroRNA (miR) are small non-coding RNA fragments that modulate messenger RNA (RNAm) at a post-transcriptional level, playing a critical role in many biological processes. Little is known about the influence of miR in the response to CS in UC. Objective: To compare the transcriptomic profile (miR and RNAm) in rectal mucosa of patients with active UC responding and non-responding to CS.

Methods: Rectal biopsies were obtained from UC patients before and after three days of CS treatment for a moderate-to-severe flares. Patients were grouped according to clinical response (non-responder = moderate or severe activity according to Montreal's classification or need of rescue therapy at day 7; responder = mild activity or remission without rescue therapy at day 7). miR were identified by means of a sequencing method (Tru Seq Small RNA kit from Illumina) and RNAm were study by microarrays method (HumanHT-12 kit from Illumina) on those rectal biopsies with high integrity. After the comparison between groups those miR and RNAm with a fold change greater than 1.5 and adjusted p-value less than 0.05 were further studied. Potential targets of selected miR were checked in "Target Human Scan database" (www.targetscan.org), and their impact on biological activity was searched in "GeneCodis database" (http://genecodis.cnb.csic.es).

Results: 8 responders and 7 non-responders tissue samples reached an integrity that allowed miR sequencing and microarrays study. Comparison between responders and non-responders before CS showed a differential miR expression of miR-1246, miR-1291, miR-5701 and miR-625-3p. Comparison between responders before and after treatment showed differential expression of miR-183-5p, miR-3607-3p, miR-1246, miR-5701 and miR-625-3p. And comparison between non-reponders before and after treatment showed differential expression of miR-4770, miR-449, miR-145-3p, miR-1246 and miR-1291. The only gene with differential expression after microarrays study was DDIT4, which was down-regulated in responders before CS in comparison with responders after 3 days of treatment. A further in silico study reveals that DDIT4 is a potential target of three of the differential expressed miR (miR-183-5p, miR-625-3p , miR-3607-3p) and also that this gene is linked to the mTOR pathway (and indirectly with autophagy).

Conclusions: There is a different miR profile in rectal mucosa of patients with active UC responding and non-reponding to CS. Our findings suggest that regulation of mTOR and autofagy pathways by miR might be involved in the response to CS in active UC.

P043
Immunohistochemical expression of angio and lymphangiogenic factors in colonic mucosa of patients with inflammatory bowel disease.

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Background: To evaluate the possible differences between inflammatory bowel disease (IBD) and non-IBD, and between ulcerative colitis (UC) and Crohn's disease (CD), in the expression of VEGFA, -C, -D, VEGFR1, -R2, -R3, PlGF, Ang1, Ang2 and Tie2 in colonic mucosa

Methods: Biopsies from patients with and without IBD that underwent to a colonoscopy by medical criteria were prospectively included and their mucosal samples studied by immunohistochemistry. VEGFA, -C, -D, -R1, -R2, -R3 and PlGF expression Results were graded as follows: (++) over 50% of the tissue cells were stained, (+) below 50%, and (-) completely negative. Ang1, Ang2 and Tie2 were assessed as the average density of five hot spots at a magnification of x40. Endoscopic activity was assessed by endoscopic Mayo

Metabolic profiling with biofluid analysis

	CD	UC
Urine metabolites		
Upregulated	Amino acid: Glyine, leucine, isoleucine. End-product of butyrate-producing Gram negative bacteria: 3-hydroxybutyric acid. Hepatic conjugation: Formate	Urea cycle: asparate. AA: glutamine, glutathione, glutamate, ascorbate
Downregulated	Gut microbial metabolism of aromatic compounds: Hippurate	Betaine, glycerophosphocholine
Faecal metabolites		
Upregulated	Ester and alcohol derivatives of short chain fatty acids and indole	Monounsaturated fatty acids, secondary bile acids, products of phenylalanine metabolism
Serum metabolites		
Upregulated	N and O-linked oligosaccharides of serum IgA. Acetate, alanine, choline	Conjugated primary BA glycocholic acid, glycochenodeoxycholic acid, ursodeoxycholic acid. Homocysteine. Asparate, glutamine,glutathione, glutamate, ascorbate for active UC L-arginine - important AA in protein synthesis and intermediate metabolism of nitrogen in urea cycle.
Downregulated	HDL, LDL choline, isoleucine, alanine, tryptophan Total BA, conjugate and glycoconjugate decreased Ga1NAc/HP	

Subscore (UC) and SES-CD (CD) indexes. Patients were classified in accordance with the Montreal classification. In cases with active disease, biopsies were taken from both endoscopically affected and non-affected mucosa

Results: 101 biopsies from 58 patients with IBD (36 UC and 22 CD) and 19 controls were included; 56% patients were male and 20% smokers. 64% of the patients did not have endoscopic activity, 16% had moderate, 14% mild and 6% severe activity. Expression and mean count of Ang1, Ang2, VEGFR2 ($p<0.01$), and VEGFC, -R1 and Tie2 were higher in samples from patients with UC compared to CD ($p<0.05$). In patients with CD, Ang1 mean count, and expression of VEGFC, -D, -R2, PlGF, and VEGFR3, were higher ($p<0.05$), and the rest of factors were lower, than in controls. Expression of Ang2 ($p<0.05$) and of all the studied factors were higher in active samples than in non-active CD; on the opposite, VEGFD and -R3 were lower. Expression of VEGFR1 and Tie2 were higher in patients under anti-TNF treatment than in those who were not ($p<0.05$). VEGFR1 and -R2 expressions were higher in patients with extraintestinal manifestations ($p<0.05$). In UC, expression of all factors were higher in patients with UC than in controls ($p<0.05$). Mean count and expression of Ang1, Ang2 were higher, and VEGFD was lower ($p<0,05$) in samples with active disease. Patients with smoking habit had a lower expression of VEGFR2 ($p<0.05$). Patients under 5-ASA treatment had a lower expression of VEGFD ($p<0.05$), and those under thiopurine treatment had a higher expression of VEGFA and PLGF ($p<0.05$) compared to untreated ones. VEGFR2 expression was higher in patients with left-sided colitis ($p<0.05$)

Conclusions: Angiogenic factors are differentially expressed at mucosal level in patients with CD and UC. Our findings might support a role of angiogenic factors in disease activity and behaviour of IBD. Expression of these factors in colonic mucosa of IBD patients may be modulated by immunosuppressive and anti-TNF treatment

P044
Systematic Review of the use of metabonomics in inflammatory bowel disease (IBD)

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Background: The management of IBD remains a challenge. Correct diagnosis is vital for the optimal management of the disease. Metabonomic studies have been used for biomarker identification for the diagnosis of IBD and differentiating between Crohn's disease (CD) and ulcerative colitis (UC). Ideal biomarkers are required for the prediction and personalisation of treatment.

We performed a systematic review aiming to identify relevant biomarkers in multiple biofluids from IBD patients and the laboratory techniques which are used for the analysis of the metabolites.

Methods: A systematic review of the literature was carried out according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Two independent reviewers searched all publications from Pubmed, Cochrane and EMBASE using MESH terms and keyword searches with "metabonomics, metabolomics, IBD, Crohn's disease, ulcerative colitis, NMR, GC-MS, lipidomics and LC-MS".

Results: The initial search identified 128 articles, of which 48 were screened for the inclusion and exclusion criteria and 26 were finally included for the analysis. The total number of patients was 1552 of which 745 were CD and 784 UC.

Urine:

Six studies have examined urinary metabolites with a total of 188 CD and 211 UC patients. All used NMR- spectroscopy. All studies were designed with the aim of diagnostic biomarker identification.

Faeces:

Six studies analysed metabolites from faeces using NMR, LC-MS and GC-MS. Total number of patients were 164 CD and 141 UC. The main aim of 4/6 studies was biomarker identification of IBD. Two further studies used GC-MS and LC-MS to identify predictive biomarkers for flares of UC post-medical therapy due to the greater sensitivity of the techniques.

Serum:

Eight studies analysed serum using NMR and LC-MS. Total patients examined were 302 CD and 438 UC. The aims were to identify diagnostic biomarkers in addition to the prediction of treatment outcomes and monitoring disease activity.

The biofluids were urine, serum and faeces. These were analysed using three labarotory techniques: Nuclear magnetic resonance

(NMR), Gas chromatography-Mass Spectrometry (GC-MS) and Liquid Chromatography- Mass Spectrometry (LC-MS); Table 1.

Conclusions: Multiple specific metabolites have been identified in Crohn's and ulcerative colitis. The techniques for identification are non-invasive, instant and can be used to create specific profiles for CD and UC. A prospective longitudinal study is required to identify prognostic markers and predictors of response to medical therapies.

P045
Quality of Life and Coping Mechanisms in patients with Crohn's Disease treated with Biological Therapy.

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Background: Crohn's disease (CD) is a chronic and relapsing inflammatory bowel disorder with deep impact on health-related quality of life (QOL).

In the last few years several studies have focused the attention on patients (pts) subjective perception of health state, including emotional, social aspects and coping mechanisms related to the disease.

Nowadays improvement of pts' QOL is a new important goal in medical therapy.

The aim of this observational study is to investigate QOL and coping skills in patients with CD and the impact of the disease on working ability and daily activities.

Methods: We recruited 47 patients with moderate to severe CD (according to HBI Index) treated with biological therapy at the IBD Centre of Negrar Hospital (Verona, Italy).

All pts answered three questionnaires:

Short Form-36 (SF-36): a generic questionnaire which measures QOL and pts' health status.

Coping Orientation to Problems Experienced - New Italian Version (Cope-NVI): to measure different coping skills.

Work Productivity and Activity Impairment Questionnaire in CD (WPAI-CD): to measure

illness'impact on work productivity (physical impairment/ reduced productivity at

work).

Hypotheses tested with statistical Methods (Z-test) are:

- Health-related QOL is good for the majority of pts.
- CD pts have the same coping skills of healthy people when dealing with a stressful situation.
- Work productivity is not compromised.

Results: SF-36 indicates that the average score of this group of pts does not differ significantly from that of healthy individuals.

Cope NVI shows that coping mechanisms, when dealing with stressful events, are very similar in our CD pts group and in healthy people. Moreover, CD pts have the same standard deviation and overall score of healthy people.

Finally, the WPAI-CD questionnaire shows 22,15%h work loss in a week. Furthermore Work Productivity Loss, caused by disease's symptoms, is 17,15%h.

Regarding pts' daily routine 22,15%h reported difficulties in carrying out their every day's activities.

Conclusions: Interest in evaluating QOL in chronic disease pts is increasing.

Our study has demonstrated that health-related QOL and coping skills are similar in our group of pts and in healthy people.

Furthermore working ability and productivity is not significantly compromised.

These Results suggest that biological therapy can restore health-related QOL and improve daily activities, as shown in literature. However further studies are needed.

P046
CD99 and cyclophilin A correlate differently in patients with inflammatory bowel diseases

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Background: Inflammatory bowel diseases (IBD) are characterized by crypt infiltration with neutrophils, which can be stimulated by externalization of an adhesion molecule CD99. Neutrophil infiltration is associated with upregulation of cyclophilin A (CyPA). However, studies on CD99 and CyPA in IBD patients have not been performed yet. The aim of the study was to determine the CD99 gene and protein expression and extra- and intracellular concentration of CyPA in UC and CD patients in comparison to healthy subjects.

Correlations between CD99 and CyPA in non-inflamed and inflamed colon areas in UC and CD patients.

	UC / r^2 / Gene level	UC / r^2 / Protein level	CD / r^2 / Gene level	CD / r^2 / Protein level
CyPA [ng/ml] in plasma vs. CD99 in non-inflamed colon areas	+0.770	+0.530	-0.651	-0.274
CyPA [ng/ml] in plasma vs. CD99 in inflamed colon areas	-0.535	+0.090	-0.344	-0.478
CyPA [ng/ml] in non-inflamed vs. CD99 in non-inflamed colon areas	-0.580	-0.086	-0.357	-0.756
CyPA [ng/ml] in inflamed vs. CD99 in inflamed colon areas	+0.796	+0.488	+0.436	-0.333

Methods: The study incorporated 26 patients divided into: control (n=7), UC (n=7) and CD (n=12). The patients were matched by age and gender. The samples comprised serum and colonoscopy biopsies from non-inflamed and inflamed (in UC or CD) colon areas. The CD99 mRNA was analysed by RT-PCR, and CD99 and CyPA protein levels by immunoenzymatic Methods (ELISA and Western blot).
Results: The UC patients had significantly lower CD99 mRNA in non-inflamed tissue and higher in inflamed colon areas comparing to CD (p=0.035 and p=0.021, respectively). The extracellular CyPA level was 4.6- and 2.8-times higher in UC and CD than in control (p=0.017 and p=0.137, respectively). CyPA was significantly lower in non-inflamed tissue in the CD group compared to control (p=0.039). Reversed correlations were found between CyPA and CD99 in inflamed tissues of CD and UC patients.
Conclusions: Our study indicated that patients with UC had increased level of CD99 and CyPA both in plasma and tissue. Moreover, CD99 gene expression correlated inversely with intracellular CyPA level in inflamed and non-inflamed colon tissue in UC, but not CD. We suggest that there may be a link between CD99 and CyPA in IBD etiology. It is likely that CD99-CyPA interaction influences the inflammatory process in colitis, as in our study both CD99 and CyPA were increased in inflamed colon areas from UC patients. However, further studies are necessary to confirm those observations and to describe how, if at all, CyPA releasing influences CD99 signaling in IBD.

P047
The presence of primary sclerosing cholangitis does not change levels of gut barrier failure biomarkers (I - FABP and ccK18) in patients with ulcerative colitis

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Background: Primary sclerosing cholangitis (PSC) is a progressive disease of the biliary tree characterised by inflammation, fibrosis and stenoses, and often associated with ulcerative colitis (UC); condition characterized by leaky gut. However, UC associated with PSC ("PSC - UC" or "PSC - IBD") is described as a phenotype distinct from the conventional UC. Our aim was to compare serum levels of biomarkers of gut barrier damage in PSC-UC, UC and healthy subjects.
Methods: We used ELISA to analyze Intestinal fatty acids binding protein (I-FABP) and caspase-cleaved keratin 18 (ccK18) in 74 individuals (38 with PSC, 19 with UC, 17 healthy controls) and 38 individuals (23 with PSC, 9 with UC, 6 healthy controls), respectively. Furthermore, we compared the levels of either biomarker with standard clinical (e.g. colitis extent and severity) and laboratory parameters (CRP, AST, ALT, ALP, GGT, INR).
Results: There is no significant difference between PSC-UC, UC and healthy subjects in I-FABP [median (IQR)] 503.9 (0.0 - 1548.0), 454.1 (0.0 - 747.3), 769.3 (220.9 - 1027.0) or ccK18 [median (IQR)] 174.1 (99.93 - 423.0), 90.08 (67.46 - 205.9), 98.7 (51.05 - 174.7). When the liver involvement is disregarded, I-FABP have a tendency to be higher in patients with pancolitis as compared with patients with partial colon involvement (p=0.07). There is no statistically significant difference in serum I-FABP or ccK18 depending on colitis severity (without colitis, remission, mild, moderate and severe).
Conclusions: Neither I-FABP, nor ccK18 differs between PSC-UC and UC. In patients with pancolitis, I-FABP has a tendency to be higher compared to patients with smaller extent of colitis.

P048
The peripheral pool of gut-homing CD4+beta7+ T-cells and regulatory CD4+FoxP3+ T-cells is maintained in Crohn's disease patients with small bowel inflammation

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Background: There are some data suggesting that the peripheral blood pool of gut-homing CD4+beta7+ pool and of T-regulatory cells CD4+is reduced in patients with active IBD, presumably due to enhanced recruitment to the gut. Our aim was to investigate these T-cell subsets in Crohn's disease (CD) patients included in a prospective study evaluating small bowel inflammation by inflammatory markers, MRE and capsule endoscopy.
Methods: Patients with known small bowel CD in clinical remission or mild disease (CDAI<220) were prospectively recruited and underwent MRE, followed by a video capsule endoscopy (CE). PBMC were obtained, and FACS analysis of CD4+ and CD8+ gut homing beta7 integrin expressing cells and of expression of the transcription factor FoxP3 were performed.
Results: Fifty three patients were studied. Capsule endoscopy documented no active inflammation and complete mucosal healing in 15 patients, and active inflammation in 38 patients (12 with severe inflammation with a Lewis score above 790, and 26 with milder inflammation and Lewis score of 135-790). The median percentage of CD4+FoxP3+ T-regulatory cells in the peripheral blood of patients with any active small bowel inflammation was not different than in patients with complete mucosal healing (5.3% versus 5.1%, respectively, p=0.8,), and was also similar when only patients with severely active mucosal inflammation (Lewis score>790) were considered. Percentage of CD4+CD45RO+Beta7+ gut-homing memory cells within the total CD4+CD45RO+ pool was also similar between patients with active inflammation and patients with healed mucosa (30.1% vs 30.2%, respectively, p=0.94). Similar Results for beta7 expression were found for the CD8+ T-cell subset.
Conclusions: Contrary to prior reports, when patients are fully evaluated for verified small bowel inflammation by capsule endoscopy, there does not seem to be a mucosal-inflammation induced depletion of the peripheral blood pool of gut-homing memory CD4+CD45RO+beta7+ T-cells, nor of the regulatory CD4+FoxP3+ T-cell subset.
RE, SBH- Equal contribution
The study was sponsored by the Helmsley Charitable Trust.

P049
H2S confers colonoprotection against TNBS-induced colitis by HO-1 upregulation in rats

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Background: Hydrogen sulfide (H2S) is an endogenous mediator that relaxes vascular smooth muscle, exhibits several antiinflammatory activities and contributes to protection

Methods: Specially, we investigated the beneficial effects of H2S and whether heme-oxygenases (HO) are involved in the H2S-induced colonal cytoprotection against 2,4,6-trinitrobenzenesulfonic acid (TNBS)-induced colitis in rats. Male Wistar rats were treated with TNBS (10 mg) to induce colitis. H2S donor (Lawesson's reagent) were used at different concentrations (60; 30; 15; 7.5; 3.75; 1.87; 0.93 µM; dissolved in carboxymethylcellulose) twice daily per os (from 0 day to 3. day). 72 h after TNBS treatment colon samples were collected to measure the extent of inflammation, myeloperoxidase (MPO), and HO activities and TNF-alpha content. In a separate experiment, HO activity was inhibited by tin protoporphyrin (SnPP, 30 µmol/kg/day, s.c) on the day of TNBS challenge (10 mg)in co-treatment with H2S donor (2 x 1.87µM, per os).

Results: Twice-daily treatment with H2S donors significantly decreased the extent of colonal inflammation in a dose dependent manner compared to vehicle-treatment. The most effective concentration was 3.75 µM daily dose of H2S donor against inflammation (27.4 ± 1.5 vs. 46.2 ± 4.3; %). Per os administration of H2S donor reduced TNBS-provoked MPO activity (19.07 ± 3.6 vs. 36.67 ± 2.95; mU/mg/protein), TNF-alpha levels (89.95 ± 9.43 vs. 531.67 ± 32; pg/mg protein),while increasing colonic HO enzyme activity (0.98 ± 0.05 vs. 0.82 ± 0.6 nmol bilirubin/h/mg protein). The protective effect of H2S was abolished by co-treatment with an inhibitor of HO activity (TNBS:35.6 ± 2.4; TNBS+H2S: 21.6 ± 5.6; TNBS+H2S+SnPP: 28.8 ± 2.6 % extent of lesion) (from 60,6 ± 15,7 to 80,89 ± 7,3 % of the extension of TNBS lesion).

Conclusions: Our findings suggest that H2S confers protection dose dependently, probably by modulation of anti-inflammatory parameters and HO enzyme activity.

P050
The influence of anti-TNF therapy on chosen angiogenesis-related processes in patients with Crohn's disease

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Background: Immune-mediated angiogenesis seems to be a crucial phenomenon in the pathogenesis of Crohn's disease (CD). Anti-TNF antibodies are believed to be the most powerful drugs in diminishing the inflammatory lesions in the gastrointestinal tract, however direct mechanisms of their action are to be elucidated. In our study we performed a complex analysis of the influence of anti-TNF agents on chosen angiogenesis-related processes in CD patients in relation to clinical efficacy of biological therapy.

Methods: The influence of the sera from CD patients on the proliferation of Human Umbilical Vein Endothelial Cells (HUVEC) of the EA.hy926 line was assessed in vitro by using the MTT formazan proliferation test. Concentrations of crucial angiogenesis-related cytokines (Vascular Endothelial Growth Factor - VEGF; Angiopoietin-1 - Ang-1; basic Fibroblast Growth Factor - bFGF; soluble Tumor Necrosis Factor Alpha - TNF) were measured by using the ELISA method. Immunohistochemical expression of VEGF and platelet/endothelial cell adhesion molecule-1 (PECAM-1) was estimated in intestinal biopsies taken from inflamed areas of the colon during colonoscopy.

All aforementioned tests were performed before and after induction phase of anti-TNF therapy (adalimumab, infliximab). Patients who achieved a decrease in the Crohn's Disease Activity Index of 100 or more (CDAI-100 response) were considered as primary responders.

Results: 24 CD patients were enrolled into the study, proliferation of HUVEC was assessed in case of 6 patients. We found a significant reduction in proliferating vessels in intestinal biopsies assessed by PECAM-1 expression after anti-TNF therapy, what was accompanied by a significant decrease in VEGF-positive staining. Proliferation of HUVEC decreased when exposed to sera of CD patients who achieved clinical response, and it increased in case of failure of the anti-TNF therapy. Concentration of VEGF and Ang-1 significantly decreased (350.8 ± 578.9 to 300.4 ± 583.3 g/ml, p=0.04 for VEGF; and 55.7 ± 15.5 to 44.9 ± 15.7 ng/ml, p=0.02 for Ang-1) after anti-TNF therapy in the responders group, and it did not change significantly in non-responders group. Moreover, high baseline VEGF concentration was predictive for clinical improvement after anti-TNF therapy. Concentrations of bFGF and TNF did not change in the course of anti-TNF treatment independently on its clinical efficacy.

Conclusions: Clinical efficacy of anti-TNF agents is at least partly dependent on the reduction of the immune-mediated angiogenesis in inflamed intestinal tissues in CD. This could be mediated by a decrease in proliferating endothelial cells after anti-TNF therapy, what is related to a significant change in the concentrations of crucial pro-angiogenic cytokines.

P051
The N- acyl-homoserine lactone 3-oxo-C12, an inter-bacterial signaling molecule (involved in quorum sensing), exerts effects on the host: thus implicating quorum sensing in inflammatory bowel disease.

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Background: Inflammatory bowel disease (IBD) associated dysbiosis causes profound changes in the gut ecosystem. We have shown that the profile of inter-bacterial signaling molecules, the N-acyl-homoserine lactones (AHLs), is altered during the course of dysbiosis. In particular, we observed a decrease in 3-oxo-C12:2, the dominant gut ecosystem AHL. These Results prompted us to study the functional role of this AHL on the gut microbiota and the host. As synthesized 3-oxo-C12:2 was unavailable, we focused our research on the structurally similar AHL, 3-oxo-C12. Existing knowledge of the host enzymes (the paraoxonases) involvement in quorum quenching and their deficiency in IBD, rendered it interesting to explore the functional role of 3-oxo-C12 on the inflammatory pathway. The aim of this study was to explore 3-oxo-C12 ability to interact with eukaryotic cells, such as intestinal epithelial cells and immune cells.

Methods: Firstly, the sub cellular localization of 3-oxo-C12, was visualized, in a human epithelial cell model, by confocal microscopy. We examined the effect of 3-oxo-C12, compared with the effect of a short chain AHL (C4), on macrophage cell line. Experiments for both AHLs were carried out under a range of conditions including: presence of 1-10 µM DMSO, with/without the paraoxanase inhibitor, 2-hydroxyquinoline (2HQ) (100µM) and with/without INF- γ (20UI/mL) and LPS (50ng/mL) stimulation. Macrophage cell response was quantified by measurement of TNF-α and IL-6 levels.
Results: Confocal microscopy showed intracellular localization of 3-oxo-C12 (1µM) after 1 hour. We observed co-localization with euchromatin suggesting a transcriptional factor role for 3-oxo-C12 within the host cells. Fluorescence diminished after addition to the media of non-fluorescent 3-oxo-C12 in excess (20 µM). No intracellular fluorescence was observed after treatment with fluorescein alone (negative control). When examining the effect of 3-oxo-C12 on raw cells, we observed a significant decrease in IL-6, 6 hours post stimulation with IFN- γ and LPS, in the presence of both 3-oxo-C12 (5µM) and 2HQ compare to the negative control (DMSO +2HQ): 23208 +/- 4639 vs 95373 +/-12875 pg/mg protein, p = 0.03. Decrease was also observed for TNF- α under the same conditions (non-significant). Finally, no significant decrease in IL-6 or TNF- α was observed 6 hours post stimulation with C4 (5µM).
Conclusions: We have demonstrated that 3-oxo-C12, an AHL structurally close to 3-oxo-C12:2 present in the human gut ecosystem, interacts with eukaryotic cells by penetration of intestinal epithelial cells. Additionally, 3-oxo-C12 exerts an anti-inflammatory effect, at low concentrations, in the presence of paraoxonases inhibitors in a murine macrophage model.

P052
Allograft inflammatory factor-1 (AIF-1) stimulates Th1 differentiation of human T-cells and protects them from apoptosis

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Background: In previous studies, we have demonstrated that AIF-1 is predominantly found in naïve CD4+ T cells. Activation with anti-CD3/CD28-coated magnetic beads of T-cells stimulated the AIF-1 expression and its secretion to extracellular medium *(Cano-Martínez et al. Gastroenterology 2014. 146(5): s822)*.
The aim of this study was to determinate AIF-1 effect on differentiation of human PBMC (peripheral blood mononuclear cells) stimulated with anti-CD3/CD28-coated magnetic beads. Furthermore, the effect of AIF-1 on proliferation and apoptosis was evaluated in human PBMC.
Methods: Blood of healthy volunteers was used after the application of informed consent. T-cell differentiation was studied by qRT-PCR of Il-2 (interleukin-2), IFN- ϒ (interferon ϒ), IL-4 (interleukin 4), IL-17 (interleukin 17), IL-10 (interleukin 10) and TGF β -1 (transforming growth factor-beta) of human PBMC in vitro. Four conditions were compared: a) basal conditions (incubation of PBMC during 24h in presence of FBS); b) clonal T-cell expansion (addition of anti-CD3/CD28-coated magnetic beads); c and d) Th1 differentiation (addition of anti-CD3/CD28-coated magnetic beads, IL-12 and anti-IL-4) in presence or absence of AIF-1 (6 nM). Proliferation of human PBMC was evaluated by cell counting and by propidium iodide-flow cytometry. Regulation of cell cycle was analyzed and Western blot analysis of Rb, pRb, E2-F and STAT-1 and pSTAT-1. Apoptosis of the different cell populations was studied by multiparametric flow cytometry using Annexin-V and by Western blot of caspase-3.
Results: After incubation of human PBMC during 24h with anti-CD3/CD28-coated beads, we observed an increased expression of IL-2 (p<0,001) without changes in CD25, the alpha chain of the IL-2 receptor; these data were in accordance with the increase in the number of cells and with the phosphorylation of Rb and STAT-1. The clonal expansion seems to affect the cells producing IFN- ϒ (Th1 response), IL-4 (Th2 response) and IL-10 (Treg response) (p<0,001). Not changes were observed in the levels of IL-17 (Th17 response). After incubation of PBMC with anti-CD3/CD28-coated beads, IL-12 and anti-IL-4 (Th1 differentiation), we observed an increase in IFN- ϒ (p<0,001) without changes in the other cytokines previously studied. The presence of AIF-1 in the medium during Th1 differentiation increased the levels of IL-2 and IFN- ϒ (p<0,001), but not IL-4, Il-17, Il-10 and TGF- β mRNA levels. Moreover, AIF-1 protected CD4+ T cells from the apoptosis observed during Th1 differentiation
Conclusions: Our Results demonstrate that exogenous AIF-1 amplified Th1 differentiation induced in vitro by increasing IL-2 and IFN-ϒ*** and by protecting $CD4^+$ T from apoptosis

P053
Mitochondrial dysfunction impairs epithelial proliferative control and stemness in the intestinal crypts

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Background: Heat shock protein 60 (HSP60), a mitochondrial unfolded protein response (mtUPR)-associated chaperone, is highly expressed in intestinal epithelial cells (IEC) of mouse models with chronic inflammation and in patients with inflammatory bowel disease (IBD).

Methods: This study investigates the impact of mitochondrial function and mtUPR on epithelial homeostasis using novel tissue-specific *Hsp60* knockout mouse models.

Results: Postnatal induction of HSP60 deficiency in IEC (*Hsp60*$^{flox/flox}$X*Villin*CreER$^{T2\text{-}Tg}$) caused substantial aberrations in cryptal architecture of the proximal and less in the distal intestine. MT-UPR induction in HSP60-deficient IEC was associated with an abrogated expression of *Ki67*, *Lgr5* and *Olfm4*, indicating a significant loss of epithelial stemness and proliferative capacity. Mitochondria in the HSP60-deficient epithelium showed a decreased expression of functional markers like the mitochondrial encoded subunit I of the cytochrome c oxidase (*mtCoxI*) complex as part of the respiratory chain. Tamoxifen-induced deletion of *Hsp60* in small intestinal crypt organoids *ex vivo* diminished mitochondrial respiration and ATP production, suggesting a role of mitochondrial function in regulating crypt homeostasis. Consistent with the release of growth factors WNT10a, WNT2b and RSPO1 from HSP60-deficient IEC, hyperproliferative stem cell nodules developed in regions with sporadic failure of Cre-mediated Hsp60 deletion, strongly supporting a role for HSP60 in regulating the proliferative response of the epithelium.

Conclusions: In conclusion, tissue-specific deletion of *Hsp60* disrupts epithelial cell homeostasis, largely independent of an inflammation-associated pathology. HSP60 deficiency in the intestinal epithelium triggers mtUPR and affects mitochondrial function, leading to an impaired proliferative response and a loss of stemness.

P054
A simple biomarker for IBD associated dysbiosis : the ratio of iso-LCA/LCA indicates alteration of isomeration of bile acids in the intestinal lumen.

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Background: IBD associated dysbiosis is linked to bile acids (BA) dysmetabolism in the intestinal lumen such as alteration in the deconjugation, transformation and desulphatation of this pool of BA. Isomerization activity leads to isoforms with altered physiochemical properties and functions, quantifiable by mass spectrometry (MS). The objective of our research was to study the impact of IBD associated dysbiosis on the alterations of luminal BA including the isomerization of BA and in particular isomerization of LCA (lithocholic acid) to iso-LCA, with the aim of identifying a biomarker for dysbiosis.

Methods: Faecal samples from patients with IBD (sex ratio M/F 0.75; average age 34 +/- 2.4 years, Crohn's disease n=25, ulcerative colitis n =27) in which activity was evaluated by the Harvey Bradshaw index and from 28 healthy subjects (Sex ratio 1.1, average age 28 +/- 2.7 years) were collected. The composition of the faecal microbiota was determined by qPCR and expressed as log10 bacteria per g stool; in parallel, concentration of faecal BA, expressed as percentage of total BA, was measured by LC-MS. Non-parametric statistical analysis, Wilcoxon, was used to compare microbiota composition and BA levels between patient and control groups. Correlation between groups was analysed by Spearman test. Search for a threshold of different markers of dysmetabolism was carried for the best diagnostic performance (IBD vs control).

Results: Dysbiosis was observed in patients suffering from IBD, compared to control, characterized by a deficit in Firmicutes, notably in C. leptum (8,9+/-0,1 vs 9,8+/-0,1 ; p<10-2) and in F. prausnitzii (9,5+/-0,2 vs 10,9+/-0,2 ; p<10-2) and an increase in E. coli (8,9+/-0,2 vs 8,4+/-0,2 ; p<0,05). Further, a decrease in conjugation, transformation and desulphatation was observed in IBD patients compared with control. Isomerisation of LCA (reported as Iso-LCA/LCA) was also decreased compared with control (10%+/-9 vs 20%+/-5 ; p <0,05) and was lower for patients in flare compared with those in remission (8,5%+/-8 vs 14%+/-4 ; p<0,05). Furthermore, ratio of iso-LCA/LCA was positively correlated with concentrations of C. Leptum (r=0.57) and F. prausnitzii (r=0.50). Using the ratio of iso-LCA/LCA as a marker for the diagnosis of IBD, threshold of 0.73, was superior to all other BA dysmetabolism markers giving a sensibility of 0.85, a specificity of 0.56, a positive predictive value of 0.79, a negative predictive value of 0.65 and an AUC of the ROC curve of 0.82.

Conclusions: In IBD associated dysbiosis, BA dysmetabolism Results in a decrease in isomerisation of BAs. Ratio of iso-LCA/LCA appears to be correlated with dysbiosis, IBD diagnosis and IBD activity, and in this context could provide a simple biomarker for dysbiosis.

P055
Increased Matrix stiffness Modulates MicroRNA expression and fibrogenesis in an in vitro model of intestinal fibrosis

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Background: Fibrosis is the common endpoint of organ failure in many organ systems and disease states, including the intestine and

Crohn's disease (CD). In colonic myofibroblasts, extracellular matrix stiffness characteristic of CD can activate fibrogenesis. microRNAs, small non-coding RNAs (miRNAs), have been shown to regulate fibrosis by targeting and fine-tuning gene expression. We postulated that pathological matrix stiffness may regulate fibrogenesis in vitro by modulation of miRNAs.

Methods: Normal human colonic myofibroblasts (Ccd-18co cells) were cultured on either physiologically soft or pathologically stiff matrices for 48 hours. Candidate stiffness responsive miRNAs were identified by screening a fibrosis-specific miRNA array. Stiffness responsiveness was confirmed by QPCR using individual miRNAs. miRNAs mimics were used to determine whether miRNAs alone induce fibrogenic gene expression.

Results: Eight stiffness-responsive miRNAs were identified and subsequently validated by QPCR. Of interest, two bicistronic miRNAs, miR-143 and miR-145, which are two key regulators of intestinal smooth muscle were strongly induced (9.5 and 7-fold respectively) by high matrix stiffness. Transfection of Ccd-18co cells grown on low stiffness (4.3 kPa) with miR-143 and miR-145 mimics recapitulated the fibrogenic effects of high matrix stiffness. Stiffness-responsive fibrogenic genes fibronectin (FN1), myosin light chain kinase (MYLK) and smooth muscle actin (ACTA2) were induced while the pro-inflammatory gene COX-2 (PTGS2) was repressed.

Conclusions: Pathological matrix stiffness induces pro-fibrogenic miRNAs in normal human myofibroblasts. Addition of miRNAs mimics to cells in a normal physiologically soft (compliant) environment, recapitulates the effects of increased matrix stiffness on fibrogenic gene expression. miRNAs may be a novel mechanism for regulation/auto-propagation of matrix stiffness-mediated intestinal fibrosis in Crohn's disease.

P056
Soluble factors from the inflamed mucosa of patients with Crohn's disease (CD) or from cytokine-stimulated epithelial cells induce the expression of TL1A/TNFSF15 in human intestinal subepithelial myofibroblasts (ISMFs)

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Background: TL1A (TNFSF15) and DR3 (TNFRSF25) are a ligand/receptor pair of the TNF/TNFR superfamilies of proteins. Both proteins are highly upregulated and functionally involved in experimental intestinal inflammation and Inflammatory Bowel Disease. Recent studies in TL1A transgenic mice implicated TL1A/DR3 signalling in inflammation-induced intestinal fibrosis. Our aim was to examine whether the pro-inflammatory mucosal environment that exists in CD may provide stimulatory signals to ISMFs that lead to upregulation of TL1A.

Methods: ISMFs were isolated from endoscopically-obtained colonic biopsies from healthy controls (HC) and patients with CD. Cultured ISMFs were stimulated for 6h with supernatants from overnight cultures of colonic mucosal biopsies. Total RNA was extracted from cultured ISMF and HT-29 cells and TL1A mRNA expression was measured by real-time RT-PCR. HT-29 epithelial cells were cultured unstimulated or stimulated with rhIL-1α and/or rhTNF-α and/or rhIFN-γ and tested for upregulation of DR3 mRNA. Finally, the supernatants from cultured HT-29 epithelial cells were tested for their ability to induce the expression of TL1A in ISMFs.

Results: Supernatants from CD-derived colonic tissue cultures induced a significantly higher upregulation of TL1A expression in cultured ISMFs (>3-fold increase over HC, $P<0.05$). HT-29 epithelial cells significantly upregulated the expression of DR3 (the functional receptor for TL1A) when stimulated with the pro-inflammatory cytokines IL-1α, TNF-α and IFN-γ. Finally, supernatants from HT-29 epithelial cells cultures significantly induced the expression of TL1A in ISMFs when TNF-α was used for stimulation of the epithelial cells either alone or in combination with IL-1α and/or IFN-γ ($P<0.05$ for any combination vs. unstimulated HT-29 cell supernatant).

Conclusions: The pro-inflammatory mucosal milieu in CD contains soluble factors that induce the expression of TL1A in ISMFs and of its functional receptor, DR3, in intestinal epithelial cells. The latter further stimulate ISMFs to express TL1A. We conclude that interactions between ISMF derived TL1A and its receptor, DR3 on epithelial cells may contribute to the pathogenesis of chronic intestinal inflammation.

P057
The T-cell compartment of the adipose tissue-differences of Crohn's disease and obesity

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Background: Creeping fat (CF), a hyperplasia of the mesenteric fat adjacent to the inflamed segments of the intestine, is pathognomonic for Crohn's disease (CD). While fat accumulation in CD is locally restricted, it is generalized in obesity (OB). Today OB is categorized not only as a form of body constitution but rather as a chronic inflammatory state. Since a destroyed mucosal barrier is pathophysiolocically highly relevant in CD, it seems interesting that OB induces an impaired barrier function and intestinal inflammation in rodents. In both diseases distinct alterations within the cellular, humoral, and stromal compartments have been described. While adipose tissue inflammation is believed to be a main player in the systemic consequences of OB, the impact of adipose tissue immune cells in CD is less defined. Whether the immunological processes within the fat contribute to the intestinal inflammation or if the hyperplastic fat might exert a protective function for the organism, is still controversially discussed.

We aim to perform a comparative characterization of the immune-cell department of CD and OB patients in order to reveal the contribution of adipose tissue immune cells for both inflammatory conditions.

Methods: Mesenteric/visceral fat (5-10g) was collected from patients with CD, undergoing surgery because of disease-related complications, and visceral fat from obese patients, undergoing bariatric surgery. Small fractions were fixed in formalin and paraffin. Immune histological staining was performed. Immune cells were isolated from the tissue and lymphocytes were analyzed by flow cytometry.

Results: The morphological pattern of immune cell infiltration differs in CD and OB. While in OB, infiltrating cells are arranged in small groups, widespread inside the tissue; In CD cells accumulate close to the mucosal border. With over 20%, lymphocytes represent a major group of non-adipocytes within the CF. In OB their percentage is significantly lower. In both conditions $CD4^+$ T-cells are higher in number compared to $CD8^+$ T-cells. Interestingly, their activation status differs significantly. While in OB memory-T-cells represent the majority, there is a strong infiltration of naive T-cells into the CF in CD.

Conclusions: Inflammatory processes within the intra-abdominal adipose-tissue impact (intestinal) inflammation in CD and OB. Adipose tissue immune cells contribute to the systemic consequences of OB. The inflammatory processes in intra-abdominal adipose tissue in OB and CD differ significantly; hence adipose tissue inflammation in CD might impact inflammatory processes in other, probably even protective, ways.

P058
Inhibition of microRNA-29a in human bone marrow mesenchymal stem cells augments their immunosuppressive properties

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Background: Mesenchymal stem cells (MSC) offer new therapeutic strategies for refractory IBD due to their potent immunosuppressive properties that can be augmented by stimulation (priming) with pro-inflammatory cytokines. MSC have been proven beneficial in various immunological disorders, including graft versus host disease, ulcerative colitis and Crohn's disease. However, the exact regulatory mechanisms of the MSC immunosuppressive properties remain elusive. MicroRNAs (miRNA) are non-coding RNAs that regulate gene expression, participating in the pathogenesis of several disorders, IBD included. The role of miRNA on the immunosuppressive properties of MSC remains unknown. We hypothesized that miRNA may be involved in the molecular regulation of the immunosuppressive properties of adult BMMSC and that manipulation of miRNA levels might potentiate the salutary properties of BMMSC.

Methods: Human donor derived bone marrow MSC (BMMSC) (n=3) were primed with IFN-γ (50ng/mL, 24 hours). MiRNA profiling (800 miRNAs) was performed by Nanostring nCounter hybridization assays (n=3). Cytokine expression was determined in primed BMMSC via multiplex immunoassays (Bioplex, 40 cytokines) (n=3). MSC immunomodulatory properties were accessed via co-culture assays (n=3) of resting and primed BMMSC with human CFSE-loaded peripheral blood mononuclear cells (PBMC). Gene expression was determined by quantitative RT-PCR. Transfection of BMMSC with miRNA-29a oligonucleotides (inhibitors) or with scramble was performed by lipofectamine assays.

Results: MiRNA-29a was found to be the most robustly expressed miRNA in rested (non-primed) BMMSC and it was the most highly up-regulated following IFN-γ priming (1.7-fold). MiRNA-29a was found to be 2-fold up-regulated in independent samples of IFN-γ primed BMMSC by conventional real-time PCR. Cytokine profiling revealed that IFN-γ induces the expression of numerous immunomodulators including IDO1, CCL5, TNFSF10, CCL2, CXCL16, CCL7, CCL13, CX3CL1, CXCL9, and CCL8. Inhibition of miRNA-29a altered the expression of various cytokines such as IDO1, CCL5, CCL2 and TNFSF10. Finally, co-culture assays between resting and primed BMMSC with human PBMC revealed that inhibition of miRNA-29a in IFN-γ primed BMMSC augments their immunosuppressive properties in comparison to scramble transfected counterparts.

Conclusions: Our data strongly support the notion that miRNA-29a is a novel regulator of the immunosuppressive properties of human BMMSC. MiRNA-29a regulates the expression of numerous cytokines in BMMSC. Understanding the molecular circuits controlling the immunomodulatory functions of MSC will facilitate the design of cell therapy trials for IBD and other inflammatory diseases.

P059
Human alpha-Defensin 6 regulated by both Atoh1 and beta-catenin might be the pathogenesis of Japanese Crohn's Disease

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Background: Antimicrobial mucosal barrier dysfunction, including the reduction of Human alpha-Defensin (HD) 5, is one of the most crucial pathogenesis of Crohn's disease (CD). Human Paneth cells produce two α-defensin peptides, which called HD5 and HD6. Recently, it has been reported that HD6 promotes mucosal innate immunity through self-assembled peptide "nanonets" whereas HD5 has the antimicrobial activity. The transcriptional regulation of HD6 has not been elucidated. Moreover the association of HD6 expression with CD also remains unknown.

We therefore aimed to elucidate the transcriptional regulation of HD6 and the pathogenesis of CD by HD6 expression.

Methods: To investigate the regulation of HD6 expression, We transgened Atoh1 into colon cancer cell line; SW480 by lentivirus infection. The expression of HD6 was assessed by quantitative RT-PCR. The transcriptional activity of HD6 promoter was assessed by the luciferase reporter assay. For the analysis of the HD6 expression in CD, non-inflamed jejunum biopsy specimens of 15 CD patients and 9 healthy controls using double balloon endoscopy (DBE) were assessed.

Results: HD6 was significantly increased by Atoh1 expression in SW480 whereas other antimicrobial peptides such as HD5, Lysozyme and phospholipase A2 were not changed. Atoh1 also enhanced the transcriptional activity of HD6 promoter. We found that HD6 promoter within 200-bp from ATG contains a transcription factor (TCF) binding site and four E-box binding site. The deletion of each binding sites revealed that not only TCF4/β-catenin protein complex but also Atoh1 is indispensable for HD6 expression. Moreover, ChIP assay showed that Atoh1 directly binds to the promoter region of HD6.

Finally, we assessed the HD6 expression in non-inflamed mucosa CD. The microarray using mapping biopsy of entire small intestine in 4 CD patients showed that almost inflammatory related genes were not shown in jejunum compared with 4 non-IBD healthy controls, suggesting that the pathogenesis before the onset of CD might remain in jejunum. HD6 positive Paneth cells of CD patients were significantly lower than that of healthy controls. Moreover, immunostaining showed that β-catenin and Atoh1 are co-expressed in the nuclei of HD6 positive cells, whereas β-catenin is not expressed in the nuclei of HD6 negative crypts.

Conclusions: Both TCF4/β-catenin protein and Atoh1 are essential to express HD6 in different from HD5. The decrease of HD6 in small intestine might cause mucosal barrier dysfunction suggesting that HD6 might be one of the pathogenesis of CD.

P060
Inflammatory bowel disease associates with pro-inflammatory potential of the IgG glycome

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Background: Glycobiology is an underexplored research area in Inflammatory Bowel Disease (IBD), and glycans are relevant to many aetiological mechanisms described in IBD. Alterations in N-glycans attached to the IgG Fc fragment can affect molecular structure and immunological function. Recent genome-wide association studies reveal pleiotropy between IBD and IgG glycosylation. This study aims to explore IgG glycan changes in ulcerative colitis (UC) and Crohn's disease (CD).

Methods: IgG glycome composition in patients with UC (n=507), CD (n=287) and controls (n=320) was analyzed by ultra-performance liquid chromatography.

Results: Statistically significant differences in IgG glycome composition between patients with UC, or CD, compared to controls, were observed. Both UC and CD were associated with significantly decreased IgG galactosylation (digalactosylation, UC Odds ratio[OR]=0.71, 95% confidence interval[CI] 0.5-0.9, p=0.01, CD OR=0.41, CI 0.3-0.6, p=1.4x10-9) and significant decrease in the proportion of sialylated structures in CD (OR=0.46, CI 0.3-0.6, p=8.4x10-8).

Logistic regression models incorporating measured IgG glycan traits were able to distinguish UC and CD from controls (UC p=2.13x10-6, CD p =2.20x10-16), with receiver operator characteristic curves demonstrating better performance of the CD model (Area under curve[AUC]=0.77) over the UC model (AUC=0.72) (p=0.026).

The ratio of presence to absence of bisecting GlcNAc in monogalactosylated structures was increased in patients with UC undergoing colectomy compared to no colectomy (FDR adjusted p=0.05).

Conclusions: The observed differences indicate significantly increased inflammatory potential of IgG in IBD. Changes in IgG glycosylation may contribute to IBD pathogenesis and could alter monoclonal antibody therapeutic efficacy. IgG glycan profiles have translational potential as IBD biomarkers.

P061
The efficacy of tonsil-derived mesenchymal stem cell in chronic murine colitis model

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Background: Stem cell therapy has come into the limelight as a potential therapeutic approach for various diseases, including inflammatory bowel disease (IBD). Tonsil-derived mesenchymal stem cells (T-MSC), a newly-established source of MSC, have many advantages including shorter doubling time, retaining stemness, high differentiating capacity and immune modulatory activity. IBD undergoes a chronic relapsing-remitting condition rather than acute one, here, we aimed to examine whether T-MSC have the therapeutic effect in chronic mice model of IBD.

Methods: Seven to eight week old C57BL/6 mice were randomly assigned to 3 groups: normal control, DSS colitis group (DSS + saline), low-dose T-MSC group (DSS + T-MSC 1x106 per injection) and high-dose T-MSC group (DSS+ T-MSC 2x106 per injection). For the induction of chronic colitis, the mice were treated with 1.5 % DSS for 5 days followed by 5 days of drinking water continuously for 3 cycles (30 days). T-MSC was administered to the treated mice via intraperitoneal route on day 6 and day 16. The severity of the colitis was assessed by the disease activity index (DAI) on every day, colon length, histologic grading and inflammatory cytokines such as IL-6, TNF- σ , IL-10.

Results: Mice with DSS induced chronic colitis suffered pancolitis in 43.5%. 72.9% of mice colon specimen showed infiltration of inflammatory cells at submucosal level or more. The colon length was significantly shortened in the DSS colitis group compared with the normal control group (64.3±5.5 vs 82.7±6.7mm, $p < 0.01$). The T-MSC treated group showed less shortening of colon compared to the DSS colitis group (68.7±4.2 vs 64.3±5.5, $p = 0.057$). The injection of T-MSC improved the DAI at D7 (3.4±1.4 vs 4.8±1.5, $p = 0.016$), but, the improvement was not significant at D14, D21

and D28. The histopathologic grading appeared to be lower in the T-MSC group than the DSS colitis group, but, there was no statistically significant difference (9.2 ± 1.9 vs 8.0 ± 0.9, p = 0.086). The expressions of IL-6, TNF- σ , IL-10 did not differ between the DSS colitis and T-MSC groups.

Conclusions: In our study, intraperitoneal administration of T-MSC reduced the shortening of colon length, disease activity and histopathological inflammation in chronic murine colitis model, but with no statistically significant differences. Whether T-MSC has indeed the therapeutic potential for chronic colitis warrants further evaluation with large scale.

P062
Metabolic phenotyping of healthy and IBD children: Perspectives for individual metabolic monitoring

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Background: Whilst the prevalence of Inflammatory Bowel Disease (IBD) has increased considerably over the last decades, its clinical feature does not allow accurate prediction of disease progression or response to specific therapy. In this context, we used omics technologies to generate a systemic view of IBD pathogenesis and generate further working hypothesis for multiple pathway-integrated therapies.

Methods: A total of 21 paediatric patients with IBD (mean age 14.8 years (range 12.7 - 16.7), 8 males) have been enrolled from the pediatric gastroenterology outpatient clinic over two years. The protocol was approved by the local Swiss Ethical Committee. Clinical and anthropometric data were collected at baseline, 6 and 12 months. A control group of 29 healthy children (mean age 13.1 years (range 10.1 - 16.7), 17 males) has been assessed at baseline. Anthropometric parameters, total and resting energy expenditure have been performed in all individuals, inflammatory and growth markers only in IBD patients. Morning spot urine samples were collected at each visit and subjected to 1H Nuclear Magnetic Resonance (NMR) spectroscopy.

Results: Metabolic profiling of urine samples based on 1H NMR spectroscopy combined with multivariate analysis described two phenotypes corresponding to IBD and healthy children. Orthogonal Projection to Latent Structure Discriminant Analysis (OPLS-DA, explained variance in metabolic data: R2X=0.11, indicator of model robustness: Q2Y=0.28 using 1 predictive and 1 orthogonal components), described distinct central energy metabolic status and gut microbial metabolic signatures. Based on clinical and anthropometric data, sub-populations of IBD patients could be stratified in active disease states, or in remission with either body weight catch-up or body weight and height catch-up. OPLS-DA model generated with 2 predictive and 2 orthogonal components showed statistically significant differences between groups (R2X=0.23, Q2Y=0.24). Children with active disease had higher urinary excretion in purines and pyrimidines, which may reflect immune cell and drug metabolism. Children with body weight catch-up had a differential excretion of gut microbial metabolites (aromatic and short-chain organic acids), whilst children with body weight and height catch-up showed increased IFG-1, IGF-3, and urinary excretion of intermediates in urea metabolism.

Conclusions: The use of metabonomics in chronically ill pediatric patients might be useful in defining the metabolic requirements at the different stages of the disease. Integration of metabolic trajectories as a next step may provide additional insights on metabolic readouts, which might be relevant for individual status monitoring.

P063
Mesalazine and cigarette smoke inhibit neutrophil extracellular trap formation in vitro

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Background: The mucosal infiltrate in ulcerative colitis (UC) is dominated by neutrophils. NET formation is a form of neutrophil cell death used to trap micro-organisms. These neutrophil extracellular traps (NETs) are not only involved in innate immunity, but also in proinflammatory responses. NETs are characterized by the release of DNA and other intracellular components. Citrullination of histones by PAD4 is one of the first steps in a cascade inducing NET formation. Both treatment with mesalazine and cigarette smoking are known to have a beneficial effect on UC, possibly through inhibition of NET formation. The aim of this study was to determine the effect of mesalazine and cigarette smoke extract (CSE) on NET formation in vitro.

Methods: Neutrophils were obtained from the peripheral blood of 15 healthy volunteers and stimulated with Phorbol 12-myristate 13-acetate (PMA), after which they were treated with prednisolon (0-5 ug/ml), mesalazine (0-5mM), hydroxychloroquine (5- 20 uM) or CSE (0-30%). NET-formation was quantitatively assessed by measuring the amount of extracellular DNA. To visualize the presence of NETs we used immunofluorescence (IF) staining for neutrophil elastase (NE), myeloperoxidase (MPO), high-mobility group protein B1 (HMGB1) and Citrulinated Histone H3 (citr. H3).

Results: Both mesalazine and CSE showed a dose dependent inhibition of NET formation (figure 1), while prednisolon and hydroxychloroquine did not. IF showed the presence of MPO, NE and HMGB1 in the NETs. The inhibitory effect of mesalazine and CSE on NET formation was confirmed by IF: MPO and NE remained visible in the cytoplasm, while HMGB1 and citr.H3 stayed within the nuclei. Pretreatment with mesalazine and CSE induced differences in the morphology of the neutrophils: after mesalazine the neutrophils were more stretched with round nuclei, while after CSE treatment the shape was more rounded with polymorph shaped nuclei.

Conclusions: Mesalazine and CSE inhibit NET-formation in a dose dependent manner in vitro. Inhibition of NET-formation, for instance by blocking PAD4 activity, might be a promising target for future UC therapy.

P064
The role of fecal calprotectin in the prediction of ankylosing spondylitis associated with early IBD

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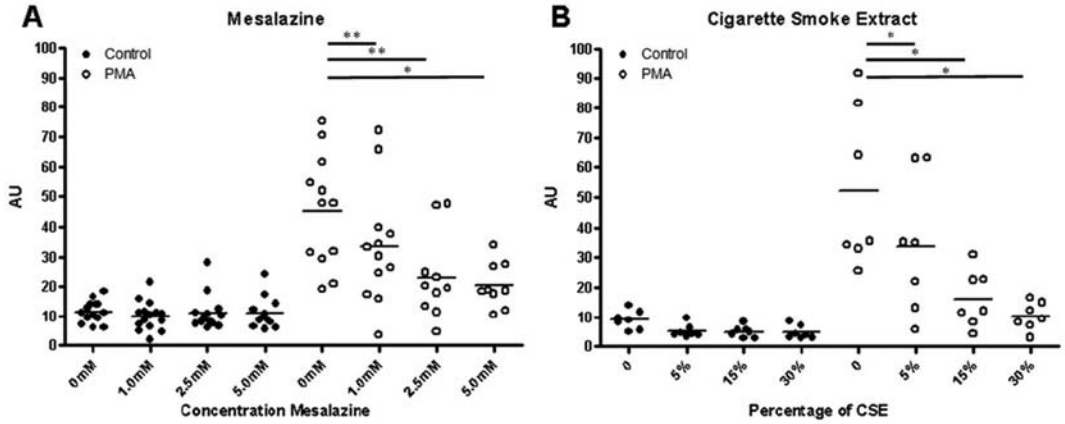

"Figure 1 The effects of mesalazine (A) and CSE (B) on unstimulated and PMA-stimulated neutrophils, measured using extracellular DNA-analysis."

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Background: Ankylosing spondylitis (AS) and inflammatory bowel diseases (IBD) are both chronic inflammatory diseases with unknown etiology, their pathogenic and ethiological characteristics are similar in many ways. 20 percent of patients with IBD have musculoskeletal involvement, whereas in 40-60 percent of patients with AS microscopic or macroscopic signs of inflammation concerning the gastrointestinal tract can be detected.

Methods: The aim of the study was to detect gut inflammation by measuring fecal calprotectin (fCal) levels, performing colonoscopy with multiple biopsy samples. We investigated the relationship of fecal calprotectin levels with symptoms, endoscopic lesions, activity indices.

Results: 19 patients were recruited (12M, 7 FM). The average age of AS patients were 40 years (19-63 years), the average disease duration was 13,4 years. 63% of the patients were male, 84% were HLA-B27 positive. Median fCal level was 162 µg/g. The stool samples of 57% of AS patients were positive for fCal when using the manufacturer's cutoff value for positivity of 30 ug/g. The colonoscopies showed macroscopic and/or microscopic signs of inflammation in ileum or colon in 58% of patients, and in the fCal positive group 81,8% of patients showed evidence of inflammation during colonoscopy (in the fCal negative group only 12,5%). The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was not significantly different in the fCal positive and negative group (3,84 points vs. 3,74 points). Fecal calprotectin levels showed no association with disease duration, ESR level. The CRP levels were significantly higher in the fCal positive group than in the negative group (15,42 mg/L vs 4,68 mg/L). Before our study 3 of the patients were already diagnosed with IBD, the bowel disease appeared years after the diagnosis of the spondylarthropathy.

Conclusions: AS and IBD may associate with each other, therefore on patients with AS a screening fecal calprotectin test should be performed to diagnose early IBD. The detected endoscopic lesions and microscopic colitis can be regarded as early IBD forms, these patients are suggested to be monitored.

P065
Identification of DSG3, MAGI1 and TFF1 as functionally important genes in inflammatory bowel disease pathogenesis

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Background: Genetic and functional studies have implicated an intestinal epithelial barrier dysfunction ('leaky mucosal barrier') in inflammatory bowel disease (IBD). However, it remains unclear whether this dysfunction is a causal event in IBD or rather a consequence of mucosal inflammation. In this study, we investigated the role of intestinal epithelial barrier genes in IBD.

Methods: The mRNA expression of 128 genes involved in different aspects of intestinal epithelial barrier function was studied in 116 colonic mucosal biopsies (74 active ulcerative colitis (UC), 23 inactive UC, 8 active Crohn's disease (CD) and 11 controls) and in 78 ileal biopsies (51 active CD, 16 inactive CD and 11 controls). Disease activity was based on endoscopic findings. Total RNA from biopsies was used to analyse the gene expression with Affymetrix Human Gene 1.0 ST arrays (false discovery rate <0.05 and >2-fold change). We also compared allele frequencies of 3220 SNPs within 104 of the selected genes in our cohort of IBD patients (n=2804; 1856 CD, 948 UC) and 1013 healthy controls using immunochip data. In addition, we tested if these SNPs influenced expression of the differentially expressed genes (eQTL).

Results: No significant difference in colonic barrier gene expression was seen between active UC and active CD. In active IBD, the colonic expression of *MUC1*, *MUC5B*, *EMCN*, *MCAM*, *TFF1*, *CLDN1*, *JAM2*, *DSG3*, *LAMA4*, *LAMC1*, *TCF4* and *F2RL2* was upregulated compared to controls, whereas the colonic expression of *RETNLB*, *CLDN8*, *OCLN*, *MAGI1* and *MEP1A* was downregulated. In inactive colonic IBD, no significant changes were observed compared to controls.

The ileal expression of *MUC1*, *MUC4*, *MUC5B*, *MUC6*, *TFF1*, *CLDN1*, *CLDN18* and *F2RL2* was significantly upregulated in active CD compared to controls, while only the ileal expression of *CLDN8* was significantly downregulated. In inactive CD, *MUC1* and *MUC4* ileal expression remained upregulated, and *CLDN8* downregulated compared to controls.

Forty-six genes showed a significant association (≥1 SNP with $p_{uncorrected}<0.05$) with IBD, of which 8 belonged to the differentially expressed genes (*MUC1*, *MUC4*, *TFF1*, *CLDN8*, *DSG3*, *MAGI1*, *TCF4*, *MEP1A*). Interestingly, SNPs in *DSG3*, *MAGI1*, and *TFF1* did not only confer risk to IBD, but also were eQTLs for their expression in inflamed colon and ileum respectively.

Conclusions: Our data show a dysregulated expression of several barrier genes in active IBD patients, while only in inactive ileal CD patients few barrier genes remained dysregulated, suggesting a primary barrier defect in these patients. The expression data, but also genetic data and eQTL analysis point to *DSG3*, *MAGI1* and *TFF1* as possibly important and functional candidate genes for IBD pathogenesis.

P066
Crohn's disease-associated adherent-invasive Escherichia coli induce secretion of exosomes with pro-inflammatory activity by intestinal epithelial cells

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Background: Crohn's disease (CD) is a chronic inflammatory bowel disease of which the etiology involves environmental, genetic and microbial factors. Our group and others have shown a high prevalence of the invasive Escherichia coli strains, designated adherent-invasive E. coli (AIEC), in the intestinal mucosa of CD patients. Exosomes are small endosomal-derived vesicles involved in cell to cell communication and have been implicated in various diseases including cancer and infectious disorders. It has been reported that mammalian cells infected with pathogens can release exosomes containing microbial compounds. Here, we investigated the capacity of CD-associated AIEC bacteria to induce secretion of exosomes by intestinal epithelial cells and to determine the inflammatory characteristics of the released exosomes.

Methods: Human intestinal epithelial T84 cells were infected with the AIEC reference strain LF82. Exosomes were purified using the ExoQuick exosome precipitation reagent. Exosomes released by LF82-infected T84 cells were tested for their ability to promote pro-inflammatory responses in naïve macrophagic cells. Identification of exosomal proteins was performed by mass spectrometry.

Results: Electron microscopy and immunogold-labeling analyses for CD63, an exosomal marker, showed that differentiated T84 cells infected with AIEC LF82 secreted an increased amount of exosomes compared to uninfected cells. This was confirmed by increased levels of CD63 as assessed by Western blot. Stimulation of human macrophages with exosomes secreted by LF82-infected T84 cells, but not by uninfected cells, significantly induced production of the pro-inflammatory cytokines TNF-alpha and IL-6, and this was not due to the presence of lipopolysaccharide, known to induce a pro-inflammatory response. Mass spectrometry analysis revealed that exosomes released by T84 cells upon LF82 infection carried microbial antigens such as the outer membrane protein C, known to be involved in AIEC adhesion and invasion.

Conclusions: Our study shows that in response to CD-associated AIEC infection, intestinal epithelial cells release exosomes that can trigger pro-inflammatory responses in naïve macrophagic recipient cells.

P067
Binding of infliximab (IFX) to human serum exosomes.

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Background: The loss of response to infliximab has been associated with the presence of antidrug antibodies (ATI). However, other protein complexes in blood could bind this drug blocking its effect. Several studies have suggested that the exosomes (30-100 nm) present in plasma could bind biological drugs decreasing their bioavailability.

Aims: To analyze the molecules that bind IFX. To assess the interaction of IFX with exoxomes. To know the composition of exoxomes by proteomic methods

Methods: Human sera from healthy volunteers (n=3) were analized. The samples were incubated with IFX-alexa 488 and the mixture was injected onto SE-HPLC column. Exosomes were isolated from human serum by Size Exclusion-HPLC using a Yarra3000 column from Phenomenex, USA. The void volume from the chromatographic profile was submitted to ultracentrifugation (160,000 g at 4ºC for 90 min). The pellet was analysed by western blot and using a Nano LC ESI-MSMS shotgun proteomics approach. In the last method was used an Eksigent 1D- nano HPLC coupled via a nanospray source to a 5600TripleTOF QTOF mass spectrometer (ABSciex, Framinghan, MA, USA).

Results: We observed IFX-alexa 488 bound to protein complexes that eluted in the void volume, indicating a diameter (greater than 30 nm) consistent with the size of exosomes. After ultracentrifugation of this last fraction, the pellet was characterized by western blot against CD63 (a classical marker of exosomes). Another part of the sample was used to identify by proteomic Methods, other molecules that co-eluted with IFX-alexa 488. Interestingly, we observed new proteins in the exosomes, as polymeric immunoglobulin receptor (PIGR), fibulin-1, utrophin, complement factor H, dermcidin, immunoglobulin J chain, among others. As predictable, we also identified proteins previously described in exosomes such as keratins, Ig alpha-2 chain C region, Ig gamma-4 chain C region, or thrombospondin-1. At present, we have immunoprecipitated the protein complexes from exosomes using IFX aiming to define news targets of this therapeutic antibody.

Conclusions: Our study demonstrated that IFX was able to bind to human serum exosomes, which were characterized by immunological and proteomic Methods. That should be taken into account when measuring antibodies to IFX as they could be wrongly considered ATI. The study of the structure and the functions of these exosomes could be important to evaluate the bioavailability and efficacy of IFX in patients with inflammatory bowel disease

P068
PSC - IBD is associated with different microbiota composition as compared to UC

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Background: Primary sclerosing cholangitis (PSC) is a progressive disease of the biliary tree characterised by inflammation, fibrosis and stenoses. Inflammatory bowel disease (IBD) in patients with primary sclerosing cholangitis (PSC - IBD) is considered to be a distinct phenotype of IBD with a multi - factorial origin where microbiota most likely have a substantial role. In our pilot study, our aim was to compare the microbiota composition in PSC and/or IBD groups with ulcerative colitis (UC) and healthy controls.

Methods: Total number of 15 individuals was used in presented study: 4 control healthy samples, 4 UC patients, 4 PSC-IBD patients and 3 PSC (without IBD).

Fecal microbiota composition was assesed by sequencing of variable V4 and V5 region of 16S rRNA gene on Personal Genome Machine platform (Fisher Scientific). Library preparation, template preparation and template sequencing was performed according to manufacturer's protocols. Obtained data were filtered by quality and length and processed for alpha and beta diversity analyses using QIIME software package.

Results: Following significant changes in bacterial numbers were observed among tested groups:

PSC versus PSC-IBD:

Higher Bifidobacterium sp. (18 vs 2.71 %), Lachnospira (4.58 vs 0,68 %) and Dorea sp (5.7 vs 1.55 %) and lower Enterococcus sp. (0 vs 9.14 %), Faecallibacterium sp. (1.31 vs 4.12 %) and Prevotella/Paraprevotella sp. (0 vs 9.71 %) numbers.

PSC-IBD versus UC:

Higher Bacteroides sp. (17.13 vs. 4.86 %), Enterococcus sp. (9.14 vs 0 %) and Prevotella/Paraprevotella sp. (9.71 vs 2.13 %) and lower Bifidobacterium sp (2.71 vs 12.95 %) and Faecallibacterium sp. (4.12 vs 16.4 %) numbers.

The clustering of samples according to the type is stronger with the unweighted UniFrac metric than with the weighted metric, suggesting that differences in community membership (rather than community structure) discriminate better among groups.

Conclusions: Members of genus Faecallibacterium and Prevotella showed highest variations with regards to PSC /PSC-IBD/UC groups comparison. Control samples showed higher species richness than patients´ samples. Our data suggest that microbiota composition differs among patients with PSC (without IBD), PSC - IBD and UC. Presented data should be considered as preliminary, as more samples are needed for statistical analyses to support detected observations.

P069
Interleukin 35 and 37 Intestinal Expression and Peripheral Synthesis by Subsets of Regulatory Cells in Patients with Inflammatory Bowel Disease.

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Background: Inflammatory Bowel Disease is characterized by an imbalance between the effectors and regulatory mediators of intestinal immunity with preponderance of pro-inflammatory cytokines. Decrease production of regulatory cytokines such as: IL-10, IL-35 and IL-37 Results in inflammation and autoimmune disease. However, IL-35 and IL-37 intestinal expression and peripheral synthesis by regulatory cells in IBD patients has not been yet described.

Methods: We studied a total of 149 patients divided in different groups: 38 active UC, 31 inactive UC, 17 active CD, and 13 inactive CD and 50 individuals as control group. Gene expression was measured by real time polymerase chain reaction (RT-PCR). Protein expression was detected in tissue by immunohistochemistry and in freshly isolated peripheral blood mononuclear cells by flow cytometry. Descriptive statistics were performed, and categorical variables were compared using the $\chi 2$ test or Fisher's exact test. One way analysis of variance on ranks by Holm-Sidak Method and Dunn's test was performed for all pairwise multiple comparison procedures. Statistical analysis was done using the Sigma Stat 11.2 program. Data were expressed as the median, range, and mean ± standard deviation (SD)/standard Error of the mean (SEM). A p value < 0.05 was considered as significant.

Results: The IDO, IL-35 (p35-EBI3 subunits) and IL-37 gene expression was significantly increased in patients with active IBD versus inactive disease and control group (P<0.05). The IL-37 high expression was significantly associated with a mild clinical course of UC characterized by long-term remission (P= 0.03, OR=0.09, IC 95%: 0.01-0.47). Conversely, UC patients in remission had significantly higher IL-10 gene expression compared with active UC patients (P<0.001) control group and CD patients (P<0.001).However, IDO, IL-35 and IL-37 -producing cells were only increased in active CD versus active UC and non-inflamed tissues (P<0.05). The IL-35 was produced by intestinal B regulatory cells and circulating T regulatory cells in patients with inactive disease (P< 0.05). The IL-37 was synthesized by peripheral activate and regulatory B cells, natural killers and monocytes

Conclusions: This is the first depiction of the expression and peripheral production by regulatory cells IL-35+ and IL-37+ in IBD. These Results suggest that tolerogenic mechanisms in IBD patients might be based on the increase of IL-35 and IL-37-expressing by T and B regulatory cells. Additional studies about IL-35 and IL-37 in the gut mucosal immune response and epithelial restitution can begin to support the immunoregulatory role of these cytokines in patients with IBD.

P070
Ferrous sulphate but not iron polymaltose complex aggravates local and systemic inflammation and oxidative stress in DSS-induced colitis in rats

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Background: Blood loss and impaired absorption in inflammatory bowel disease (IBD) often leads to iron deficiency with or without anaemia (ID(A)). Yet, it has been shown that treatment with oral ferrous sulphate (FS) may worsen the disease symptoms and increase oxidative stress [1] . In this study, we compared the

effects of oral FS and iron polymaltose complex (IPC) on inflammatory and oxidative stress markers in rats with chemically-induced colitis.

Methods: The rats were divided into four groups with ten animals each. Three groups received dextran sodium sulphate (DSS) in the drinking water to induce colitis, and in two of these groups the animals received 5 mg iron/kg body weight a day as FS (group DSS+FS) or IPC (group DSS+IPC) for seven days. The fourth group served as a control. Among others, histology, L-ferritin, tumour necrosis factor-α , interleukin-6, hepcidin, and oxidative stress markers in colon and liver, as well as gross colon anatomy, and serum levels of hepcidin and iron markers were assessed.

Results: All DSS-treated animals developed severe colitis and anaemia. Animals with colitis that were treated with IPC did not show significant differences to animals with colitis but without iron treatment in body weight, gross colon anatomy, crypt injury and inflammation scores, inflammatory parameters in liver and colon, as well as serum and liver hepcidin levels (Table 1). In contrast, treatment with FS caused significant ($p<0.05$) worsening of these parameters. Increasing oxidative stress in liver and colon was observed in the different groups in the order Control < DSS ≤ DSS+IPC ≤ DSS+FS. L-ferritin stainings, serum iron, and TSAT values indicated that iron absorption from IPC and FS took place, although they did not correct anaemia in this model of severe colitis.

Conclusions: In contrast to FS, IPC treatment did not significantly exacerbate colonic tissue erosion, local or systemic inflammation and caused only a minor increase in oxidative stress even at high therapeutic doses in rats with DSS-induced colitis. IPC may thus represent a valuable oral treatment of ID(A) in IBD patients, especially with regard to the typically long duration of oral iron treatments and the often re-emergent nature of ID(A) in IBD.

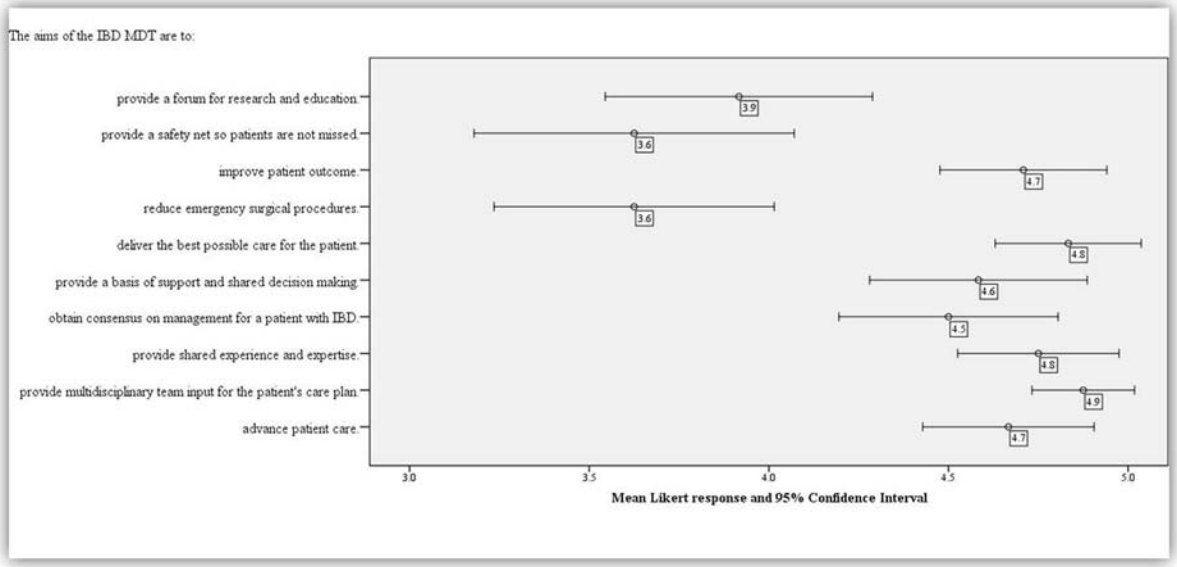
References:

[1] Kulnigg S, Gasche C, (2006), Systematic review: managing anaemia in Crohn's disease, Aliment Pharmacol Ther, 24:1507-1523

"Table 1 Selected parameters with standard deviations for each group at the end of the study."

		Group			
Parameter		Control	DSS	DSS + IPC	DSS + FS
Body weight change	(g/week)	29 ±3.8 *	−16.5 ±2.4	−18.2 ±3.3	−28.8 ±5.5 *
Colon gross anatomy	(score)	0.1 ±0.3 *	4.6 ±1.9	6.4 ±2.7	10.2 ±1.5 *
Crypt injury	(score)	0.1 ±0.3 *	3.5 ±0.7	5.9 ±2.4	11.4 ±3.3 *
IL-6 positive staining, colon	(%/area)	1.1 ±0.3 *	13.4 ±3.0	13.5 ±3.1	30.6 ±7.8 *
IL-6 positive staining, liver	(%/area)	1 ±0.5 *	7.8 ±2.5	9.8 ±3.3	25.8 ±4.7 *
TNF-α positive staining, colon	(%/area)	0.8 ±0.3 *	8.1 ±3.1	9.5 ±2.7	24.5 ±6.2 *
TNF-α positive staining, liver	(%/area)	0.9 ±0.3 *	7.1 ±2.2	8.7 ±2.3	21.7 ±5.0 *
Serum hepcidin	(pg/ml)	12.1 ±0.9 *	18.6 ±2.0	22.6 ±3.9	37.9 ±4.5 *
Hepcidin positive staining colon	(%/area)	1.4 ±0.4 *	6.7 ±1.0 *	9.1 ±1.4 *	15.5 ±1.7 *
Hepcidin positive staining liver	(%/area)	1.5 ±0.3 *	5.4 ±0.9	7.7 ±1.6	19.1 ±2.6 *
GSH:GSSG, colon	(ratio)	11.2 ±0.6 *	5.9 ±0.3 *	4.8 ±0.3 *	3.7 ±0.3 *
GSH:GSSG, liver	(ratio)	7.4 ±0.3 *	4.9 ±0.4	4.8 ±0.5	3.5 ±0.5 *

*significant difference vs. all groups ($p<0.05$)



"Figure 1 Error bar graph representing the aims of the IBD MDT - Mean scores for each stem are represented in the centre of each bar with the bar width representing the 95% confidence interval limits."

P071
Defining the aims of multi-disciplinary team driven care within an inflammatory bowel disease service provision - Results from a Delphi consensus-building methodology

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Background: Multidisciplinary Team (MDT) driven care is arising intuitively within the Inflammatory Bowel Disease (IBD) setting. There are no clear evidence-based definitions of what the aims of the IBD MDT should be. Providing a standardised framework, with clearly defined aims that characterise the purpose of the IBD MDT, may enhance its capacity to establish effective quality improvement. The objective of this study was to obtain a definition of the aims of the IBD MDT, through expert-based consensus.

Methods: This was a prospective, qualitative study using a Delphi formal consensus-building methodology. An eligibility criterion was established to ensure panel members had recognised expertise in the field of IBD. The online survey contained stems, developed on the basis of themes that emerged from prior semi-structured interviews with IBD experts. Participants were asked to rank each stem with a Likert scale (1= not relevant to 5= highly relevant). Likert ratings were represented as mean scores. Consensus was defined with a standard deviation (SD) < 1. Stems with a mean score of ≥4 were included into the primary aim, and those <4 were included into the secondary aim.

Results: A multidisciplinary sample of 24 experts were recruited. The mean number of years of experience in the field of IBD was 11. Stems that described the aims of the IBD MDT [mean; SD] (from highest to lowest relevance) were to provide multidisciplinary input for the patient's care plan [4.9; 0.3], deliver the best possible care for the patient [4.8; 0.5], provide shared experience and expertise [4.8; 0.5], improve patient outcome [4.7; 0.6], advance patient care [4.7; 0.6], provide a basis of support and shared decision making [4.6; 0.7], obtain a consensus on the patient's management plan [4.5; 0.7], provide a forum for research and education [3.9; 0.9], reduce emergency surgical procedures [3.6; 0.9], and provide a safety net so patients are not missed [3.6; 1.1]

Conclusions: The IBD MDT should primarily aim to deliver the best possible care for the patient, improve patient outcome and advance patient care by obtaining multidisciplinary input and consensus on the patient's management plan through a basis that provides support, shared experience, expertise and decision-making. Secondary aims are to reduce emergency surgery and provide a forum for research and education. This definition provides a focus for key specialists, enhancing the MDT as a tool that delivers a high quality IBD service provision. Further validation is required prior to implementation into standards.

P072
Flow cytometric detection of vitamin D receptor changes during vitamin D treatment in Crohn's disease

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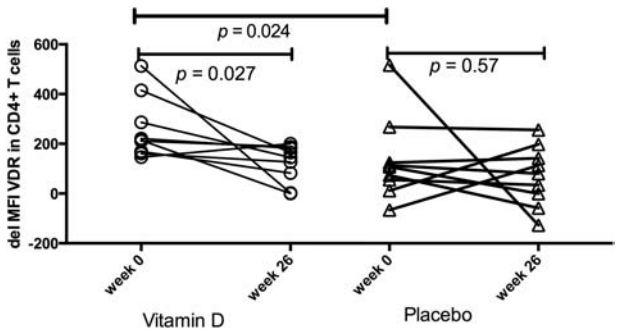

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Background: Crohn's disease (CD) is characterized by a dysregulated T cell response towards intestinal microflora in genetically predisposed hosts. Vitamin D deficiency is common in CD. Vitamin D has immune modulatory effects on T cells through the nuclear vitamin D receptor (VDR) in vitro. It is unclear how oral vitamin D treatment affects VDR expression. We aimed to establish a flow cytometric protocol, including nuclear and cytoplasmic VDR expression, and to investigate the effects of vitamin D treatment on T cell VDR expression in CD patients.

Methods: The flow cytometric protocol for VDR staining was developed using the THP-1 cell line. The protocol was evaluated in anti-CD3/CD28-stimulated peripheral blood mononuclear cells (PBMCs) from vitamin D3- (n = 9) and placebo-treated (n = 9) CD patients. Anti-VDR-stained PBMCs were examined by flow cytometry, and their cytokine production was determined by cytokine bead array. VDR, CYP27B1 and RXR α mRNA expression levels in CD4+ T cells were measured by quantitative reverse transcriptase PCR.

Results: The flow cytometry protocol enabled detection of cytoplasmic and nuclear VDR expression. The Results were confirmed by confocal microscopy and supported by correlation with VDR mRNA expression. VDR expression in CD4+ T cells increased following stimulation. This VDR upregulation was inhibited with 30% by vitamin D treatment compared to placebo in CD patients ($p = 0.027$)(Figure 1).

VDR expression was correlated with in vitro interferon-γ production in stimulated PBMCs ($p = 0.01$).

Conclusions: Flow cytometry is a useful method to measure intracellular VDR expression. Vitamin D treatment in CD patients reduces T cell receptor-mediated VDR upregulation.

P073
The role of eicosanoids in Inflammatory Bowel Disease

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Background: Inflammatory molecules from the class of eicosanoids, in particular prostaglandin E2 (PGE2) and leukotriene B4 (LTB4), are associated with more severe forms of Inflammatory Bowel Disease (IBD) and in contrast, prostaglandin D2 (PGD2) and lipoxin A4 (LXA4) have been described in increased quantity during disease remission.
Methods: A metabolomic analysis of longitudinal samples of serum collected over 2 years from 30 patients affected by UC and CD. The presence of eicosanoids was evaluated with tandem HPLC - MS (High Performance Liquid Chromatography - Mass Spectrometry) and correlated with clinical indices of activity, the Simple Clinical Colitis Activity Index (SCCAI) and the Harvey-Bradshaw Index (HBI). Quantitative variables were analyzed using a Spearman's correlation coefficient; difference in distribution between dichotomous variables was sought with the Mann-Whitney U test.
Results: There was no correlation between the pro-inflammatory eicosanoid LTB4 and clinical activity (Spearman's rho -0.17, p=0.36). Median concentration levels of PGE2 did correlate with activity scores (Spearman's rho, 0.457; p=0.01). A negative correlation between PGD2 and clinical activity could not be demonstrated (Spearman' rho 0.035, p=0.85). LXA4, despite being expected to be associated with disease remission, featured an almost significant correlation coefficient of 0.39 (p=0.07). LXA4 was increased in patients receiving anti-TNF therapy (Mann-Whitney, p=0.044), who also had a more severe clinical activity score (p=0.081).
Conclusions: Although certain eicosanoids have been shown to reflect disease activity when isolated from intestinal biopsies and serum, to our knowledge a longitudinal study that evaluates different eicosanoids using state of the art HPLC-MS represents a novel approach. While a recent study reported the lipoxin concentration to be immeasurable in healthy volunteers, we successfully isolated LXA4 in half of our samples, from patients with more severe disease. This experimental pilot study constitutes the basis for a successive pragmatic assessment of the role of eicosanoids in IBD: patients seen with worsening symptoms in secondary and tertiary care will be prospectively recruited for clinical and biological data collection before medical and surgical therapy. Variation of PGE2 and LXA4 concentration will be used to predict disease severity and identify patterns of remission.

P074
Circulating adipokynes and Paraoxonase-1 activity in overweight Crohn's disease patients

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Background: Inflammatory bowel diseases (IBD) and especially Crohn's disease (CD) are associated with low BMI (body mass index). Although obesity was considered unusual a growing percentage of over weighted IBD patients could be observed, encountering a group with special characteristics Adipose tissue specially characterizing this population by the secretion of different adypocytokines could have an active role in inflammatory changes. Close relationship between PON1 and metabolic markers rise the possibility of the association of PON1 with nutritional status.
Aim of this study was to investigate the possible relationship between adipocitokynes leptin and adiponectin and PON1 activity in CD patients related to nutritional status, disease activity, treatment modalities, and different laboratory parameters.
Methods: Altogether 61 patient were recruited in the study. Groups were developed considering body mass index (BMI), biological therapy (untreated and treated with antiTNF-alfa infliximab respectively) and the status of Crohn's disease (active, inactive) as well.
Adiponectin and leptin concentrations of the sera were measured by sandwich enzyme immunoassays . PON1 paraoxonase activity was analyzed by kinetic semiautomated method, using salt-stimulated and arylesterase substrates. The dual substrate method was used to determine the phenotypic distribution of PON1, (ratio of salt-stimulated paraoxonase to the hydrolysis of phenyl acetate): ratio < 3.0 for AA, ratio between 3.0 and 7 for AB and ratio >7.0 for BB phenotype.
Results: Patients having active disease (CDAI>250) before biological treatment showed elevated leptin level which decreased during infliximab treatment in line with CDAI. (Median: 5.9111 vs. 4.7123, p=0.0236) Arylesterase activity rise in level during anti-TNF alpha treatment, restoring normal level. (Median 123.7441 vs. 106.2700, p=0.0185 respectively).No correlation regarding adiponectin level, paraoxonase activity and cholesterin fractions was found in biological treatment and untreated group. Positive correlation was detected between BMI and CDAI (r2=0.072001, p=0.058408), se LDL (r2=0.225477, p=0.006030) and leptin (r2=0.229931, p=0.005487) respectively. Significant differences were found in leptin levels when over weighted patients compared to the underweighted group (p=0.005487). No difference was observed to adiponectin (p=0.1086), aryl (p=0.6228) and PON (p=0.5527) respectively .
Conclusions: The link between inflammatory a metabolic processes seems to be more evident in owerweighted IBD patients. In this patient type inflammatory processe could be driven in different way needed new innovative therapeutic strategies. Further studies are required to elucidate the underlying immunopathogenesis.

P075
OCT4B1, a spliced variant of OCT4, is expressed in Inflammatory Bowel Disease

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Background: OCT4, a POU-domain transcription factor is considered to be a key factor in maintaining the pluripotency of stem cells. Several OCT4 isoforms are differentially expressed in human pluripotent and non-pluripotent cells. Aim of our study was to identify the presence of developmentally early cells in both peripheral blood and intestinal tissue from patients with Crohn's disease (CD) and ulcerative colitis (UC).
Methods: Both blood and tissue samples were collected from 17 patients with active CD and 13 UC, as well as form 4 healthy individuals. Total RNA was extracted and cDNA was prepared. OCT4 expression and isoform determination were documented by reverse transcription-PCR and real-time PCR. SOX-2 expression levels were

also examined by real-time PCR. The isoforms expressed in the studied cases were confirmed by sequencing.

Results: In all samples, OCT4B1 isoform was expressed. OCT4B1 expression levels were higher in blood samples from CD and UC. More specifically, in blood samples OCT4B1 was expressed 6.87 ± 1.94-fold greater in CD and 3.37 ± 0.53-fold greater in UC compared with healthy controls. Similar Results were obtained in tissues samples, also. On the other hand, the mRNA levels of SOX2 were found slightly increased compared to healthy controls, in both blood and tissue samples of CD patients only.

Conclusions: Our Results are in agreement with previous studies, showing that OCT4 is expressed in peripheral blood in patients with CD. Developmentally early cells, such as hematopoietic stem progenitor cells (HSPCs), mesenchymal stem cells (MSCs), endothelial progenitor cells (EPCs), and very small embryonic-like stem cells (VSELs), are mobilized into peripheral blood in response to tissue/organ injury, suggesting a role of these cells in repair of damaged intestinal tract.

P076
Specific mRNA Expression Profile in Inflamed Colonic Mucosa Derived from Patients with Inflammatory Bowel Disease

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Background: Recent studies indicated that the dynamic interplay between Th17 cells and FoxP3+ T regulatory cells is essential for gut homeostasis maintaining. Cytokines related to these T cells subsets are crucial mediators of tissue damage closely connected to the intestinal inflammation in Inflammatory Bowel Disease (IBD).

The aim of this study was to investigate expression of IL-17A, TGF β 1, IL-6, IL-23, IL-10 and transcription factor FoxP3 in mucosal samples from IBD patients in order to specify the cytokine milieu in the inflamed tissue.

Methods: We examined mRNA relative quantities of these parameters in inflamed and adjacent normal colonic mucosa samples derived from 37 IBD patients (23 with ulcerative colitis - UC and 14 with Crohn`s disease - CD) and in normal mucosa from 12 non-IBD persons by performing qRT-PCR assay. We further investigated IL-17A, TGF β 1, IL-6, IL-10 serum and tissue protein levels by enzyme immunoassay.

Results: Our Results showed that gene expression of FoxP3 and IL-6 were significantly higher in inflamed mucosal tissue of the IBD patients than in the adjacent normal mucosa (p=0.035, p=0.03 respectively), borderline significance for IL-10 (p=0.05), and no significance for IL-17A, IL-23 and TGFbeta. Overall all investigated genes are upregulated according to RQ value in inflamed mucosa in the following order: IL-6>FoxP3>TGFbeta>IL-23>IL-17A>IL-10. We also observed significant differences between higher gene expression of FoxP3 and IL-6 in inflamed tissue in UC (p=0.011, p=0.000 respectively) and CD (p=0.008, p=0.000 respectively) compared to normal mucosa of non-IBD persons and increased TGFbeta in CD patients alone (p=0.041). Moreover IL-6 and TGFbeta were overexpressed (RQ>10) in non-inflamed mucosa from IBD patients in comparison with normal mucosa from the controls. We found also increased levels of IL-17A, IL-6, IL-10 and decreased level of TGF β 1 in inflamed tissue compared to serum levels of patients with IBD. We did not define significant correlation between gene and protein expression of the target cytokines within the IBD patients group. The serum and tissue levels of IL-17A and IL-6 were lower in the non-IBD patients compared to IBD ones. None surprisingly, tissue level of IL-10 and serum level of TGF β 1 in IBD patients were similar to these obtained in non-IBD controls.

Conclusions: Our Results demonstrated significant differences in the expression of some mRNA-encoded effector and regulatory cytokines in IBD. Specific expression profile obtained in mucosa of IBD patients including IL-6, TGF β 1 and IL-10 cytokines simultaneously with the transcription factor FoxP3 may represent a transcriptional hallmark for IBD.

P077
The acquisition of cancer stemness by Atoh1 in colitis associated cancer

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Background: The patients with inflammatory bowel disease have an increased risk of developing colitis-associated colorectal cancer (CAC). CAC often acquires the chemoresistance, resulting in the poorer prognosis than that of sporadic colorectal cancer (CRC). However, how CAC have enhanced malignant potential remains unknown. We therefore focus the pathological characteristic of CAC that shows the enrichment of mucinous carcinoma. We have assessed that APC deletion in CRC directly suppressed the differentiation system of intestinal epithelial cells (IEC), resulting in the non-mucinous form of CRC. The transcription factor Atonal homolog 1 (Atoh1) plays crucial roles in the differentiation of IECs. We have reported that aberrant Wnt signal by APC deletion causes Atoh1 protein degradation by GSK3, resulting in maintaining the undifferentiated state of CRC.

Methods: The expression of Atoh1 in mucinous cancer of four patients with CAC were assessed by immunofluorescence. The expression of Atoh1 fused with mCherry in CRC derived cell line was assessed by fluorescence microscopy. The function of GSK3 was assessed by Western blotting. Cancer stemness was assessed by spheroid-forming assay. Cell cycle was assessed using FUCCI system. Chemo-resistance was assessed by MTS assay.

Results: Atoh1 protein was expressed in mucinous cancer of the patients with CAC. The treatment with TNF- α resulted in the stable expression of Atoh1 in CRC cell line by inducing the dysfunction of GSK3 β phosphorylated by AKT. Microarray analysis revealed the acquisition of the mucus-secreting form by Atoh1 protein stabilization. Moreover, Atoh1 protein enriched cancer stem cells with enhanced cell migration. Furthermore, Atoh1 protein induced cell cycle arrest in G0/G1 phase, resulting in the chemo-resistance to oxaliplatin.

Conclusions: Atoh1 protein stabilized by TNF- α might acquire both mucinous phenotype and more malignant potential in CAC, suggesting that the inflammation on carcinogenesis might preserve the differentiation system of IEC, resulting in the acquisition of both mucinous phenotype and enhanced malignant potential including the enrichment of cancer stem cells.

P078
Evaluating the efficacy of potential drugs for intestinal fibrosis using precision-cut tissue slices

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Background: Intestinal fibrosis (IF) is a common complication in Crohn's disease. Currently, there are no drugs registered to treat IF and the sole therapy is intestinal resection. Transforming growth factor (TGF)-beta and platelet-derived growth factor (PDGF) play a key role in IF and are the main targets for potential treatment. Recently, we developed a novel model for the early onset of IF using precision-cut intestinal slices (PCIS). Our objective was to investigate the antifibrotic effect of some potential antifibrotic compounds, including TGF-beta and PDGF-pathway inhibitors, by using the murine PCIS fibrosis model.

Methods: Murine PCIS were incubated up to 48 h. The viability was assessed by evaluating the ATP content of the PCIS. Gene expression of the fibrosis markers pro-collagen 1a1 (Col1a1), heat shock protein 47 (Hsp47) and fibronectin (Fn2) were determined by qPCR. The effects of antifibrotic drugs mainly inhibiting the TGF-beta pathway: valproic acid (VPA), tetrandrine (Tet), pirfenidone (Pir), and LY2109761 (LY) and mainly inhibiting the PDGF pathway: imatinib (Ima), sorafenib (Sor), and sunitinib (Sun) were determined at the maximal non-toxic concentrations.

Results: Murine PCIS remained viable up to 48 h of incubation and showed increased gene expression of the fibrosis markers (Col1a1, 0.6; Hsp47, 4.0 and Fn2, 4.4 fold). After 48 h, VPA and Tet down-regulated Hsp47 gene expression 2.0 and 1.7 fold, respectively. Furthermore, Fn2 gene expression was also decreased 2.1 fold by Tet. Meanwhile, Pir decreased Col1a1, Hsp47, and Fn2 gene expression 2.2, 1.5, and 1.2 fold, respectively. All investigated markers of fibrosis were down-regulated by LY (Col1a1, 9.0; Hsp47, 1.9 and Fn2, 2.7 fold). Sun decreased the expression of Col1a1, 1.6; Hsp47, 3.3 and Fn2, 2.3 fold, while Sor only down-regulated Hsp47, 1.3 fold. In contrast, Ima did not affect the expression of fibrosis markers.

Conclusions: From the compounds studied, the TGF-beta-inhibitors; Tet, Pir, and LY and only one PDGF-inhibitor, Sun, showed potential antifibrotic effect on gene expression of fibrosis markers in murine PCIS. Thus, PCIS is a promising model to evaluate the antifibrotic effect of potential drugs for intestinal fibrosis.

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Poster presentations

OXFORD

Clinical: Diagnosis & outcome

P079
Predicting the risk of acute severe colitis (ASC) at diagnosis of Ulcerative Colitis (UC): external validation

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Background: A simple prognostic index applied at diagnosis of UC appears to predict the likelihood of patients developing ASC and therefore those at high risk of colectomy. This study evaluated the index in two independent cohorts of patients

Methods: An episode of ASC was defined by hospital admission with bloody diarrhoea >6/d and 1 or more Truelove & Witts' criteria. The index, calculated by the sum of 1 point each for extensive disease, CRP >10mg/L and haemoglobin <12.1g/dL (F) or < 13.8g/dL (M) at diagnosis to give a total score of 0/3 to 3/3, was applied retrospectively to two external validation cohorts (patients diagnosed and followed up for >3y in Cambridge (UK) and Uppsala (Sweden), excluding presentation with ASC within a month of diagnosis). Performance characteristics of the prognostic index were verified by discrimination and calibration.

Results: Table 1 shows the characteristics of development and validation cohorts. Patients in Oxford (n = 111) and Cambridge (n = 96) had much higher rates of ASC during a median 3 years follow up (31% and 26% respectively) than patients in Uppsala (n = 296, 6% ASC). Nevertheless, the mean predicted risk of ASC using the index was similar in the three cohorts: 73%, 72% and 72% (Oxford, Cambridge, Uppsala). Of those who scored 3/3 at diagnosis, 8/11

Table 1

Characteristic		Oxford development (n=111)		Cambridge validation (n=96)		Uppsala validation (n=298)	
		No ASC (n=77; 69%)	ASC (n=34; 31%)	No ASC (n=71; 74%)	ASC (n=25; 26%)	No ASC (n=280; 94%)	ASC (n=18; 6%)
Gender	M	35 (45%)	15 (44%)	44 (62%)	15 (60%)	157 (56%)	9 (50%)
	F	42 (55%)	19 (56%)	27 (38%)	10 (40%)	123 (44%)	9 (50%)
Age at diagnosis	Years	33.5 (23.5, 50.8)	36 (23.5, 42.8)	34 (25, 52)	48 (28, 63)	36 (25, 54.3)	30.5 (22.5, 54.8)
Extent	E1	18 (23%)	1 (3%)	18 (25%)	0	111 (40%)	0
	E2	42 (55%)	17 (50%)	44 (62%	5 (20%)	153 (55%)	3 (17%)
	E3	16 (21%)	16 (47%)	9 (9%)	20 (80%)	16 (6%)	15 (83%)
CRP	mg/L	3.5 (2, 11)	14 (9.25, 43.75)	3 (2, 6)	23 (17, 36)	7.4 (3.2, 10)	19 (11.3, 53)
Hb	g/dL	13.4 (12.5, 14.6)	12 (11.3, 13.9)	13.5 (12.5, 14.4)	11.2 (10.2, 12)	13.9 (13, 14.8)	10.4 (9.7, 11.2)

Table 2

Prognostic Score	0	1	2	3
Number of patients				
Oxford	39	32	29	11
Cambridge	35	29	14	18
Uppsala	163	89	32	14
Number with ASC (%)				
Oxford	4/39 (10%)	6/32 (19%)	16/29 (55%)	8/11 (73%)
Cambridge	0/35 (0%)	2/29 (7%)	5/14 (36%)	18/18(100%)
Uppsala	0/163 (0%)	1/89 (1%)	4/32 (12%)	13/14 (93%)
Mean predicted risk				
Oxford	11%	27%	46%	73%
Cambridge	13%	23%	47%	72%
Uppsala	13%	24%	39%	72%
IQR				
Oxford	8 to 13%	18 to 28%	32 to 52%	61 to 82%
Cambridge	9 to 16%	18 to 27%	39 to 54%	63 to 78%
Uppsala	9 to 16%	17 to 27%	25 to 45%	65 to 80%

(O: 73%), 18/18 (C: 100%) and 13/14 (U: 93%) subsequently developed ASC. The ability of the index to discriminate (c-index, where 1.0 = perfect discrimination) was 0.81 (Oxford), 0.95 (Cambridge), 0.97 (Uppsala).

The distribution of the predicted risks (from score = 0/3 to 3/3) was similar across each of the cohorts, indicating good calibration and the ability of the model to identify those at low or high risk of developing ASC. A nomogram allows individual risk to be estimated.

Conclusions: Despite geographic and demographic differences among three cohorts, this simple index has been verified as a reliable tool to predict ASC within 3 years from diagnosis. Patients with a score of 3/3 at diagnosis may merit early immunomodulator therapy.

P080
Persistence and sensitivity of colonic biopsies for microscopic colitis in a regional cohort

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Background: Microscopic colitis (MC) includes collagenous (CC), lymphocytic (LC) and incomplete microscopic colitis (MCi). The ECCO guideline recommend that a diagnosis of inflammatory bowel disease should be based on separate biopsies from several colonic segments. If applied to patients with chronic diarrhoea this would markedly increase the pathologists' work load.

We estimate the sensitivity of left- and right-sided colonic biopsies for the diagnosis of MC and MC subgroups in a non-selected population of patients and identify histological changes before and after the diagnostic endoscopy.

Methods: All consecutive MC patients diagnosed from January 2000 through March 2014 were identified and included. From the Danish National Pathology Database we extracted for each patient the indication, time and type of all endoscopies, number of biopsies obtained, and biopsysegment. The diagnostic criteria were as previously described. Biopsies from the colon oral to the splenic flexure were classified as right sided and biopsies from the sigmoid and descending colon as left sided. Rectal biopsies were excluded.

Persistence of MC

	CC	LC	MCi
Early (≤ 1 year)	76% (41/54)	58% (18/31)	27% (12/45)
Late (> 1 year)	61% (46/75)	53% (17/32)	18% (3/17)

Results: MC was diagnosed in 749 patients; 354 with CC, 245 with LC and 196 with MCi. The diagnostic procedure was colonoscopy in 221 with CC, 159 with LC and 120 with MCi. The median number of biopsies taken at the diagnostic endoscopy was 7. The sensitivity of biopsies from the left and right colon for the three MC subtypes was 98%-100% and 89%-98%, respectively. 4 patients had histological changes of MC in the right colon only and 17 in the left colon only. Endoscopies prior to the diagnostic endoscopy had been performed in 132 patients a median of 12 (0-218), 5 (1-53) and 16 (1-188) months before the diagnosis of CC, LC and MCi, respectively. The pre-diagnostic histology was normal in 26%, 17% and 22% and chronic inflammation in 40%, 43% and 24% in the three MC subgroups. Post-diagnostic endoscopies were preformed in 129 (37%) with CC, 63 (27%) with LC and 62 (32%) with MCi. The histology was normal in 12%, 10% and 8%. Change to a different MC subgroups occurred in 5%, 11% and 27%. Persistence of MC in the first post-diagnostic endoscopy according to primary diagnosis and time to endoscopy is shown in the table.

Conclusions: The diagnostic sensitivity does not differ between the right and left colon. Chronic inflammation in colonic biopsies from patients with chronic diarrhoea should raise suspicion of MC. The histological findings of CC and LC persist in half of the patients, but rarely normalises. MCi frequently changes to LC or CC.

P081
Matrix Metalloproteinase Degraded Biglycan (BGM) and Citrullinated and MMP-degraded Vimentin (VICM) differentiates Crohn's disease from ulcerative colitis.

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Background: The hallmark of IBD is inflammation, which leads to excessive extracellular matrix remodeling and release of protein fragments into the circulation. Early and accurate diagnosis is essential for optimal treatment. We investigated whether UC or CD contains disease-specific tissue turnover profile, which could be assessed by serological biomarkers

Methods: 72 CD patients (37 with active disease,>150 CDAI), 56 patients with active UC (St. Marks score>2), and 22 patients with irritable bowel syndrome (IBS) were included. Biomarkers of neutrophil elastase degraded elastin (EL-NE), matrix metalloproteinase (MMP) degraded biglycan (BGM), vimentin (VICM) type 5 collagen (C5M), as well as type % collagen formation (Pro-C5), were evaluated by

Table 1 AUC, sensitivity and specificity of each ROC-analysis

	AUC (CI)	Sensitivity %	Specificity %	Percent of cases correctly classified
CD vs. UC: BGM	0.95 (0.92–0.98)	98	80	87 %
CD vs. UC: EL-NE	0.85 (0.77–0.91)	76	77	75 %
CD vs. UC: Pro-C5/C5M ratio	0.66 (0.57–0.74)	43	85	64 %
CD vs. UC: VICM	0.77 (0.72–0.86)	73	86	70 %
CD vs. UC: Biomarker combination (BGM, VICM)	0.98 (0.93–0.97)	94	96	94 %
CD vs. IBS Biomarker combination (Pro-C5, EL-NE)	0.70 (0.60–0.79)	77	56	77 %
UC vs. IBS: BGM	0.97 (0.91–1.0)	98	91	95 %
UC vs. IBS: EL-NE	0.93 (0.85–0.97)	86	86	86 %
UC vs. IBS: Biomarker combination (BGM, EL-NE)	0.99 (0.94–1.0)	90	100	96 %

a competitive ELISA assay system. One way-analysis of variance, Mann-Whitney U-test, and area receiver operator characteristics (ROC) curve analysis were carried out to evaluate the discriminative power of the biomarkers. The biomarkers were adjusted for confounders (age, gender, BMI and smoking). Combination of biomarkers was investigated by a backwards logistic regression model.

Results: BGM (P<0.0001), EL-NE (P<0.0001), Pro-C5/C5M (P<0.001) were significantly elevated in UC patients compared to CD and IBS patients. VICM was significantly elevated in CD patients compared to UC patients (P<0.0001), and Pro-C5 was significantly elevated in CD patients with active disease compared to UC (P<0.001) and IBS patients (P<0.01). The biomarkers with highest diagnostic accuracy to discriminate CD from UC was BGM (AUC=0.95), EL-NE (AUC=0.85), VICM (AUC=0.76) (table 1) . BGM (AUC=0.97) and EL-NE (AUC=0.93) had the highest diagnostic accuracy to discriminate UC from IBS (table 1). The combination of biomarkers with the highest diagnostic accuracy to differentiate CD from UC was BGM and VICM (AUC=0.98) and Pro-C5 and El-NE to CD from IBS (AUC=0.71)(tabel 1). In addition, Pro-C5 (P<0.05) was significant elevated in CD patients with moderate/severe disease activity compared with low disease activity.

Conclusions: These data provide new insights into the molecular patho-physiological differences of CD and UC. The combined accuracy of the biomarkers, BGM and VICM, demonstrated almost a 100% discriminatory diagnostic power. The role of macrophages (VICM) and MMP-mediated biglycan degradation (BGM) warrants further attention to understand the molecular differences between these related diseases.

P082
The relationship between onset days and clinical characteristics of pouchitis after ileal pouch-anal anastomosis in Ulcerative Colitis

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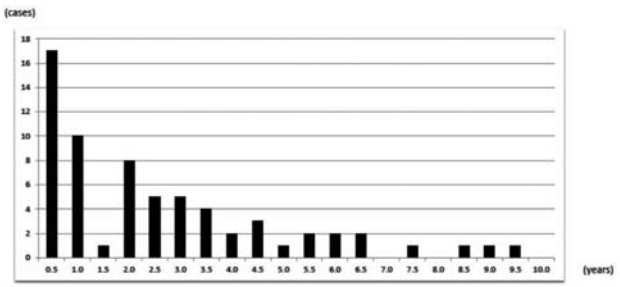
Background: Pouchitis, a nonspecific inflammatory condition of the ileal pouch reservoir, is the most common long-term complication in patients who have undergone ileal pouch-anal anastomosis (IPAA), and it significantly affects patients' quality of life.

It is known the first episode of pouchitis occurred within 6 months of restoration of gastrointestinal continuity in almost half of patients who developed pouchitis

However, no previous studies have examined the relationship between onset days and clinical characteristics of pouchitis.



"Distribution of onset days in patients with pouchitis"

We compare the difference between early and late-onset pouchitis and aim to reveal the characteristics of early-onset pouchitis.

Methods: This retrospective study involved 244 consecutive patients from January 2000 to January 2013 who underwent ileal pouch-anal anastomosis for ulcerative colitis with a minimum follow-up of 12 months. Early-onset pouchitis was defined as pouchitis developing within one year of restoration of gastrointestinal continuity. Patients with pouchitis were divided into early-onset pouchitis and late-onset pouchitis groups for comparison. Pouchitis was defined as a modified Pouchitis Disease Activity Index (PDAI) score of ≥ 5 points. Antibiotic-dependent, antibiotic-refractory, and relapsing pouchitis were categorized as chronic pouchitis.

Results: Two hundred thirty-one patients met the inclusion criteria. Sixty-six (28.5%) patients developed pouchitis. Twenty-seven (40.9%) patients developed early-onset pouchitis(Figure).

Overall pouchitis was finally classified into 35 acute pouchitis and 31 chronic pouchitis cases. Univariate and multivariate revealed no difference between two groups in clinical factors such as gender, age at initial surgery, disease duration, type of disease, extent of colitis, severity of colitis, extraintestinal manifestation. The total modified PDAI, symptom, and endoscopy scores are higher in early-onset pouchitis than late-onset pouchitis respectively (p=0.017, 0.048, 0.011). Proportion of chronic pouchitis was higher in early-onset pouchitis, compared to late-onset pouchitis (62.9% vs 35.9%, p=0.030).

Conclusions: Early-onset pouchitis may be more severe and refractory than pouchitis that occurs >1 year after restoration of gastrointestinal continuity. Understanding the characteristics of early-onset pouchitis may enable us to detect refractory conditions early and alleviate them by active prophylactic or treatment measures in high-risk patients.

P083
Low-grade Dysplasia in Ulcerative Colitis: Risk Factors associated with Progression to High-grade Dysplasia or Colorectal Cancer

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Background: One of the most challenging aspects of managing low-grade dysplasia (LGD) in ulcerative colitis (UC) is the identification of patients who will progress to high-grade dysplasia (HGD) or colorectal cancer (CRC). The aim of this study was to identify risk factors associated with progression to HGD or CRC in UC patients diagnosed with LGD.

Methods: This was a retrospective cohort study. Patients with histologically confirmed long-standing extensive UC who were diagnosed with LGD between 1990 and 2011 were identified from the UC surveillance database of a large tertiary centre in the UK and followed up to 1st January 2013. Data on patient demographics, endoscopic and histological variables at the time of the first LGD episode were collected and correlated with progression to HGD or

"Table 1. Variables associated with progression to HGD or CRC in univariate analysis"

Variables	Categories	Hazards ratio (95% confidence interval)	P-value
Lesion shape	Polypoid §	1	
	Non-polypoid¶	20.4 (8.5 – 48.9)	
	Invisible♯	7.7 (2.7 – 22.0)	<0.001
Lesion size	<1cm	1	
	≥1cm	8.6 (4.0 – 18.6)	<0.001
Colonic stricture	No	1	
	Yes	7.1 (2.4 – 21.1)	<0.001
Previous Indefinite dysplasia	No	1	
	Yes	4.0 (1.9 – 8.4)	<0.001
Multifocal dysplasia	No	1	
	Yes	3.1 (1.6 – 6.0)	.001

§: Paris type 0-I lesions (discrete pedunculated or sessile).

¶: Paris type 0-II (macroscopically visible flat, slightly elevated or depressed), 0-III (excavated), irregular, or plaque-like lesions.

♯: Presence of LGD in the histological examination without evidence of endoscopically visible lesions.

CRC, our primary outcome measure. Time to event analysis was performed using Cox proportional hazards Methods with a Bonferroni adjusted significance level (p=0.0022).

Results: A total of 189 patients were evaluated during 1,100 patient-years of follow-up from the date of the initial LGD diagnosis (median, 53 months; interquartile range, 19 - 92 months). Overall, 38 (20.1% of study population) had progressed to HGD (16 patients) or CRC (22 patients). Table 1 demonstrates the variables significantly associated with progression to HGD or CRC on univariate analysis.

In addition, a statistically non-significant trend towards the progression to HGD or CRC was observed in those patients with history of primary sclerosing cholangitis (hazard ratio (HR), 3.5; 95% confidence interval (CI), 1.2–10.1; p=0.02), a shortened colon (HR, 2.8; 95% CI, 1.1–6.6; P=0.02), metachronous dysplasia (HR, 2.6; 95% CI, 1.3–5.0; P=0.005), and histological active inflammation in the segment of LGD (HR, 2.30; 95% CI, 1.1–4.9; P=0.02). At multivariate level, macroscopically non-polypoid (HR, 12.1; 95% CI, 4.0 - 36.8; P=0.001) or invisible (HR, 6.0; 95% CI, 1.8 - 19.7; P=0.003) lesions, lesions 1cm or larger in size (HR, 3.3; 95% CI, 1.4 - 8.2; P=0.008), and a previous history of "indefinite for dysplasia" diagnosis (HR, 3.0; 95% CI, 1.4 - 6.8; P=0.007) remained significant contributory factors for developing HGD or CRC.

Conclusions: Lesions that are large (1cm or larger), non-polypoid, and endoscopically invisible or proceeded by "indefinite for dysplasia" diagnosis are independent risk factors for the development of HGD or CRC in UC patients with LGD. Patients with these risk factors require careful counseling of management options including colectomy.

P084
Attributes of anti-TNF treatment that impact on preferences of patients with Crohn's disease candidates for biological treatment (IMPLICA Study)

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scenario	Route of Administration	Person Administering Treatment	Place of Administration
A	Intravenous	Healthcare staff	Hospital
B	Intravenous	Healthcare staff	Outpatients
C	Subcutaneous	Healthcare staff	Hospital
D	Subcutaneous	Healthcare staff	Outpatients
E	Subcutaneous	Healthcare staff	At home
F	Subcutaneous	Self-administration	At home
G	Subcutaneous	Family member or carer	At home

Background: To identify attributes related to the biological treatment (BT) of moderate-severe Crohn's disease (CD) most highly valued by patients.

Methods: Observational, cross-sectional, multicentre study. Patients included were diagnosed with moderate-severe CD and were potential candidates for receiving any BT for CD. Patients answered IMPLICA-questionnaire to evaluate the preferences regarding treatment attributes. The questionnaire had 7 scenarios (A to F) with a combination of 3 attributes related to different characteristics of BT The scenarios were scored from 0 (I would never choose it) to 4 (I would always choose it). Conjoint analysis was used to measure the treatment preferences of patients. IMPLICA-questionnaire was provided prior to the visit. Investigator was aware of patient's preferred treatment but whose prescription was based on routine clinical practice.

Results: 201 patients recruited by 19 Spanish gastroenterologists were included. 55.7% were male and mean(SD) age was 38.9(12.3) years. The mean(SD) disease duration was 8.6(8.1) years. Scenarios E and F were the most preferred (57.3% and 53.7% respectively). The place where the treatment is administered is the most influencing factor on patient's preference (importance of 50.7%). Patients who prefer treatment administered at home have a higher perceived health status versus patients who prefer treatment administered in hospital (p<0.01). Regarding route of administration, more patients preferred subcutaneous than intravenous treatment (70.1% vs 29.9%). Up to 68.7% of patients that preferred subcutaneous treatment chose treatment administered at home and 31.3% preferred treatment administered in hospital (by healthcare personnel). Patients aged 37 or older, students and housekeepers give the highest importance to whom administers the treatment, while patients aged <36 years and active workers give the highest importance to the place where the treatment is administered. Demographic and clinical profile was similar between patients that prefer hospital administration versus "at home" administration.

Conclusions: This study demonstrates that place and route of treatment administration have the greatest impact on patient preference for BT and that administration at home by subcutaneous via was the most preferred option of potential candidates for receiving BT. Age and working status have significant relevance in the patient's choice of BT. Knowing reasons for patient's election could help to optimize BT.

P085
Pregnancy-onset IBD is not associated with adverse maternal or neonatal pregnancy outcomes

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Background: Inflammatory bowel diseases (IBD), mainly Crohn's disease (CD) and ulcerative colitis (UC), may affect young female patients, including their childbearing years. In some cases, IBD may also first manifest during pregnancy (pregnancy-onset IBD). Given the fact immune tolerance during pregnancy may be associated with amelioration in disease severity; it may be intuitive to expect IBD cases which first manifest during pregnancy to have a more severe course, with possible adverse pregnancy outcomes. In our center, a dedicated IBD-MOM clinic, comprised of a multidisciplinary team, manages the diagnosis and treatment of IBD patients before, during and after pregnancy.We aimed to evaluate the pregnancy outcomes of female patients with pregnancy- onset IBD.

Methods: Data regarding pregnant patients with IBD is prospectively gathered at our IBD-MOM clinic. Out of the pregnancies followed during 2011-2014, patients whose IBD first manifested during pregnancy (pregnancy-onset IBD) were identified. Maternal and neonatal outcomes were compared between this group and those in the group of non-pregnancy onset IBD. Diagnosis of UC during pregnancy was performed by flexible sigmoidoscopy and mucosal biopsies. Diagnosis of CD during pregnancy was done by MRE and subsequently confirmed by colonoscopy and ileoscopy with mucosal biopsies post-partum. Statistical analysis was done to assess the profile of these two study populations including characteristics of their IBD and pregnancy outcome variables.

Results: During 2011-2014, 81 pregnancies of IBD patients were prospectively followed in our IBD-MOM clinic, 70 with previously known IBD, and 11 patients first diagnosed with IBD during pregnancy (mean age 29 ± 5 and 28 ± 5 years, respectively). Within the pregnancy-onset IBD, 4 patients were diagnosed with CD and 7 with UC compared to 46, 22, and 2 patients with CD, UC and IBD-undetermined respectively in the non pregnancy-onset IBD group. No differences were noted between the two groups in the ethnic origin, type of the disease, extent of disease involvement, pattern of IBD, need of steroids or hospitalization rate. Spontaneous vaginal delivery was achieved in 73% and 90%, respectively (p=0.48). Mean week of delivery was 38.3 ± 3 and 39.6 ± 1.3, respectively (p=0.11). Mean birth weight was 2942 ± 590 gram and 3167 ± 688, respectively (p= 0.27). Normal Apgar scores (9-10) were noted in most of the newborns in both groups (97% vs 100%, p= 0.72). Similar Postpartum exacerbation rate was observed (27% and 33%, p=0.48).

Conclusions: Pregnancy-onset IBD is not associated with negative impact on maternal or neonatal pregnancy outcomes compared to non pregnancy onset IBD.

P086
The presence of the Epstein-Barr virus is associated to a higher colectomy requirement in patients with Ulcerative Colitis

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Background: The Epstein Barr (EBV) infection has been related to Inflammatory Bowel Diseases (IBD), but its relevance in the course of the disease is not well established. Our objective is to investigate the relation between EBV and the clinical course in patients with ulcerative colitis (UC).

Methods: The presence of EBV was determined in the colectomy pieces of 27 patients with UC who had been colectomized by medical treatment refractory disease. The presence of EBV was studied by using in situ hybridation (EBER). The clinical caracteristics of the disease were compared between EBV positive patients and EBV negative ones. As an additional comparing group, it was studied the prevalence of the virus in patients with ulcerative colitis with cortico-refractory disease who did not require colectomy (patients who responded to cyclosporine or anti TNF treatment).

Results: Fourteen (52%) from the 27 colectomized patients with refractory disease were found to be positive to EBV in the surgical piece (+EBV). Fifty percent of them were men. The age expressed in median at the time of the colectomy was 46 years old (+/- 16). The comparison with 13 EBV negative patients did not show any significant differences regarding sex, age at the colectomy or in the evolution time of the disease. It was found that a hundred percent of the patients of the + EBV group had severe clinical activity at the moment of the colectomy vs. 53% of the EBV - group (p=0,006). Three patients (23%) of the + EBV group were receiving thiopurines vs. 11 (77%) of the patients of the - EBV group (p= 0,007). Significant differences in the proportions of patients treated with cyclosporine or anti TNF were not found. The EBV presence in colonic tissue was able to be analyzed in 10 of the 14 patients, and it was positive in all of them. The EBV presence in the tissue was also analyzed in 19 corticorrefractory patients who did not required colectomy. It was observed that only 2 (10,5%) patients of these group were + EBV vs. 10 of the group that require colectomy (p=0,03).

Conclusions: In patients with severe, corticorrefractory ulcerative colitis, the EBV presence in colonic tissue is associated with a higher requirement of colectomy. Further reserch is needed to evaluate if the treatment of this infection improve the clinical course of the disease.

P087
The study of the related risk factors of steroid resistance with Ulcerative Colitis in the Chinese Han polulation

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Background: Ulcerative colitis (UC) is a chronic non-specific colonic inflammatory disease with uncertain etiologies. Recently, the incidence of IBD in China has increased rapidly. The trerapy strategy of UC has been got more and more attention especially about steroid resistance. However, the related risk factors of steroid resistance in patients with UC are uncertain. With this aim, we detected the association between gene polymorphism, disease phenotype, infection etc and steroid resistance.

Methods: 165 UC patients from Peking Union Medical College Hospital were enrolled in this study, with 83 males (50.3%) and 82 females (49.7%). The median age at diagnosis was 39 (31-51). A total of 137 patients had used oral or intravenous corticosteroid, among which 43.8% were steroid-effective, 39.4% steroid-dependent, and 16.8% steroid-resistant. We also enrolled 199 healthy controls, matching for age and gender. Genotypes of C3435T, C1236T loci of MDR1 and -173G/C locus of MIF were detected.

Results: Multivariate analysis showed patients with MDR1 3435TT and 3435CT genotypes had decreased risk of steroid dependence (OR=0.183, 95%CI: 0.039~0.856; P=0.031; OR=0.268, 95%CI: 0.094~0.768). Patients with extensive UC had higher of steroid dependence than proctitis and left-sided colitis (OR=7.602, 95%CI: 2.223~26.001; P=0.001). Patients with elevated ESR had decreased risk of steroid dependence by two thirds (OR=0.312, 95%CI: 0.119~0.818; P=0.018).

Comparing between steroid-resistant group and steroid-effective group, all these three loci were associated with steroid resistance by univariate and multivariate analysis. Multivariate analysis showed that patients with extensive UC had higher risk of steroid resistance than patients with proctitis and left-sided colitis (OR=6.604, 95%CI: 1.104~ 39.510; P=0.039). patients complicated by CMV infection had increased risk of steroid resistance (OR=10.681, 95%CI: 1.490~76.549; P=0.006) . Moderate anemia was also a risk factor for steroid resistance (OR=3.247, 95%CI: 1.066~9.890; P=0.006) .

Conclusions: 1. C3435T locus of MDR1 and -173G/C locus of MIF were associated with steroid-dependent UC, not associated with steroid-resistant UC. There was no significant association between C1236T locus of MDR1 and steroid dependence or resistance.

2. Patients with extensive UC had increased risk of steroid dependence. Patients with extensive colitis, CMV infection and moderate anemia had higher risk of steroid resistance.

P088
Serum Matrix Metalloproteinase-3 Concentration Correlates with Clinical and Endoscopic Evidence of Ulcerative Colitis

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Background: Matrix metalloproteinase-3 (MMP-3), a 59-kDa protein and one of 4 known stromelysins among MMPs, has been reported to be up-regulated in inflamed areas in ulcerative colitis (UC) and is considered to play an important role in mucosal injury. However, the levels of MMP-3 in UC patient serum and its clinical effects remain unknown. We examined whether serum MMP-3 levels are correlated with clinical and endoscopic evidence of UC.

Methods: This study was prospectively conducted from February 2013 to April 2014 at 2 hospitals in Japan. Patients with a history of colorectal surgery and coexisting collagen disease were excluded. Serum samples were collected at the first visit during the study period and serum MMP-3 was assessed in relation to the clinical activity index (CAI) of Rachmilwitz, defined as 5 or more active phases, as previously reported. Serum MMP-3 level was also measured on the day or within 1 week of a complete colonoscopy procedure, with those patients scored according to Mayo endoscopic subscore (MES), with scores of 2 and 3 used to denote an active phase. We then assessed the correlation of serum MMP-3 with MES.

Results: One hundred thirteen patients with UC (mean age 47.6 ± 18.5 years; 65 males, 48 females) were enrolled in the study. Mean serum MMP-3 level was significantly higher in the active (n=22, 155.6 ± 22.2 ng/ml) as compared to inactive (n=91, 58.4 ± 5.0 ng/ml) phase (p<0.001) and significantly correlated with CAI (Spearman's rank correlation coefficient r=0.43, p<0.001). A complete colonoscopy was performed 110 times in 89 patients during the study period. In those, median serum MMP-3 for MES 0 (n=26), 1 (n=46), 2 (n=28), and 3 (n=10), was 45.5 ng/ml (range 12-108 ng/ml), 55.0 ng/ml (17-456 ng/ml), 88.4 ng/ml (24-367 ng/ml), and 127 ng/ml (50-388 ng/ml), respectively. That level in MES 2 and 3 cases was significantly elevated as compared to both MES 0 and 1, though that in MES 1 was not significantly elevated as compared to MES 0 cases. Serum MMP-3 levels showed a significant correlation with MES (r=0.45, p<0.001). For detection of endoscopic evidence in males, serum MMP-3 levels with a cutoff of 92.4 ng/ml had a sensitivity of 69% and a specificity of 82% (MES 2-3), while in females with a cutoff of 36.7 ng/ml those were 83% and 74%, respectively.

Conclusions: Our Results showed that serum MMP-3 levels are elevated during active phases of UC and have a significant correlation with colonoscopic findings. Thus, MMP-3 may be useful as a clinical biomarker in UC patients.

P089
Disease course, phenotype, and medication use in elderly-onset Crohn's disease patients - A population-based IBD-SL cohort study

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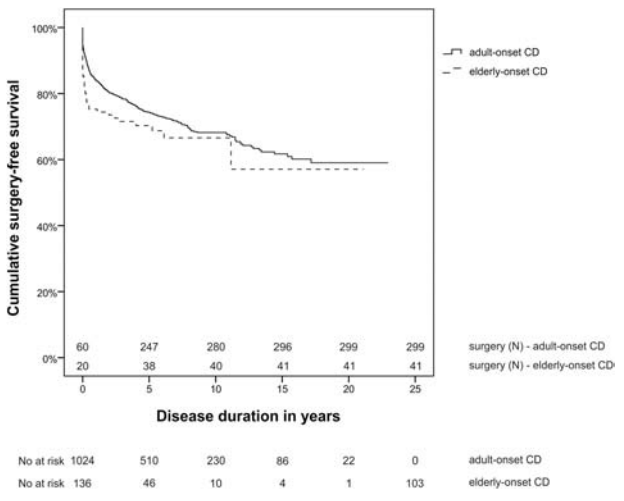
Background: Population ageing is a demographic phenomenon seen in many Western countries. This may result in an increased prevalence of elderly-onset Crohn's disease (CD) patients in our outpatient



"Risk of surgery in elderly-onset and adult-onset Crohn's disease patients"

clinics. For optimal patient information and treatment, insight in the disease course of elderly-onset CD is mandatory. However, data are scarce and often derived from small, selected populations. Therefore, we aimed to study the disease course of elderly-onset CD compared to adult-onset CD in our population-based IBD-SL cohort.

Methods: Since 1991, incident IBD cases in the South-Limburg (SL) area are included in our population-based IBD-SL cohort, with over 93% completeness. CD patients were divided in two groups, based on their age at diagnosis: adult-onset (AO) CD (<60 years at diagnosis) and elderly-onset (EO) CD (≥ 60 years at diagnosis). Disease behaviour was classified according to the Montreal classification as B1 (non-stricturing, non-penetrating), B2 (stricturing), or B3 (penetrating). The disease course of CD was compared between groups for progression to B2 or B3 phenotype, need for immunomodulators or biologicals, hospitalisation and surgery. Data were analysed with a Kaplan-Meier survival curve, and hazard ratios (HR) were calculated using a Cox regression model.

Results: In total, 136 EO and 1026 AO CD patients were included. Mean follow-up was 6.4 (SD 4.9) and 9.0 (SD 5.8) years, respectively. At diagnosis, B1 phenotype was most common in both groups (79.4% and 77.2%) and no difference was found in behaviour distribution (p=0.49). More EO patients than AO patients underwent surgery at diagnosis (14.7% vs. 5.9%, HR 2.49; 95%CI 1.40-4.43). During follow-up, the risk of progression from B1 to B2 or B3 phenotype (47.8% vs. 49.7%, HR 0.92; 95%CI 0.68-1.26), hospitalisation (71.4% vs. 73.1%, HR 0.99; 0.77-1.29) and two or more hospitalisations (36.5% vs. 39.1%, HR 0.87; 95%CI 0.56-1.35) did not differ between groups, nor did the risk of surgery during follow-up (33.1% vs. 37.3%, HR 0.91; 95%CI 0.58-1.43). EO patients were less often treated with immunomodulators (61.8% vs. 77.1%, HR 0.71; 95%CI 0.54-0.95) and biological agents (25.1% vs. 55.2%, HR 0.59; 95%CI 0.37-0.93).

Conclusions: In this population-based IBD cohort, disease presentation was different in elderly-onset CD patients as more surgery was performed at diagnosis. Although elderly-onset CD patients less often used immunomodulators and biologicals, rates of disease progression, hospitalisation and surgery during disease course were similar to adult-onset CD.

P090
Evaluation of NT-proBNP in Inflammatory Bowel Disease

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Background: N-Terminal pro-Brain Natriuretic peptide (NT-proBNP) is currently used as a diagnostic marker in heart failure. Elevated NT-proBNP and significant correlation between NT-proBNP and CRP was recently reported in rheumatoid arthritis (1) and in Crohn's Disease (CD) (2). The purpose of this study was to evaluate NT-proBNP as a marker of inflammatory bowel disease (IBD) activity.

Methods: In this single-center study, NTproBNP assay was performed in patients with CD or ulcerative colitis (UC), irritable bowel syndrome (IBS) and in healthy controls. Clinical characteristics (Harvey-Bradshaw score (HB), Mayo Clinic score (Mayo)), biological (CRP) and endoscopic (CDEIS, UCEIS) data were collected at the time of NTproBNP dosage. Echocardiography was performed in case of NT-proBNP serum levels> 124pg/ml.

Results: To date, 118 patients with CD, 26 with UC, 20 with IBS and 18 healthy controls were included. The median serum NT-proBNP was 50.5 pg/ml [Q1=28-Q3=94] in CD group, 72 pg/ml [46-138] in the UC group, 43.5 pg/ml [27-111] in IBS Group and 34,5pg/ml [26-49] in the control group. A significant increase of NT-proBNP levels was observed in CD patients with HB>4 (p=0.02) or UC with Mayo>2 (p=0.03) as compared to inactive patients. There was a significant correlation between NTproBNP and, the HB score (r=0.31, p=0.0005), and the Mayo score (r=0.45, p=0.01) respectively. A significant increase in NT-proBNP was observed in CD (p<0.001) and UC (p< 0.0016) patients having CRP >10 mg/l as compared to patients with CRP<10. There was a significant correlation between NT-proBNP and CRP in both CD (r=0.64, p<0.001) and UC (r=0.8, p<0.001). Among the 34 patients who had a colonoscopy a significant correlation between NT-proBNP and, CDEIS (r=0.85, p< 0.001), and UCEIS (r=0.78, p=0.007) was observed respectively. A NTproBNP level of 57pg/ml had a sensitivity (Se) of 70% and a specificity (Sp) of 63% (AUC 0.73, 95%CI [0.63-0.83]) to predict a CRP >10 mg/l in CD. In UC, a rate of NTproBNP of 75 pg/ml had a Se of 88% and a Sp of 75% (AUC 0.87, 95%CI [0.71-1]) to predict a CRP>10 mg/l. All echocardiograms performed were normal.

Conclusions: NT-proBNP is correlated to the clinical, biological and endoscopic activity of CD and UC and may be a new biomarker in IBD.

(1) Provan SA et al. Arthritis Res Ther 2008
(2) Colombel JF et al. ECCO 2012.

P091
The impact of a value-based health program for inflammatory bowel disease management on healthcare utilization

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Background: Standardized care pathways, task differentiation, and knowledge of costs in clinical decision making are all likely to contribute to improved outcomes and cost-effective care delivery. The UCLA Center for Inflammatory Bowel Diseases (IBD) launched a value-based health program for IBD management in February 2012 including all these aspects. The aim of this study was to compare utilization patterns observed at the UCLA Center for IBD to IBD care across California.

Methods: Administrative data were obtained from Anthem Blue Cross California. IBD patients and UCLA IBD Center providers were identified, as well as IBD non-program patients who were included as control group. Controls were matched 5:1 with the cases based on disease type, age, relapse rate, and Charlson Comorbidity Index in 2012. IBD-related office visits, laboratory tests, imaging studies, procedures, emergency department (ED) visits, hospitalizations, and pharmacy use in 2013 were compared.

Results: Forty-nine UCLA IBD Center patients were matched to 245 controls. Demographics were similar in groups with a mean age of 39 years (SD 12), 57% Crohn's disease and 43% ulcerative colitis, and 22% severe disease course in the year prior to analysis. We observed significantly less corticosteroid use in the UCLA IBD Center group (12% and 31%, respectively, p=0.03) and numerically more methotrexate (1% and 6%, p=0.11) and adalimumab (15% and 21%, p=0.43) use. Thiopurine (35% and 33%, p=1.00) and infliximab (14% and 15%, p=1.00) use were comparable in both groups. Patients in the UCLA IBD group had 25% fewer IBD-related office visits per year (1.7 and 2.2 visits per year, p=0.06), 12% to 100% fewer imaging studies (p=0.99), 10% less colonoscopies (p=0.91) and 1.3 to 3.4 times more biomarker testing (p<0.0002). Lastly, we observed 89% fewer hospitalizations (p=0.06) in the UCLA IBD Center group and 75% fewer ED visits (p=0.52).

Conclusions: An administrative database was utilized to identify IBD patients treated at the UCLA Center for IBD and to compare those patients with a matched control population in California. We found a significant decrease in corticosteroid use and a trend towards more use of steroid-sparing medications in the UCLA IBD group. Furthermore, UCLA IBD Center patients' disease activity was monitored more frequently using biomarkers, and fewer hospitalizations and ED visits were observed. This study indicates that a comprehensive, value-based care pathway is likely to improve outcomes and decrease unnecessary health care utilization. Future more powerful larger sample studies will be needed to confirm these positive findings.

P092
Risk factors for active tuberculosis in patients with inflammatory bowel disease: A case-control study

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Background: Patients with inflammatory bowel disease (IBD) who receive anti-tumor necrosis factor (antiTNF) therapy are at increased risk of active tuberculosis (TB), mainly by reactivation of latent TB infection. Other risk factors for active TB in IBD patients are still poorly understood.

Methods: A retrospective, case-control, multicenter study was conducted. Patients who developed active TB after the IBD diagnosis were identified from the IBD databases of four hospitals in Northern Spain. As controls, 3 IBD patients per TB case were randomly selected from the same databases, matched on sex, age and year of IBD diagnosis. Both in cases and controls, IBD characteristics and risk factors for active TB were collected. Features of TB episode were described.

Results: A total of 34 cases and 102 matched controls were included, of whom 50% were women; the mean age at IBD diagnosis was 36 years. 9 out of 34 cases were diagnosed between 1989-1999, and 25 cases from 2000 to 2012 (15 cases associated to antiTNF therapy). The cases were current or former smokers, and had received immunomodulator (IMM) or antiTNF treatment, more often than controls; also, the penetrating pattern was more common among cases with Crohn's disease than among controls.

In the univariate analysis, hospitalization and exposure to corticosteroids, IMM or anti TNF in the previous 3, 6 or 12 months, were associated to higher risk for active TB; on the other hand, higher levels of hemoglobin and albumin were associated to lower risk for TB. In the multivariate analysis, only antiTNF therapy in the previous 12 months (OR 8.34 [2.46-28.22], p: 0.001), hospitalization in the previous 3 months (OR 6.25 [1.45-26.90], p: 0.014), and albumin level at the TB diagnosis (OR 0.90 [0.82-0.98], p: 0.013), were significantly associated to active TB. A case of nosocomial infection was demonstrated by the genotyping of Mycobacterium tuberculosis.

Mean age at TB diagnosis was 43 ± 16 years; IMM therapy in the previous 12 months and extrapulmonary presentation were more frequent among TB cases associated to antiTNF treatment (80% vs 37%, p: 0.017; 63% vs 32%, p: 0.03, respectively). Active TB was diagnosed an average of 13 months after starting antiTNF therapy, and only 47% took place after 12 months of starting antiTNF.

Conclusions: In addition to the antiTNF treatment, hospitalization is associated with increased risk of active TB in IBD patients; a mechanism of nosocomial transmission of TB is possible in patients with IBD. Less than 50% of active TB associated with antiTNF occur in the first 12 months after starting this treatment; TB screening should be mandatory after starting treatment with antiTNF.

P094
Prediction of patency capsule retention by MR Enterography in patients with known Crohn's disease:

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Background: The main complication of capsule endoscopy (CE) in Crohn's disease (CD) patients is capsule retention. Evaluation of small bowel patency is recommended before CE administration by using cross-sectional imaging or patency capsule (PC). Our aim was to evaluate the ability of magnetic resonance enterography (MRE) to predict PC retention in CD patients, and to identify the most predictive imaging features for PC retention.

Methods: Fifty seven patients underwent MRE followed by PC. A radiologist blinded to the PC Results gave a positive or negative prediction for PC retention based on the MRE and thereafter all patients swallowed a PC. Diseased segments (DS) on the MRE were evaluated for the following imaging features: mean number of segments, stenosis and prestenotic dilatations, maximal stenosis length, maximal wall thickness and ***presence of enhancement.

The association of these imaging features with the risk of PC retention was evaluated.

Results: The radiologist gave a positive prediction of PC retention in 30/57 patients. Actual PC retention occurred in 13/57 patients and was predicted by MRE in 12/13 cases. The sensitivity, specificity, positive and negative predictive values (PPV/NPV) for prediction of PC retention were 92.3%, 59%, 40% and 96.3% respectively.

Diseased segments were found in 45 /57 patients. The mean maximal stenosis length (9.7 cm vs 7 cm, p=0.04) and the mean number of prestenotic dilatations (2 vs 1.1, p=0.02) were significantly associated with PC retention. One case of symptomatic PC retention occurred in the study which resolved with steroid treatment. No cases of CE retention occurred.

Conclusions: MRE has high NPV and sensitivity but low PPV and specificity for PC retention.

Capsule retention suggested by MRE should not preclude performance of PC to determine the feasibility and safety of diagnostic CE. Longer stenosed strictures and higher number of prestenotic dilatations on MRE were significantly associated with PC retention.

RE, SBH- equal contribution

The study was sponsored by the Helmsley Charitable trust

P095
Lewis Score - prognostic value in patients with isolated small bowel Crohn's disease

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Background: Small bowel capsule endoscopy (SBCE) allows for the characterization of inflammatory activity and distribution of small bowel lesions in Crohn's disease (CD), contributing to therapeutic strategy in these patients. We aimed to assess the prognostic value of the severity of inflammatory lesions, quantified by the Lewis Score (LS), in patients with isolated small bowel CD.

Methods: Retrospective study, between 2008 and 2013, including 49 patients with isolated small-bowel CD, submitted to SBCE at the time of diagnosis. LS was assessed and patients included had at least 12 months of follow-up after diagnosis. The variables defined as adverse events were corticosteroid therapy, hospitalization and surgery during follow-up. The incidence of adverse events were analysed and compared in patients with higher LS (LS ≥ 790), corresponding to moderate or severe inflammatory activity, versus patients with mild inflammatory activity (LS between 135 and 790). Statistics were performed with SPSS v.20.0.

Results: 49 patients included, 63,3% were female with mean age 33 years and mean follow-up of 44 months. Global LS was ≥ 790 in 21 patients (43%), while 57% presented with LS between 135 and 790. The two groups were similar for mean follow-up, family history of CD, extraintestinal manifestations, history of appendicectomy, perianal disease and mean levels of haemoglobin, erythrocyte sedimentation rate, C-reactive protein and ferritin at the time of SBCE. Patients with higher LS were more frequently smokers (p=0,01), were more frequently under immunosuppressive therapy (p=0,006), had more often incomplete SBCE examinations (p=0,01) and had lower albumin mean levels (p=0,002). During follow-up, patients with moderate to severe inflammatory activity in SBCE were more frequently submitted to surgery (p=0,045), had more hospitalizations for CD flares (p=0,008) and needed more frequently corticosteroid therapy (p=0,009) in comparison to those patients with mild inflammatory activity.

Conclusions: in patients with moderate to severe inflammatory activity (LS ≥ 790) there was a higher prevalence of corticosteroid therapy demand, hospitalizations and surgeries during follow-up compared with patients with mild inflammatory activity (LS<135). Thus, the stratification of the degree of inflammatory activity in EC by the LS at the time of diagnosis may have a relevant prognostic value in patients with isolated small-bowel CD.

P096
Transperineal ultrasound: first level exam in the management of perianal disease?

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Background: Pelvic magnetic resonance imaging (MRI) has become the method of choice for evaluating perianal fistulae and abscesses in patients with inflammatory bowel diseases (IBD). Recently, transperinealultrasound (TPUS) has been proposed has a simple, safe and useful diagnostic tecnique to assess different pathological conditions of the pelvic floor including perineal disease in IBD patients.

Aim of this prospective single center study was to evaluate the accuracy of TPUS versus MRI for the detection and classification of perineal fistulae in IBD patients.

Methods: Twenty-eight consecutive IBD patients (17 males, mean age 37,6 ± 16 years) with known or suspected diagnosis of perineal disease were enrolled from November 2013 to November 2014. All patient underwent both TPUS and MRI within 30 days (median). Fistulae and abscesses were classified according to the classification of Parks and the American Gastroenterological Association (AGA) Technical Review Panel. Concordance between the two techniques was assessed by k statistics.

Results: Overall, 33 fistulae (4 superficial, 13 intersphinteric, 8 transphinteric, 2 extrasphinteric and 6 rectovaginal) and 8 abscesses were recognized (1 large and horseshoe-shaped, 2 large deep, 5 small and superficial) on TPUS. Conversely MRI identified 30 fistulae (7 superficial, 11 intersphinteric, 8 transphinteric, 1 extrasphinteric and 3 rectovaginal) and 8 abscess (1 large horseshoe-shaped, 2 large and deep, 3 small and deep, 1 superficial). Two rectovaginal, one intersphinteric and one transphinteric fistulae, and four small and superficial abscessess were not detected on MRI; while one intersphinteric fistula, three small and deep abscesses were not detected on TPUS. The agreement between TPUS and MRI for classyfing perianal fistulae was 75% according to Parks' classification (k = 0,67) and 92% according to AGA classification (k = 0,92).

Conclusions: TPUS is a simple and accurate diagnostic method for classifyng perineal fistulae, especially according AGA classification, and for detecting superficial and small abscesses in IBD patients. Being painless, easily repeatable and cheap method, it could be used in conbination with MRI to evaluate IBD patients with complicated perinel disease.

P097
The Thromboembolism in Inflammatory Bowel Disease - apropos of 28 cases

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Background: Patients with Inflammatory Bowel Disease (IBD) have an increased risk of thromboembolism (TE). Estimating the

magnitude of this risk is important in the decision to start thromboembolic prophylaxis in patients who are already naturally predisposed to bleeding events.
Objective: Characterization of TE in IBD.
Methods: Retrospective study including all patients with IBD and hospitalization between 01-08-2006 and 31-05-2013 with episodes of thromboembolism, venous/arterial. Characterization of the population by the variables: IBD (diagnosis age, type, location, behavior, therapy), thromboembolic event (diagnosis age, type, location, associated risk factors - surgery / trauma, smoking, hypertension, diabetes mellitus, dyslipidaemia; prophylaxis), complications (recurrence, death to 30days).
Results: We recorded 774 admissions of patients with IBD, 28 (3.6%) with thromboembolic episode - 57% male; mean age 58 ± 17 years (21 % <40 years); average duration IBD 13 ± 13years; Ulcerative Colitis 57% (E1-21%, E2-43% and E3-36%) and 39% with Crohn's disease (L1-70%, L2-10%, L3-20 %, B1-25%, B2-42% , B3-33%). Medication: 5-ASA (57%), thiopurines (23%), corticosteroids (15%), anti-TNF (12%). 17 showed arterial complications (10-ischemic stroke, 6-myocardial ischemia, 1-peripheral arterial ischaemia); 7 had pulmonary thromboembolism, 3 deep vein thrombosis, 1 superior mesenteric vein thrombosis. At least 39% of these patients had active IBD. Six venous complications (54%) and 8 arterial complications (47%) had other concomitant risk factors. One case recurred. No deaths were registered.
Conclusions: The TE in IBD is not uncommon, and arterial events seem to be more frequent. However, the concomitant presence of other risk factors requires further study to ascertain the true role of IBD in the pathogenesis of TE.

P098
An endoscopic therapeutic goal to maintain remission with tacrolimus in refractory ulcerative colitis

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Background: Tacrolimus (TAC) is effective as remission induction therapy for refractory ulcerative colitis (UC). Although the drug is principally administered for 3 months, no therapeutic goal to maintain remission has been established. Thus, to explore this goal, we divided patients into two groups: one group of patients who achieved remission maintenance (remission maintenance group), and another group who showed relapse (relapse group) after remission induction with TAC.
Methods: The subjects were divided into the remission maintenance or relapse group. In the groups, the sex, age at disease onset, disease extent, disease duration, pre-TAC CAI (Lichtiger score), Hb, CRP, total amount of PSL until remission, admission period, TAC administration period, post-TAC CAI, Hb, and CRP, and endoscopic score (Mayo score 1 or lower versus 2 or higher) were examined. Relapse was defined as CAI at 4 weeks post-TAC and thereafter being 4 or lower. Subjects with relapse were defined as those who required an intensive intravenous regimen of PSL, switching to a biological product, repeated TAC administration, or repeated remission induction at an increased dose to achieve a higher blood trough level (10 ng/dL or higher).
Results: Between the two groups, no significant difference was noted in the sex, age at disease onset, disease extent, disease duration, pre-TAC CAI, Hb, or CRP, total amount of PSL until remission, admission period, TAC administration period (257 ± 178 and 174 ± 96 days for the remission maintenance and relapse groups, respectively), or post-TAC CAI, Hb, or CRP, whereas a significant difference was observed in the post-TAC endoscopic scores ($P < 0.05$). Adverse reactions including nephropathy (6 patients), tremor (5), and headache (2) occurred, but no significant reaction was noted.
Conclusions: The therapeutic goal to maintain remission with TAC treatment may be an endoscopic Mayo score of 1 or lower. Thus, in patients with a Mayo score of 2 or higher who showed clinical remission induction but persistent endoscopic inflammation, TAC should be continued to achieve a Mayo score of 1 or lower. Additionally, in patients who cannot achieve a Mayo score of 1 or lower in spite of continuous TAC, it is necessary to consider additional therapy or a change in therapy. In treatment with TAC, a goal to maintain remission may be the achievement of an endoscopic Mayo score of 1 or lower.

P099
Efficacy, safety and predictors of response to Adalimumab in Crohn's disease (CD)- a nationwide cohort study

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Background: Adalimumab, a human anti-TNF, is an effective induction and maintenance therapy for patients with moderate to severe Crohn's disease, The aim of this study was to evaluate its efficacy in a large Romanian population and to identify predictor factors of response
Methods: We performed a retrospective cohort study using data from Romanian National Insurrance House. 136 patients with CD received Adalimumab (ADA) between December 2008 and June 2014. Binary logistic regression was performed with the aid of statistical program SPSS, in order to identify predictors of response to ADA .
Results: Patients were half women, with a median age of 36 years, a median disease duration of 2 years, and most of them (82%) received Azathioprine before biologic therapy. Mean therapy duration was 20 months (standard deviation 10 months). 67% of patients had moderate flare of the disease, while 16% had mild disease activity. Regarding disease extension, most of them had ileocolonic involvement (49%), followed by colonic extension (29%), and inflammatory behaviour predominates (61%). 21% of subjects suffered surgical resections of small bowel and/or colon before ADA, and 12% had perianal disease. 104 patients (77%) had complete response on Adalimumab, while secondary loss of response was recorded in 24(17.7%). Non-response appeared in 5 cases (3.7%), and 3 patients responded partially. Adverse events reported were:

local erythema 1, tuberculosis (located in lymph nodes) 1, psoriasis 1, fever of unexplained origin 1, arthralgia 3. 2 deaths were reported, both disease related, and not-related to Adalimumab. Predictors of poor response to ADA were: severe active disease (CDAI more than 450 points): OR 5.67 (95% CI 0.17, 185.65), presence of perianal fistulae: OR 5.87 (95% CI 0.26, 131.15), fistulising behaviour of the disease OR 3.71 (95% CI 0.18, 73.72).

Conclusions: Adalimumab is higly efficient and well tolerated in Crohn's disease, with a complete response rate of 77%. Predictors of poor response to ADA were: severe active disease, perianal disease and fistulising behaviour.

P100
Motivational interviewing in Inflammatory Bowel Disease patients counselling: Data from a case-control study

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Background: Motivational interviewing (MI) is a patient-centered counselling also proven useful in inflammatory bowel disease patients. Some skills are at the base of a successful MI: the ability to ask open ended questions, the ability to provide affirmations, the capacity for reflective listening, and the ability to periodically provide summary statements to the patients. We report data from a case-control study (1:2 ratio) on MI applied to IBD patients.

Methods: Between June 2014 and October 2014 we collected data from 2 IBD referral centers both with knowledge on MI skills but only one of these (case group) currently applied this technique during the visits. At the end of visit all patients filled out an anonymous questionnaire.

Results: 150 patients (85 males [57%]) with a mean age of 41.3 ± 15.3 years were evaluated. Sixty-eight patients were affected by Crohn's disease (45%), 70 by ulcerative colitis (47%), and 12 by indeterminate colitis (8%). In table 1 are summarized all patients' characteristics.

At final analysis 132 patients (88%) were previously evaluated by a gastroenterologist with an high satisfaction rate (77%) which significantly decreased in those at the first outpatient visit (61%, p<0.001). Satisfaction rate on general practitioner was low both in all patients and in those at the first visit (57% and 39%). The lowest satisfaction rate was reported in patients at the first visit (p<0.001), in patients affected by indeterminate colitis (p=0.007), in patients with long disease duration (p=0.002); 83% of patients would have liked the use of explanatory pictures. Patients already followed-up in the referral centers reported a good overall satisfaction rate (98%) which reached 100% in those at the first visit. Nevertheless in the latter group, on a scale from 1 to 5, "5" (100% satisfied) was reported by 98% of patients on MI-group (case group) compared to 54% of controls: p<0.001. No differences in terms "physician's communication skills", "perceived empathy" and duration of visits (41.4±8.2 vs. 40.1±9.2 minutes) were observed.

Conclusions: Our study showed as IBD patients followed-up in referral centers are satisfied of their physician rather than gastroenterologists without experience on IBD. MI is a communication tool very well appreciated by IBD patients and can help "IBD experts" to reach the best communication skills especially in pts at the first visit. Explanatory pictures should be used to help patients to better understand their clinical condition.

Patietns' characteristics"

	N=50	N=100
Male, N (%)	28 (56)	57 (57)
Mean age±sd, years	35.9.1±14.4	44±15.1
Median of disease duration (range), months	16 (1-120)	96 (2-612)
Median of symptoms duration before the diagnosis (range), months	7 (1-41)	11.5 (1-276)
Disease, N (%): Crohn's disease Ulcerative colitis Indeterminate colitis	 24 (48) 20 (40) 6 (12)	 44 (44) 50 (50) 6 (6)
Family history of inflammatory bowel disease, N (%)	11 (22)	25 (25)
Patients previously evaluated by a gastroenterologist, N (%)	35 (70)	97 (97)
Patients previously evaluated by a general practitioner, N (%)	15 (30)	77 (77)

P101
Fecal Calprotectin is a valuable marker for detecting active Crohn`s disease with colon involvement

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Background: Fecal Calprotectin has been detected as a biomarker for active Crohn`s disease(CD). But its diagnostic value in different disease phenotype was not clear.

Methods: 60 active CD (CDAI>150) patients were enrolled. Small bowel lesions were detected by CTE/MRE. Colon lesions were detected by ileocolonoscopy and Simple Endoscopic Score for Crohn's Disease (SES-CD) was assessed by an experienced endoscopist. Fecal Calprotectin(FC), Erythrocyte Sedimentation Rate (ESR), high sensitive C reactive protein(hs-CRP), Platelets count(PLT) were tested simultaneously.

Results: 80% patients had colon involvement (L1: n=12, 20%. L2+L3: n=48.80%). 26.7% had a stricturing or penetrating disease (B1: n=9, 15%. B2: n=8, 13%. B3: n=43, 72%).In patients with colon involvement, FC levels were correlated well with CDAI and SES-CD (P<0.01). ROC curve analysis indicated that for a FC cut-off of 350ug/g, the sensitivity for detecting active CD was 95% and the specificity was 80% (area under curve [AUC], 0.95; P<0.01) that was superior to hs-CRP,ESR and PLT. In patients with small bowel involvement only, although FC levels were correlated with CDAI (P<0.01), but ROC curve analysis indicated that FC was failed in detecting active CD. Among disease pattern, disease location, combination with abdominal complication, and SES-CD, multiple liner regression suggested that SES-CD was the only independent risk factor for high FC levels.

Conclusions: FC is a valuable surrogate marker for detecting active CD in patients with colon involvement. SES-CD was the only independent risk factor of high FC levels.

P102
Hemophagocytic lymphohistiocytosis in Crohn's Disease associated to citomegalovirus (CMV) or Epstein-Barr virus (EBV)

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Background: Infection by CMV or EBV is the most frequent cause of hemophagocytic lymphohistiocytosis (HLH) in patients with Inflammatory Bowel Disease (IBD). We want to know the clinical, epidemiological and analytical characteristics of the appearance of HLH in our patients (for an early diagnosis) and assessing the response to treatment.

Methods: Series of three cases of patients with Crohn's disease (CD), diagnosed with HLH between 2010 and 2014. We analyse basal features of the patient and the IBD. The way of presentation clinical-analytic, diagnostic Methods used and response to treatment.

Results: The three patients with HLH were males with an average age of 35 years old and CD. Two of them were treated with azathioprine and the rest with infliximab.

The three patients presented high fever (39-40ºC), hepatosplenomegaly (slight hipertransaminasemia), cytopenia, hypertriglyceridemia and high levels of ferritine when they came in (see table1). The bone marrow aspiration was positive in two of them. Macrophagic activation and erythrophagocytosis were appreciated. Low levels of NK cells were also observed in two of the cases.

Microbiological diagnosis was performed using PCR techniques in blood. In two of the patients the PCR was positive for CMV and the third, positive for EBV. In two patients it was produced for a primoinfection (cases 1 and 2) while the other one for CMV reactivation.

The three patients were treated with ganciclovir (in an empirical way in case 1 for EBV) as well as standard treatment with corticotherapy, ciclosporine and etoposide, beginning in the fourth, third and fifth day respectively from the day of entry to hospital.

Table 1. Summary of clinical and laboratory manifestations *(diagnostic criteria)*

	Case 1	Case 2	Case 3
Age (years)	24	36	43
Sex	Male	Male	Male
Treatment for CD	Infliximab	Azathioprine	Azathioprine
Clinical manifestations			
Fever	+	+	+
Splenomegaly	+	+	+
Cytopenia			
Hemoglobin	75 mg/L	100 mg/L	89 mg/L
Platelets	19000	79000	79000
Neutrophils	0	600	700
Hypertriglyceridemia	1269 mg/dl	238 mg/dl	194 mg/dl
Hypofibrinogenemia	0.7 g/dl	-	-
Hiperferritinemia	> 5000	4597	1333
Bone marrow aspiration			
Erytrophagocytosis	-	+	+
Macrophagic hyperplasia/activation	-	+	+
Low level cells NK	±	±	:
Microbiology			
Serology			
IgM VEB	-	-	+
IgG VEB	-	-	+
IgM CMV	-	-	+
IgG CMV	-	-	+
PCR VEB	+	-	-
PCR CMV	-	+	+
Treatment			
Corticotherapy	+	+	+
Ciclosporine	+	+	+
Etoposide	+	+	+
Ganciclovir/valganciclovir	+	+	+
Inmunoglobulins	+	-	-
Days between admission hospital and treatment	4	3	5

The three patients evolved favourably after the start of the treatment. The clinical symptoms diminished and the cytopenia (progressive improvement) in 2-4 weeks, without requiring hematopoietic cell transplantation.

Conclusions: All patients who have IBD with immunosuppressive treatment who show high fever and cytopenia should be monitored for HLH, the diagnostic criteria for which are in the enclosed table. The early treatment influences the prognosis of this disease (sometimes fatal), may check in these cases that showed good performance thanks to the early establishment of it. We believe it is important to perform a serum bank of the main viruses (including EBV/ CMV) before treatment for IBD, in order to be able to suspect primoinfeccions /reactivations thereof.

P103
Assessment of QOL using internet web system in Japanese patients with Inflammatory Bowel Disease: The 3I survey

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Background: Little is known about the QOL of patients with inflammatory bowel disease (IBD) in Japan. The aim of this survey was to compare the current living conditions and QOL between patients with IBD and healthy people in Japan, using a questionnaire through Internet-Web system (3I survey).

Methods: Through the Internet, we asked 464 patients with Crohn's disease (CD), 360 patients with ulcerative colitis (UC) and 4100 healthy controls (HC) for a questionnaire including SF-8 to. The survey was conducted until the predetermined numbers of CD patients (120), UC patients (120) and HCs (240) could be achieved.

Results: Responses to the questionnaire were obtained from 120 CD patients, 120 UC patients, and 240 HCs. While there were significant differences in gender with male predominance in CD patients (73%) and UC patients (76%) when compared to HCs (57%), other demographics were no different among the three groups. The marriage rate in adults was significantly lower in CD group than in UC group and HCs. The mean annual income and the unemployment rate were also significantly lower in CD group than in the other two groups. QOL assessment by means of SF-8 revealed that five of the eight items showed significantly lower values in CD and UC groups than HCs. Furthermore, the five items were lower in CD group than in UC group. The overall analysis of CD and UC patients showed that there was a significant and negative correlation between each score of SF-8 and the 4-grade degree of symptoms (diarrhea and abdominal pain).

Conclusions: The Results of the survey suggested that the marriage rate and income are lower in Japanese patients with IBD, and this is especially the case for patients with CD. The QOL seems to be disturbed in Japanese patients with IBD, presumably due to abdominal symptoms.

P104
Fecal calprotectin as a non-invasive biomarker for intestinal involvement of Behçet's disease

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Background: Little is known about the usefulness of fecal calprotectin (FC) measurement in predicting intestinal involvement of Behçet's disease (BD).

Methods: Forty four consecutive patients with systemic BD who underwent colonoscopy for the evaluation of gastrointestinal symptoms were prospectively enrolled between November, 2012 and March, 2014 in a single tertiary medical center. Fecal specimens from the patients were obtained the day before bowel cleansing.

Results: Twenty five patients showed intestinal ulcerations on colonoscopy [12 (48.0%) typical and 13 (48.0%) atypical ulcerations]. Of them, six (24.0%) definite, eighteen (72.0%) probable, and one (4.0%) suspected intestinal BD were diagnosed according to the validated criteria for intestinal BD. Mean FC level of intestinal BD group was significantly higher than of non-diagnostic group (306.5 ± 367.7 vs. 59.9 ± 85.4, respectively, P=0.012). Moreover, typical ulceration group showed significantly higher FC level than atypical ulceration group in patients with intestinal BD (476.3 ± 444.5 vs. 149.7 ± 183.8, respectively, P=0.033). Multivariate analysis revealed higher FC as an independent predictor of intestinal BD (OR=1.014; 95% CI = 1.000-1.028; P=0.043). The cut-off levels of FC were 110.44 µ g/g (83.3% sensitivity and 81.2% specificity) for predicting typical ulceration and 68.89 µ g/g (75.0% sensitivity and 75.5% specificity) for predicting intestinal BD.

Conclusions: FC level might have a significant role as a non-invasive surrogate marker of intestinal involvement of BD.

P105
Evaluating the frequency of MEFV gene mutation and its impact on the clinical course in patient with inflammatory bowel disease

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Background: Inflammatory bowel disease (IBD) and familial mediterranean fever (FMF) have similar clinic and pathologic features. Here in the frequency of MEFV gene mutation and the effect of its presence on the outcome of IBD was evaluated.

Methods: Genetic variants on 2nd and 10th exon of MEFV gene were determined by DNA sequence analysis in blood samples of IBD patients. The relation between presence of MEFV gene mutation and the requirement of steroid, immunomodulator, biologics and surgical intervention was analyzed.

Results: Hundred IBD patients (55 ulcerative colitis and 45 Crohn's disease) were evaluated. The frequency of MEVF gene mutation was 20% (n=20). Although no relation was found between the presence of MEFV gene mutation and the requirement of steroid (p=0.917), immunomodulator (p=0.468) and biologic agent (p=0.585), there was a statistically significant relation between the need for surgery (p=0.021). In logistic regression analysis the presence of E148Q and M694V mutations were associated with the requirement of surgical intervention [Odds ratio, 6,25 (95% CI, 1.1-34.6)].

Conclusions: It was determined that the mutation related to FMF in the MEVF gene encoding substances important in inflammatory function, was high in IBD patients that required surgery. Given the fact that these patients have frequent and severe attacks it should be confirmed whether the mutations are related to the clinical severity.

P106
Screening for melanoma and non melanoma skin cancer in IBD patients before and after thiopurines and anti-TNFs: A single-center prospective cohort study

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Background: An increased frequency of skin cancers has been reported in Inflammatory Bowel Disease (IBD). An increased risk of Non Melanoma Skin Cancer (NMSC) and melanoma has recently been associated with thiopurines (IS) and anti-TNFs use, respectively. In a prospective study, we aimed to assess the frequency of NMSC and melanoma in a cohort of IBD patients (pts.) screened for skin cancer before and 1 year after IS o anti-TNFs treatments.

Methods: From January 2012 to November 2014, IBD pts. with indication for IS or anti-TNFs were screened by a dedicated dermatologist. Assessments were performed by the same IBD-dedicated team. Dermatological assessment focused in detecting NMSC and melanoma was performed before (T0), at 6 (T6) and 12 mos (T12) after IS. Data were expressed as median (range).

Results: Dermatological screening was performed in 110 IBD pts. (55 M,age 44 [21-71]; IBD duration 8.5 yrs, [1-48]). IBD pts. included 29 UC (16 M, age 46 [24-71]; duration 8 [2-48] yrs; proctits 5,left-sided 4,extensive 19, IPAA 1), 81 CD (39M,age 44 [21-67] yrs;duration 9[1-31] yrs; CD colitis 6,ileo-colitis 17,ileitis 58). Combo therapy (1 azathioprine, AZA+Infliximab, IFX;3 AZA+adalimumab,ADA) was given after T0 in 4 (4%) pts. Monotherapy included AZA in 35 (32%) IBD (13 UC,22 CD), 6-MP in 4 (4%) IBD (1 UC,3 CD), anti-TNFs in 67 (61%) IBD (14 UC,53 CD): IFX (n=37;34%)(12 UC,25 CD), ADA (n=30; 27%) pts. (2 UC,28 CD). Before IS or anti-TNFs, NMSC occurred in 2 (2%) pts, melanoma in no pts. (0%). At T0, all pts. received local photolyase to prevent skin cancer. At T6, 44 pts (40%) already completed the screening: 15 (14%) discontinued therapies due to: intolerance 8 (AZA 6,IFX 1), pregnancy (1), IFX; infections 3 (1 IFX, 2 ADA), relapse 3 (1 IFX,1AZA,1 ADA), 3 (3%), lost at follow up, death 2 (2%)(cirrhosis,sepsis), low compliance 38 (34%), 7 (6%) pts. are in follow up. At T12, 85 (77%) pts. are in follow up. Screening was completed in 31/85 (36%) pts.: 4 (5%) discontinued AZA (n=1), ADA (n=2) or IFX (n=1) for intolerance, no compliance 37 (43%), 17 (20%) pts. are in follow up. At T24, 82/110 (74%) pts. are in follow up. Screening was already performed in 21/82 (26%) pts: 2/82 (2.4%) pts. discontinued IFX (n=1; pregnancy) or ADA (n=1; relapse), 21 low compliance (26%), 40 pts. (48%) are in follow up. No cases of NMSC or melanoma occurred at 6,12 or 24 mos.

Conclusions: In a cohort of IBD pts. from a Mediterranean area, dermatologic screening before immunomodulators showed a low frequency of NMSC and no melanoma. Screening and photoprotection are however indicated during immunomodulatory treatments in IBD pts., at higher risk of skin cancer.

P107
Increased prevalence of lower GI tract abnormalities without any IBD in patients with primary biliary cirrhosis

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Background: Involvement of lower gastrointestinal (GI) tract, particularly inflammatory bowel disease (IBD) prevalence, is not known in patients with primary biliary cirrhosis (PBC). Our aim was to evaluate these involvements in patients with PBC by using lower GI tract endoscopy. Because of both diseases (IBD and PBC), have similar background, the occurence of IBD was also questioned by endoscopy with/or without biopsy.

Methods: We evaluated our PBC clinic's records, retrospectively. Lower GI tract abnormalities were evaluated by colonoscopy and rectoscopy. Patients with recent onset dyspepsia were used as a control group.

Results: Of the 82 patients with PBC, 62 had documented abdominal ultrasound and 18 patients had lower GI tract endoscopy Results. There were 61 patients without PBC as a control group. All of the patients, 8.1% in PBC and 8.1% in control were male (p> 0.05). Lower GI tract examination was performed by colonoscopy with ileum entubation (IE) in 5 patients and without IE in 8 patients as rectoscopy was in 5 patients. Colon polyps (size from 1 to 15 mm) were found in 5 patients as follows: 3 with adenomatous, 1 with tubulovillous and 1 with inflammatory changes. Ileum biopsies showed normal ileum mucosa in all 5 patients. US showed: Gallbladder polip, 1.6% in PBC vs 4.9% in controls (p> 0.05); gallbladder sludge&stone, 14.5% in PBC vs 9.8% in controls (p> 0.05); gallbladder operation, 22.6% in PBC vs 9.8% in controls (p= 0.05); gallbladder wall tickness, 6.5% in PBC vs 1.6% in controls (p> 0.05); all gallbladder abnormalities 43.5% in PBC vs 26.2% in controls (p< 0.05); pancreas abnormalities 6.5% in PBC vs 0% in controls (p< 0.05).

Conclusions: Our Results showed that colon adenomatous polyps occurence was increased in PBC. None of the patients with PBC had IBD.

P108
Mean Platelet Volume As An Inflammatory Marker In Inflammatory Bowel Disease

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Background: Many non-invasive tests have been studied for diagnosis and determining the activation degree of inflammatory bowel disease (IBD). Thrombocyte count and mean platelet volume (MPV) are influenced by the chronic inflammation. They are considered as useful markers of inflammatory bowel disease. The aim of the study was to investigate the capacity of MPV and other inflammatory markers in detecting IBD activity and also to determine whether MPV would be a useful, cheap and non-invasive biomarker for following up and determining severity of IBD.

Methods: A total of 181 patients with IBD (128 ulcerative colitis and 53 Crohn's disease) and 30 healthy volunteers were enrolled into the study. Disease activity was assessed using the Crohn's Disease Activity Index (CDAI) and the Truelove and Witts severity index. Platelet counts, MPV, and inflammatory parameters were measured for all study subjects.

Results: Eighty-one subjects had active disease and 100 subjects were in clinical remission. Total platelet count (PLT), sedimentation rate, and C- reactive protein (CRP) were significantly increased (p=0.001) and mean platelet volume was significantly reduced (p=0.015) during the clinical relapse state compared to the clinical remission state. The significant difference of MPV values was most apparent between remission and severe disease states (p=0.004). Statistical difference was not found between moderate or mild disease activity and remission state in terms of MPV values. A statistically significant decrease in MPV was noted in patients with severely active disease (8.24 ± 0.61 fL) compared with healthy controls (7.43 ± 1.07 fL) (p=0.013; p<0.05).

Conclusions: Our study showed that MPV is reduced in IBD, particularly in patients with severely active disease. Decreased MPV can be an independent laboratory marker of clinical disease activity in IBD.

		Disease	Activity		
	Remission (n=100)		Activation		
		Mild (n=39)	Moderate (n=29)	Severe (n=13)	
	Mean±SD (median)	Mean±SD (median)	Mean±SD (median)	Mean±SD (median)	p
MPV	8.56±1.33 (8.4)	8.38±1.03 (8.1)	8.00±1.34 (8.3)	7.43±1.07 (7.4)	0.015
CRP	0.63±0.76 (0.4)	0.88±1.19 (0.5)	3.93±3.42 (2.7)	7.18±5.94 (5.1)	0.001
Sedim	23.39±18.19 (17)	25.35±13.94 (24)	49.36±23.35 (51.5)	54.23±32.2 (55)	0.001
Albumin	4.02±0.43 (4.1)	4.12±0.26 (4.2)	3.70±0.49 (3.8)	3.47±0.47 (3.5)	0.001
Hemoglobin	12.86±1.74 (12.8)	13.24±1.94 (13.5)	11.93±1.67 (11.9)	10.13±1.55 (10.1)	0.001
PLT	286.05±92.42 (263.5	270.98±76.24 (268)	395.24±134.22 (365)	405.85±123.83 (436)	0.001

Labratory Findings According to Disease Activity

P109
The prevalence of liver, biliary tract and pancreas abnormalities in patients with Inflammatory Bowel Disease screened by US and confimed by echoendoscopy

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Background: It was reported that involvement of the pancreas, liver and biliary tract, including the gallbladder is rare in patients with inflammatory bowel disease (IBD). More specifically, pancreas pathologies were not well defined in patients with IBD, so far. Our aim to find the prevalance of these involvements by using transabdominal ultrasound (US). Additionally, we further characterized pancreas abnormalities by echoendoscopy (EUS).
Methods: We evaluated our IBD clinic's records which includes 2700 patients with IBD. We used US to show pancreas, liver and biliary tract abnormalities. Then, patients with pancreas abnormalities were further examined by EUS. Patients with recent onset dyspepsia were used as a control group.
Results: Of the 2700 patients with IBD, 835 had documented US Results. There was 162 patients without IBD as a control. All of the patients, 59% in IBD and 58% in control were male. The prevalence of abnormalities as follows: liver steatosis, 40% in IBD vs 45% in controls (p> 0.05); gallbladder polip, 2.4% in IBD vs 8% in controls (p> 0.05); gallbladder sludge&stone, 8.4% in IBD vs 9.9% in controls (p> 0.05); hepatomegaly, 9.7% in IBD vs 25.3% in controls (p< 0.001); gallbladder operation, 4.4% in IBD vs 7.4% in controls (p< 0.001); gallbladder pathologies (polip, sludge, and operation), 15.1% in IBD vs 22.2% in controls (p= 0.024); gastric antrum wall tickness, 0.5% in IBD vs 1.9% in controls (p> 0.05); hepatic simple cyst, 1.6% in IBD vs 2.5% in controls (p> 0.05); hemangioma, 2.8% in IBD vs 1.9% in controls (p> 0.05); pancreas parancyhmal abnormalities, 5.3% in IBD vs 0.6% in controls (p= 0.009); chronic liver disease findings, 2.2% in IBD vs 0% in controls (p: 0.057); hepatic calcification, 1.0% in IBD vs 0.6% in controls (p> 0.05). Of the 44 patients with paranchymal changes in pancreas, EUS investigation was performed in 13. EUS showed major A or B with minor single finding according to the Rosemont classification. The presentation of the disease was autoimmune pancreatitis (AIP) in 3 patients; acute pancreatitis in two; without any symptom in 6 patients. Echoendoscopy findings as follows: The size of the main duct was dilated up to 5.0 mm; pancreas atrophy in 2 patients; sausage-shaped enlargement in 2 patients with AIH; honey comb appearence in 10 patients, hyperechogen stria in the head of the pancreas in 6 patients.
Conclusions: Our Results showed that involvement of the pancreas, liver and biliary tract not frequent, but also not a rare finding in patients with IBD. Chronic paranchymal changes of the pancreas are underestimated and should be followed for any progress in clinical practice.

P110
Usefulness of magnifying endoscopy for diagnosis of colitis-associated intraepithelial neoplasia in patients with ulcerative colitis

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Background: The prognosis of ulcerative colitis-associated cancer (UCAC) is generally poor because early detection of dysplasia/UCAC is difficult. In the present study, we investigated the characteristics of magnifying endoscopic findings for dysplasia or intraepithelial neoplasia to detect the lesions in patients with UC as early as possible.
Methods: Thirty-eight cases of dysplasia/intraepithelial neoplasia from 27 patients were retrospectively reviewed and the clinical and magnifying endoscopic features were analyzed using narrow-band imaging (NBI) and crystal violet staining.
Results: 1) Median size of dysplasia/intraepithelial neoplasia was 19mm (range 5-60mm) and these lesions were mainly detected in the rectum or sigmoid colon (31/38). A total of 11 cases (30%) were recognized as flat type (n=9) or depressed type (n=2). Clinical characteristics (age, duration of disease, extent of disease, endoscopic severity at the detection of dysplasia/UCAC) were comparable between dysplasia/intraepithelial neoplasia and invasive neoplasia. 2) Using magnifying endoscopy with crystal violet staining, all lesions were recognized as neoplastic pit patterns including type IV, III_L, III_S or V pattern. 74% of flat type lesions were recognized as III_s pattern whereas all depressed type was found as type V pattern. 3) All dysplasia/intraepithelial neoplasia were distinguished from non-neoplastic lesions on the basis of NBI magnification. Irregularity vascular pattern was observed in 11/12 dysplasia/intraepithelial neoplasia and surface patterns could be recognized in these cases whereas amorphous surface pattern and/or avascular pattern was observed in submucosal or invasive neoplasia.
Conclusions: Dysplasia/intraepithelial neoplasia was recognized as neoplastic pit patterns with irregularity vascular pattern on magnifying endoscopy. Magnifying endoscopy was useful to distinct neoplastic lesions from non- neoplastic lesions.

P111
Are extraintestinal manifestations associated with disease outcomes in Ulcerative Colitis? Results from a population-based inception cohort between 2002-2012

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Background: Association between extraintestinal manifestation (EIM) and disease activity suggest a common pathogenetic link. Limited data are available on the prevalence of extraintestinal manifestation and the association with the disease outcome. The aim of this study was to analyze prospectively the association between EIMs (joint, skin, occular), treatment strategy and long-term disease outcomes in the population-based UC inception cohort from Veszprem province between 2002 and 2012.
Methods: Data of 347 incident UC patients diagnosed between January 1, 2002 and December 31, 2010 were analyzed (m/f:

200/147, median age at diagnosis: 36, IQR: 26-50 years, duration: 7, IQR 4-10 years). Both in- and outpatient records were collected and comprehensively reviewed.

Results: EIMs (joint, skin, ocular) were present in 17.3%. There was an association between the presence and number of EIMs and young age at onset (p=0.03 OR: 1.77, 95%CI: 1.00-3.08), disease extent (pextensive=0.003 OR: 3.58, 95%CI: 1.37-9.30) and female gender (p=0.07, OR: 1.57 95%CI: 0.90-2.77), but not with smoking and colectomy. Presence of EIMs was associated with need for steroids (p<0.001, OR: 3.1, 95%CI: 1.74-5.51) and azathioprine (p=0.004, OR: 2.57, 95%CI: 1.35-4.89) in both univariate and logistic regression analysis. In Kaplan-Meier analysis there was an association between the presence of EIMs and time to first IBD-related hospitalization (p=0.002). (Image1.)

Conclusions: Presence of EIMs in UC was associated with the treatment steps and need for hospitalization.

P112
Effectiveness of "Hospital Anxiety and Depression Scale" for the screening of the psychiatric treatment need in outpatients with Inflammatory Bowel Diseases

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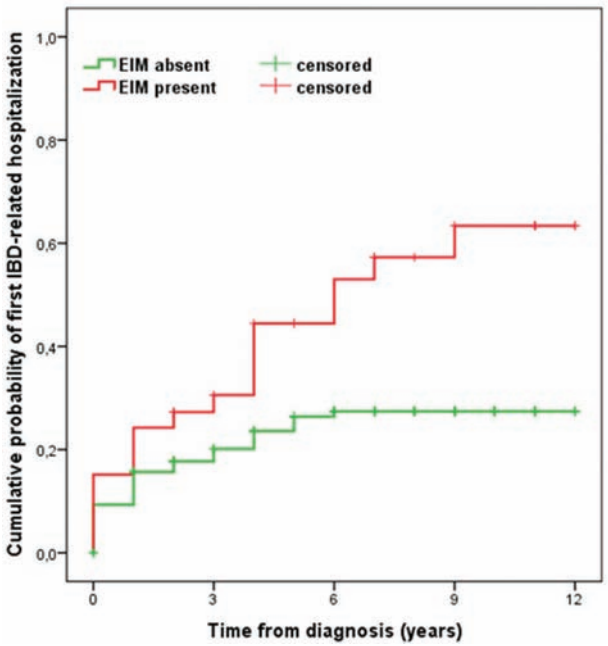
Background: Depression and anxiety disorders are reported to be decreasing the quality of life and quite frequent in Inflammatory Bowel Diseases (IBD) patients. It is important to diagnose and treat them in a timely manner. This is not easy for gastroenterologists. In that study, our aim was to determine the effectiveness of "Hospital Anxiety and Depression Scale (HADS)" for the detection of the psychiatric treatment need in IBD outpatient clinics.



"Figure 1. Cumulative probability of first IBD-related hospitalisation"

Methods: HADS is a self-report test, which measures both the risk and severity of anxiety - depression in physical diseases. It has 14 questions. A predetermined cut point of 7 for depression, 10 for anxiety are considered as a risk for diagnoses. We sent the patients with scores higher than the cut-off, to an interview with the psychiatrist in a week time to assess if there was a requirement for any psychiatric drug intervention. The consultations completed with SCID (structured clinical interview for DSM IV) which is a specially structured and validated interview technique for making psychiatric diagnoses including anxiety and depression. The SCID interview takes 25-60 minutes and can only be administered by a psychiatrist who had specially certified for performing the instrument. All interviews were done by the same psychiatrist.

Results: We prospectively offered the HADS test to a total of 214 consecutive IBD outpatients, 177 of them accepted (82.7%). Mean age was 40.8 ± 12.7 years. 99 (56%) were female, 80(45%) Crohn's Disease (CD) and 97(55%) were Ulcerative Colitis(UC) patients. Mean Modified Mayo Score and Crohn's Disease Activity Index were 2.4, 130 respectively. History of past psychiatric treatment was 20.9 % (n=37) and suicide attempt was 4.0 % (n=7). Family history of psychiatric disease was 10.2 % . Patients themselves completed the HADS test in a mean time of 7 minutes. HADS scores of seventy patients (38 UC, 32 CD) (%39.5) were higher than cut- offs and sent to psychiatric examination. After SCID interview, 95.7 % (67 out of 70) of the patients had a psychiatric diagnosis with a treatment plan. Major depressive (41.4%) and generalized anxiety disorders (14.3%). were the most common diagnoses.

Conclusions: Depression and anxiety disorders is found to be quite frequent in our IBD outpatients (%39.5). HADS is a cheap, easily applied, not medical personal depended ie. self- report, paper tool which revealed a very high consistency (%95.7) with the Results of professional SCID interview to screen the presence of depression and anxiety disorders in outpatient IBD clinics. Positive test result may alarm the gastroenterologist for a consultation to the psychiatrist.

P113
Subclinical Ultrasonographic Enthesopathy and Synovitis in patients with Inflammatory Bowel Disease (IBD) without clinical signs or symptoms of Spondyloarthritis

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Background: Musculoskeletal manifestations, as peripheral arthritis, axial disease and enthesitis, are present in 10-60% of IBD patients. As ultrasonography is more sensitive than physical examination to detect enthesopathy and synovitis, it may be useful to identify subclinical involvement.

Objectives: To evaluate the presence of subclinical enthesitis and synovitis with power Doppler ultrasonography (PDUS) in IBD patients and to investigate its correlation with clinical variables.
Methods: IBD patients without clinically overt musculoskeletal disease were prospectively recruited. Gastroenterological, rheumatological and PDUS evaluation, blind to each other, were performed. Clinical assessment included demographics, comorbidities, IBD characteristics, joint load and musculoskeletal clinical examination. PDUS evaluation consisted of the detection of grey scale (GS) and power Doppler (PD) signs of enthesopathy and synovitis in 12 enthesis scored according to the Madrid Ankylosing Spondylitis Enthesitis Index (MASEI) and in 44 joints using a LOGIQ7 General Electric machine with a 12-MHz linear array transducer.
Results: 35 (51% male) IBD patients [17 Crohn's disease (CD) and 18 ulcerative colitis (UC)], have been included so far. Clinical variables (mean±SD): Age 42 ± 12 years, CDAI 20 ± 17, Mayo index 0.4 ± 0.9, DMARD therapy in 98.6% for 5.5 ± 5 years, ESR 12 ± 8 mm/h and CRP 0.13 ± 0.19 mg/dL. A positive MASEI was present in 98.6%, with a mean score of 33 ± 9. GS enthesal abnormalities were found in at least 1 enthesis in 100% of patients: enthesophytes or calcifications (100%), altered echoestructure (100%), increased thickness (100%), erosion (17%) and bursitis (34%). The most severely affected enthesis were Achilles tendon and plantar fascia. GS joint effusion and synovial hypertrophy (SH) in at least 1 joint were present in 86% and 94%, respectively, with poliarticular (≥ 5 joints) involvement in 40% and 60%, respectively. Entheseal and joint PD signal was positive in 43% and 40% of patients, respectively. Joint effusion and synovial hypertrophy were more frequent in MTF, MCF, carpal and knee joints and PD signal in carpal and knee joints. SH scores were significantly higher in UC than in CD (p=0.003). SH and PD scores were associated with age (p<0.05). The intra-reader agreement was high (0.8 intra-class correlation variability).
Conclusions: Subclinical joint and entheseal PDUS abnormalities are common in IBD patients, regardless of clinical subtype, evolution time and intestinal activity. SH seems more severe in UC than in CD. Prospective longitudinal studies are needed to define its predictive value of clinically overt musculoskeletal disease and its association with structural deterioration

P114
Outcome of thiopurine-intolerant patients with Crohn's disease (CD)

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Background: Approximately 10% of CD patients treated with thiopurines (TP) have an early immuno-allergic intolerance that prevents continuation of treatment. The aim of this study was to assess if the impossibility to use TP jeopardizes the outcome of such patients, and to which extent, before and after the advent of anti-TNF.
Methods: From a total of 1805 consecutive CD patients who had in our center a first prescription of TP between 1994 and 2006, 114 patients (42M, 72F, 29 +/- 14 years) developed an early and definitive TP intolerance. Evolution of CD, collected prospectively, was compared in these patients and 228 controls matched 2/1 for age, sex, and disease duration, who received TP at a proximate date and tolerate this treatment. The patients were separated into 2 calendar cohorts: before (1994-2000, n=31) and after (2001-2006, n=83) the advent of anti-TNF. The primary end point was need for intestinal surgery. Secondary end points were percentage of patients-years out of clinical remission (because of flare or complication), use of anti-TNF, and occurrence of a perianal fistula or abscess.
Results: In case of intolerance, TP was replaced within the first year by methotrexate (n=60) or anti-TNF (n=18). Median follow-up was 130 months (IQR 105-158). The cumulative rate of intestinal surgery was 41% (CI 95% 30-54) at 10 years in TP-intolerant patients vs 29% (22-37) in controls (log rank p=0.01). The percentage of patient-years out of clinical remission was 41% (527/1294) in TP-intolerant patients vs. 32% (891/2813) in controls (p<0.0001). The 10-yr cumulative rates of anti-TNF use and development of a perianal perforating complication were 72% (61-81) and 20% (12-33), respectively, in TP-intolerant patients vs 48% (41-56) (p<0,001), and 17% (11-24) (p=0.12), respectively, in controls. In the first calendar cohort, differences between TP-intolerant patients and controls were significant (p<0.01) regarding cumulative rates of intestinal surgery (10-yr rates: 66% vs. 31%), anti-TNF use (67% vs 30%), and perforating anal complication (32% vs 18%), and percentage of patient-years out of clinical remission (43% vs 33%). In the cohort 2001-2006, compared to controls, TP-intolerant patients required more anti-TNF (10-yr rates: 73% vs 56%) and were more often out of remission (39% vs. 31%, p<0.01). However there was no difference regarding need for intestinal surgery (36% vs 28%) nor perianal perforating complication (15% vs 16%).
Conclusions: Compared to patients who tolerate TP, TP-intolerant patients undergo a more severe evolution of CD. The use of anti-TNF compensates only in part this disadvantage. These Results emphasize that TP still have an important room in the treatment of CD.

P115
Early and late-onset Crohn's disease: different clinical presentation and course, an Italian cohort study

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Background: Disease heterogeneity, according to age of onset, may be observed in Crohn's disease (CD). The aim of the present study was to compare CD phenotype at diagnosis and disease course in diagnosed patients ≤ 17 years (early) and ≥ 60 years (late), the more critical categories in terms of risks and benefits of therapeutic choices.
Methods: Cases included all CD patients diagnosed ≤ 17 years and ≥ 60 years with follow-up > 2 years, recorded in the registry of two IBD referral Centres in Rome. Data reported at diagnosis included gender, smoking habits, IBD family history, IBD location and CD behavior, according to the Montreal classification, extra-intestinal manifestations and medical/surgical treatments performed during the follow-up period. Statistical analysis: Chi-squared test, Kaplan-Meier survival method.

Results: Of the entire cohort of 2321 CD, 160 patients met criteria for the inclusion in the study: 92 in the early-onset (EO) and 68 in the late-onset (LO) group. The median follow-up was 10 years (range 2- 34 years). A family history of IBD occurred more frequently in EO compared to LO (26% vs 4%; p<0.0007). Ileocolonic location, upper gastrointestinal involvement and perianal disease occurred more frequently in EO compared to LO (56% vs 21% p<0.0001; 17% vs 3% p<0.009; 38% vs 19% p<0.01 respectively). Disease behavior at diagnosis was inflammatory in approximately 60% in both group, however progression to complicated disease during follow-up occurred more frequently in EO (40% vs 10% p<0.002).Compared to LO, EO had increased need for steroids and anti-tumor necrosis factor (TNF) alpha during the first two years from diagnosis (41% vs 6%, p<0.003 and 15% vs 4%, p<0.05 respectively). The cumulative probability of receiving steroids, immunosuppressant and anti-TNF alpha within 10 years from diagnosis in EO and LO was 81% and 58% (p=0.004), 58% and 35% (p=0.04), 36% and 16% (p=0.01) respectively. There was no significant difference between the two groups regarding the cumulative probability of surgery within 10 years.

Conclusions: At our knowledge, this is the first Italian study on clinical presentation and course of CD according to age of onset.

Our data are consistent with the literature being ileocolonic location and greater proportion of complicated behavior more common in EO CD. The course of disease in LO CD is more stable and less aggressive than EO CD and should be taken into account when discussing therapeutic choices.

P116
Serologic and genetic markers may predict the development of chronic pouchitis after pouch surgery in ulcerative colitis patients

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Background: Serologic markers characterize Crohn's disease (CD) and a minority of ulcerative colitis (UC) patients. *NOD2* gene single nucleotide variations (SNVs) and NOD2 InsC mutation were found to be associated with CD but not with UC. UC patients undergoing pouch surgery due to disease complications may develop inflammation in the previously normal small bowel constructing the pouch (pouchitis).The NOD2 InsC mutation is more frequent in UC patients developing pouchitis compared to those with an uninflamed pouch. Several molecular similarities between pouchitis and CD were previously detected. We hypothesized that serologic and genetic similarities characterizing CD will be found in patients with pouchitis.

Methods: Samples from IBD patients and controls were obtained. Pouch patients were defined as having a normal pouch (NP) or chronic pouchitis (CP) according to clinical definitions. Anti-glycan antibodies: anti-Saccharomyces cerevisiae (ASCA) anti-laminaribioside, anti-chitobioside, and anti-mannobioside carbohydrate antibodies (ALCA, ACCA and AMCA, respecitvely), were tested using ELISA. Two single nucleotide variations (SNVs) of missense type in *NOD2* gene (R702W/rs2066844, G908R/rs2066845) and the common frameshift alteration (1007FS/rs2066847) were analyzed using polymerase chain reaction.

Results: A total of 144 CD, 69 UC, 111 UC patients after pouch surgery (57 NP, 54 CP), and 90 healthy controls were recruited. Demographic data in pouch and UC patients were comparable except for younger age of UC diagnosis in CP patients (21.7 ± 10.3 vs 30 ± 12.6 years, respectively, p<0.05). All four serologic markers were significantly increased in CD patients compared with controls (P<0.05). In UC ALCA and AMCA levels were elevated compared to controls (P=0.023 and P=0.43, respectively). No significant alteration of serologic markers was detected in NP, however in CP both AMCA and ACCA levels were elevated compared to controls (76 and 62 IU in vs. 44 and 34 IU, respectively). Significant differences in allele frequencies of the three tested *NOD2* variants were detected in CD (P<0.05). The *NOD2* InsC allele frequencies tended to increase in CP as well: 11.2%, 7.6%, 2.9% and 1.7% in CD, CP,UC and NP, respectively). Interestingly, CD patients with the *NOD2* 1007FS mutation had significantly increased ASCA levels compared with CD patients without this mutation (77 vs. 52 IU, p=0.01) and a similar pattern was observed for CP.

Conclusions: UC patients developing pouchitis after pouch surgery have specific characteristics. Moreover, CP and CD patients have serologic and genetic similarities. This suggests that the processes causing pouchitis and CD may be similar, and that serologic and genetic markers may predict disease course after pouch surgery

P117
Risk matrix for prediction of disease progression in a referral cohort of patients with Crohn's Disease

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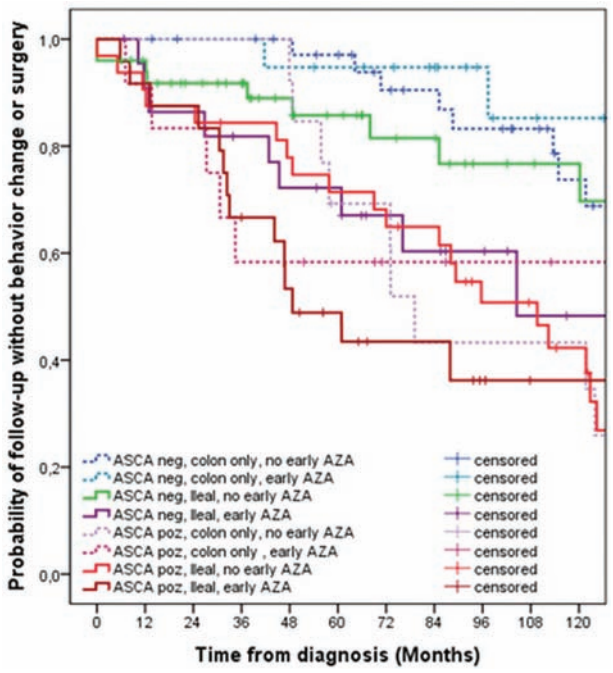
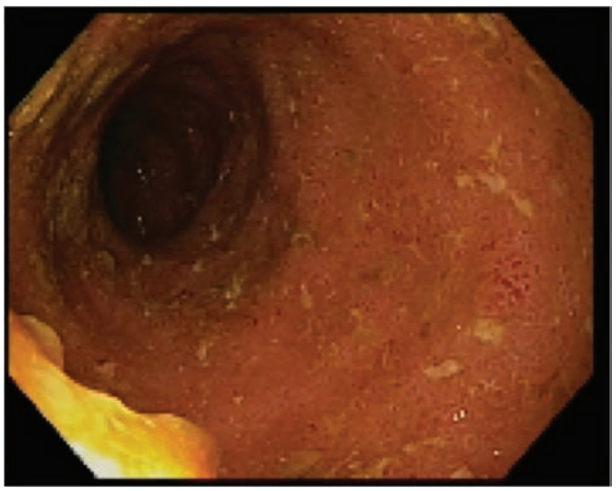
Background: Early identification of patients with at risk for subsequent complications is essential for adapting treatment strategy. The aim of the present study was to develop a prediction model including clinical and serology markers for assessing the probability of developing advanced disease 3, 5 and 7 years after diagnosis in a prospective referral CD cohort.

Methods: 271 consecutive CD patients (median follow-up: 10.9 yrs) were included. ASCA IgA,IgG and anti-OMP Plus IgA were determined by ELISA. Detailed clinical phenotypes were determined prospectively from diagnosis during the follow-up by reviewing the patients' medical charts. Analysis was limited to patients with inflammatory disease behaviour at diagnosis. Total exposure to steroids, azathioprine(AZA) or anti-TNFs were



"Association between ASCA, location, need for early azathioprine and the development of advanced disease"



"Image demonstrating pre-pouch ileitis with erythema, erosions and ulcerations seen in the afferent limb of the pouch"

88.2%, 73.8% and 41.7%, respectively. At diagnosis, 45% had ileocolonic disease and 79.7% had inflammatory behaviour, while 52% had complicated disease behaviour and 41.1% had at least one resective surgery at last follow-up. Two definitions were used for advanced disease: 1. having intestinal resection or progression in disease behaviour and 2. having intestinal resection, progression in disease behaviour, or need for thiopurines(IBSEN definition).

Results: ASCA IgA and/or IgG, disease location, and need for early AZA were included in the 5-year prediction matrix. The probabilities of advanced disease during this period varied from 6.2% to 55% depending on the combination of predictors. The 3- and 7-year ASCA-based model resulted in probabilities of advanced disease ranging from 0 to 45.5% and from 11.1% to 64.7%. In addition, the model including ASCA, disease location, and early need for steroids but not age at onset, was only predictive for the outcome at 5-years if the IBSEN definition was used. In contrast, the association was lost if the need for azathioprine was excluded from the advanced disease definition. Similar findings were obtained from in a Cox regression analysis, the combination of ASCA, location and early AZA was associated with the probability to develop advanced disease (pLogRank<0.001).

Original model combining ASCA, early steroids and location, however failed to predict disease progression.

Conclusions: Our prediction models identified substantial differences in the probability of developing advanced disease in the short and intermediate course of CD. Markers identified in this referral cohort were different from those previously published in the population-based cohort suggesting that different prediction models should be used in referral setting.

P118
Incidence and Severity of Pre-pouch Ileitis: A Distinct Disease Entity or a Manifestation of Refractory

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Background: Pre-pouch ileitis (PI) is a complication that can occur after panproctocolectomy and ileal pouch-anal anastomosis (IPAA) for ulcerative colitis (UC). It is characterised by inflammation of pre-pouch ileum in the afferent limb of the pouch. The development of PI has been noted to be associated with the presence of primary sclerosing cholangitis (PSC) in previous studies. Our aims were to assess the prevalence of PI as well as to identify predictive factors and investigate the medications needed for its management.

Methods: Data on 546 patients who underwent IPAA for UC was retrospectively collected from three tertiary inflammatory bowel disease (IBD) referral centers. Data was collected from sites in the Netherlands (Academic Medical Centre, Amsterdam), Belgium (Leuven University Hospital) and England (University College London Hospital). PI was considered present if there was endoscopic, as well as histological inflammation in the afferent limb. Wherever possible, Crohn's disease was excluded by assessing the histology of colectomy resection specimens.

Results: PI was present in 33/546 (6%) UC patients, all of these had concurrent pouchitis. 144 (26%) patients had pouchitis without PI. 369 (68%) patients did not have any inflammatory pouch problems. Of the 33 patients with PI: 6 (18%) did not require treatment, 9 (27%) responded to antibiotics and 18 (54%) required escalation in therapy, to include steroids/immunomodulators or anti-TNF agents. Rates of requiring potent immunosupressive treatment were higher

"**Table** comparing the demographics, disease characteristics and treatment of the pouchitis group with the pre-pouch ileitis group"

	PI	Pouchitis	P-value
Number of patients	33	144	
Gender (female/male)	11/22 (33%/67%)	70/74 (49%/51%)	0.056
PSC	6 (18%)	9 (6%)	0.044*
Mean age at UC diagnosis, years	25	30	0.032*
Mean age at time of surgery, years	33	37	0.107
Mean interval between diagnosis and surgery, years	7.6	6.8	0.422
Indication for colectomy			0.687
Therapy refractory disease	21 (64%)	95 (67%)	
Steroid dependent	4 (12%)	15 (10%)	
Dysplasia/CRC	5 (15%)	15 (10%)	
Other	3 (9%)	14 (10%)	
Unknown	0	5 (3%)	
Most potent treatment required			<0.01
No treatment	6 (18%)	47 (33%)	
Antibiotics	9 (27%)	79 (55%)	
Steroids or immunomodulators	6 (18%)	9 (6%)	
Anti-TNF	12 (36%)	9 (6%)	

amongst patients with PI than those with pouchitis alone. Patients who went on to develop PI were significantly younger at the time of their UC diagnosis. PSC was significantly more common in patients with PI than those with pouchitis alone.

Conclusions: PI is a much less common and more treatment refractory condition than pouchitis alone. Pouchoscopy should be considered in any patient with symptoms of pouchitis. This should include careful endoscopic evaluation of the afferent pouch limb as well as biopsies of the pre-pouch ileum. Once a diagnosis of PI is made, clinicians should commence immunomodulatory therapy early in the disease course and consider escalating to an anti-TNF if this proves ineffective.

P119
Evaluation of Crohn's disease: CRP in the midst of MRI and endoscopy

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Background: Endoscopy is the gold standard for the assessment of activity in Crohn's disease (CD) however,due to the full thickness involvement of the bowel wall or presence of complications,evaluation of CD activity should be the result of an integration of endoscopical, clinical,laboratory,and radiological approach.In this context,it is still unclear when MRI should be performed.

Aim of this study was to evaluate the capability of endoscopy and MRI to assess disease activity and severity in a series of CD patients and when and how to perform them at their best.

Methods: 50 consecutive patients with endoscopically proven CD underwent MRI enterography for the staging of disease at diagnosis and activity assessment.Endoscopic activity was measured by a quantitative score (SES-CD,range 0-40) with active mild, moderate ad severe disease defined as a scores 4-10,11-19 and >20 respectively. MRI activity was measured by a previously validated quantitative score which integrates both mural and extramural involvement (Magnetic Resonance Enterography global score,MEGS,range 0-296),with active disease being present for a ≥ 1 score.For all participants CDAI was completed and CRP and fecal calprotectin (FC) were also measured (positivity cut-off respectively >0,50 mg/dl and >150 µg/gr).

Results: We enrolled 20 males and 30 females (diagnosis in 62%, follow-up in 38%),mean age 38 ± 15 ys,mean disease duration 5 ys.SES-CD and MEGS were well correlated (r=0,42,p=0.001);both SESCD and MEGS show correlation with clinical (CDAI r=0,51,r=0,59,p<0.001) and biological activity (CRP r=0,37,r=0,43 p<0.005,FC r=0.27,p=0.02 respectively).According to SES-CD,90% of patient had active disease (64% mild,20% moderate and 6% severe);at MEGS,86% of patients had active disease (sensibility 89%,specificity 40%,VPP 93%,VPN 29% vs. endoscopy).MEGS scoring did not showed ability to distinguish severity of disease as determined at endoscopy (p=0.14),but revealed trasmural/extramural signs of inflammation,indipendently from CD activity (60% of patients in remission,84% mild,and 100% with moderate and severe disease), mostly with CRP positivity.Increasing staging of grading at endoscopy was significantly correlated to the risk of trasmural/extramural involvement,only in CRP positive patients (p=0.007). CRP positivity was associated with the presence of extraintestinal involvement (p=0.006;lymph nodes p=0.009, combsign p=0.001 and abscess p=0.005),not of mural involment(p=0.4).

Conclusions: MRI does not discriminate luminal CD severity;however,transmural inflammation,which is more frequent in severe disease,may still be present regardless of endoscopical activity.The presence of positive CRP suggests the need of MRI for the staging of patients with CD independently from endoscopic severity.

P120
Consistently low albumin level is associated with subsequent bowel stenosis, fistula or perforation in patients with Crohn's disease.

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Background: Laboratory tests are used longitudinally in the management of patients with Crohn's disease. Whether the Results of these tests correlate with the subsequent development of bowel stenosis, perforation or fistula formation is unknown.

Aim: To study the correlation between longitudinal laboratory testing and subsequent outcome in patients with Crohn's disease.

Methods: Patients diagnosed at a tertiary referral centre with Crohn's disease between 1994 and 2014, with more than five years of clinical follow-up, had objective clinical, laboratory and genetic data recorded. An objective poor outcome was defined as the development of a fistula, a bowel stenosis or a bowel perforation. Outcomes occurring within 6 months of diagnosis were excluded. Laboratory data was represented by the area under the curve of values measured when patients were well, in the complication free period leading up to development of the outcome. Cox regression was used to analyse the association between outcome and laboratory values; C reactive protein (CRP), platelet count, albumin level, faecal calprotectin, serum ferritin, serum haemoglobin and erythrocyte sedimentation rate (ESR). Laboratory values were converted to

categorical variables with optimized cut-offs. Recognized predictors of poor outcome were added to the model to assess independence of identified associations.

Results: The data of 382 patients were reviewed, 325 patients had more than five years of clinical follow-up, and 268 had a complete clinical, biochemical and genetic record. 144 outcome events (120 stenoses, 15 perforations and 9 fistulae) were observed over a median of 10.77 (IQR (interquartile range) 7.65 - 13.91) years of follow-up. Blood testing was performed a median of 4.79 (IQR 3.23 - 7.66) times per year for each patient, over a median of 3.95 (IQR 1.76 - 7.37) years prior to each event. After multivariate analysis with inclusion of recognised predictor variables, an albumin level < 36 (HR 3.19, p<0.001) maintained an independent association with outcome. ATG16L1 AG or GG genotype (HR 2.32, p=0.031) , continued smoking (HR 1.57, p=0.018) and L1 or L3 Montreal location at diagnosis (HR 1.73, p=0.032) were also independently associated with a poor outcome in the final model.

Conclusions: A longitudinally measured albumin level consistently<36 g/L correlates with subsequent development of an objective poor outcome - predominantly small bowel stenosis - in patients with Crohn's disease. This observation may represent malnutrition from sub clinical bowel obstruction, or a chronic inflammatory state. Serial monitoring of albumin may aid in identification of patients at risk of progression to bowel stenosis, peroforation or fistula formation.

P121
Delay in diagnosis of Crohn's disease: description over time and identification of associated factors. A 21-year population based study

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Background: Delay in diagnosis (DD) of Crohn's disease (CD) may be responsible for complications and a poor response to treatment. The description of DD over time in a population-based CD cohort and its determining factors are unknown and may help implementing corrective measures. The aim of this study was to report in a 21-year population-based cohort the variation over time of DD and to identify associated factors including sociodemographic factors.

Methods: Sociodemographic and clinical characteristics of all CD patients issued from the EPIMAD registry and diagnosed from 1990 to 2010 were included. DD was defined as the time between onset of symptoms and CD diagnosis (months). DD was considered as long when in the upper quartile of this time period. Sociodemographic data included the living area of each patient at the time of diagnosis (urban, periurban or rural), the distance between the patient's living area and the nearest gastroenterologist, and the deprivation index of the living area (FDep99). Clinical data were classified according to the Montreal classification. Univariate and multivariate analyses were performed using a logistic regression to identify the baseline characteristics of patients associated with a long DD.

Results: 8 704 patients with CD were recorded including 57% of females; 10% of them had < 17 years at CD diagnosis (A1), 67% between 18 and 59 years (A2) and 23% >60 years (A3). The majority (65%) of patients had an ileocolonic CD and 5% had perianal lesions; 17% had a stricturing and 10% a penetrating behaviour. During the whole study period, median DD was 3 months [Q1=1; Q3=7] with no change over time. A long DD was >7 months and was associated in univariate analysis with the absence of weight loss (p=0.04), the presence of extra-intestinal manifestations (p=0.02), pure ileal involvement (L1) (p<0.0001) and stricturing behaviour (p=0.002). In multivariate analysis, only the absence of weight loss (OR=1.16 [1.04-1.28]) and pure ileal location (OR=1.36 [1.18-1.56]) were associated with a long DD. Socioeconomic characteristics were not associated with a long DD.

Conclusions: In this 21-year population-based study of CD patients, median DD was 3 months with no change over time and no influence of socioeconomic baseline characteristics. Only two clinical features (absence of weight loss and L1 location) were associated with a long DD.

P122
Rectal bleeding accurately reflects mucosal inflammation in patients with Ulcerative Colitis

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Background: Evaluation of disease activity in ulcerative colitis (UC) clinical trials currently relies upon a symptoms-based scoring system; however, UC patients may have symptoms in the absence of active mucosal inflammation. Therefore, symptoms scores may not accurately distinguish between different levels of mucosal inflammation or healing. These symptoms scores are used for patient enrollment and efficacy in clinical trials, and an imperfect tool can dilute the treatment effect considerably.

Methods: Symptom scores from UC patients were used to compare the relationship between symptoms and mucosal inflammation. Specifically, rectal bleeding (RB) and stool frequency (SF) scores, individually and in combination, were compared to endoscopy scores for patients in two independent studies [1], [2], n=103 and

118, respectively. Mucosal inflammation was assessed by the Mayo endoscopy subscore using an active disease cut-off of 2 or greater. The symptom scores of RB and SF were individually classified as high if the score was 1 or greater. The two symptom scores were also combined using the sum of RB and SF scores with a cutoff of 1 or greater. In addition, histologic disease activity, measured by the Geboes score [3] using a cutoff of 2 or greater, was compared to symptom scores in a single study [2], n=101.

Results: RB and SF scores, both individually and in combination, are highly accurate at identifying UC patients with active disease as measured by endoscopy (sensitivity of 81% and 85% for RB; 95% and 94% for SF; 95% and 97% for the combination in the two independent studies, respectively). Additionally, the symptom scores are effective at identifying patients with active disease based on histology (sensitivity of 84% for RB, 95% for SF, and 98% for the combination). However, RB scores are superior to SF scores and the combination when identifying UC patients with low disease activity as measured by endoscopy (specificity of 77% and 81% for RB; 62% and 42% for SF; 54% and 39% for the combination in the two independent studies, respectively) and histological healing (specificity of 54% for RB, 33% for SF, and 28% for the combination).

Conclusions: Both RB scores, SF scores, and their combination identify most UC patients with active mucosal inflammation, as measured by endoscopy or histology. However, when identifying UC patients with inactive disease, RB scores are superior to SF scores and the combination of RB and SF. Thus, rectal bleeding is the most reliable symptom score for identifying the level of mucosal inflammation in UC patients taking part in clinical trials.

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P123
A single center experience with small bowel capsule endoscopy for patients with established Crohn's Disease: In which patients are lesions found?

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Background: The role of small bowel capsule endoscopy in patients with known Crohn's disease has been studied in several trials, which have shown superiority of this test over all other modalities in identifying the severity and extent of the disease. However, it is not clear how often small bowel lesions - apart from the terminal ileum - are found. The aim of our study was to determine frequency and predictors of small bowel involvement in patients with established Crohn's disease.

Methods: We reviewed the records of 3740 patients subjected to small bowel capsule endoscopy in our department from March 2003 to March 2014. Among those patients, we identified 641, with known Crohn's disease. All patients had had ileocolonoscopy and upper gastrointestinal endoscopy prior to capsule endoscopy, where biopsies established the diagnosis of Crohn's disease. Patients were then subjected to small bowel capsule endoscopy, if, based on clinical judgment and standard radiographic tests (history of the patient, plain abdominal radiography, computed tomography of the abdomen), there was no evidence of bowel obstruction. Patients in whom suspicion of obstruction could not be excluded were additionally subjected to small bowel follow through, enteroclysis or a patency capsule test prior to capsule endoscopy. Patients in whom small bowel obstruction was seen were not subjected to capsule endoscopy.

Results: Among the 641 patients with established Crohn's disease subjected to capsule endoscopy, small bowel involvement - apart from the terminal ileum - has been identified in 269 (41.96%). According to the statistical analysis predictors of small bowel involvement were age < 40 years old (OR=1.13, 95% CI=1.04-1.23, p=0.041), the presence of upper GI involvement (OR=2.13, CI=1.18-4.77, p=0.010), as well as the presence of lesions in the terminal ileum found at ileocolonoscopy (OR=2.99, 95% CI=1.21-6.14, p=0.012).

Conclusions: Small bowel capsule endoscopy identifies lesions in a substantial number of patients with established Crohn's disease. Younger age and the presence of Crohn's lesions in the terminal ileum and the upper GI tract are predictive of small bowel involvement.

P124
Iron deficiency in the absence of anemia affects the perception of health-related quality of life in IBD patients in remission

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Background: Anemia is a common complication of inflammatory bowel disease (IBD) and contributes to the deterioration of health-related quality of life (HRQOL). The IBDQ-36 is a questionnaire that assesses quality of life (QOL) in patients with IBD. It has the advantage of a validated normality cutoff value, which corresponds to a normal perception of QOL, equivalent to that of the general population of reference. Although anemia is multifactorial in IBD, iron deficiency is one of the most prevalent underlying factors and it is present in up to 90% of patients. However, in the absence of anemia, it is unclear to what extent iron deficiency can affect the restoration of the quality of life in patients with IBD. Our aim was to determine whether iron deficiency without anemia negatively affects the restoration of HRQOL in IBD patients in remission.

Methods: We carried an observational, prospective, cross-sectional study in IBD patients in clinical remission without anemia according to WHO criteria. All patients signed the informed consent and then completed the IBDQ-36. Blood samples were obtained to determine iron status. Iron deficiency was defined based on serum ferritin <30ng/mL and/or transferrin saturation index < 16%. Restoration of HRQOL score was defined as >209 points on the global IBDQ-36 score. Results were expressed as medians, percentages and percentiles. Fisher's exact test was performed for categorical variables, and for quantitative Mann-Whitney U test. A two-tailed p value <0.05 was considered statistical significant.

Results: One hundred-three patients with IBD in remission were included, 61 with Crohn's disease and 42 with ulcerative colitis. Patients were stratified into two groups: 61 with iron deficiency

without anemia and 41 with normal iron status. The median age was 37 years [31-47], and 55% were women. Median hemoglobin was 12.9g/dL in the iron deficient group and 14 in the normal iron group (p=0.02). There were no differences in age, type of IBD, treatment or illness behavior between groups. The prevalence of female patients was higher in the group with iron deficiency (RR: 1.87 95% CI 1.33-2.62, p<0.01). The median global value of the IBDQ-36 was 227 in the iron deficient group and 231 in the normal iron status group (p=ns), but restoration of health was significantly less frequent in iron deficient patients than in patients with normal iron status (RR: 2.5 IC 95% 1.15-5.51, p=0.018).

Conclusions: Iron deficiency in absence of anemia negatively impacts the normal perception of health-related quality of life in IBD patients in remission.

Correction of iron deficiency may be a new target in the treatment of these patients.

P125
Developments of novel diagnostic findings on capsule endoscopy in the small bowel of patients with Crohn's disease

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Background: Definitive diagnosis for Crohn's disease (CD) at an early stage can optimize treatment strategy and can improve prognosis. However, thus far, no specific diagnostic criteria have been established based on the small bowel (SB) findings on capsule endoscopy (CE). In the present study, we aimed to identify and confirm the novel findings using CE in the SB of patients with CD.

Methods: We investigated the derivation cohort study and subsequently performed a prospective randomized study. The derivation cohort included 90 cases (cases with established ileitis or ileocolitis CD [n=52], suspected CD [n=8], intestinal Behçet's disease [n=5], and infectious enteritis [n=5], and users of non-steroid anti-inflammatory drug [NSAIDs; n=13] and aspirin [n=7]). Thereafter, we conducted a prospective randomized controlled study to confirm the specific CE findings (UMIN000008199). Three investigators were trained to observe specific findings from among the CE videos; these investigators were then blinded to the clinical backgrounds of patients included in the prospective randomized study, and assessed the CE videos of the patients.

Results: In the derivation cohort, the specific CE findings were determined for 51 CD cases (85.0%). These novel findings included the transition from aphthae to erosion, as well as to small or longitudinal ulcers, as the capsule endoscope progressed towards the distal portion of the SB. These transition of the small bowel lesion (TSL) in patients with CD was observed significantly more frequently in patients with CD than in patients with other diseases (1 of 30 cases, 3.3%: P<0.01). Our prospective randomized controlled study included 20 patients with established ileitis or ileocolitis CD and 20 patients with long-term NSAIDs or aspirin users (11 NSAIDs, 5 aspirin, and 4 both; the control group). All 40 patients were tested for functional patency of the gastrointestinal tract using a patency capsule, of which 14 were confirmed in each group. TSL was accurately diagnosed in 12 of 14 CD patients (85.7%) and was accurately diagnosed in 1 in 14 NSAIDs or aspirin users (7.1%: P=0.02); the difference in the diagnostic accuracy rate was statistically significant. TSL was provided high availability (specificity 85.7%, sensitivity 92.9%, positive predictive value 92.3%, and negative predictive value 86.7%).

Conclusions: TSL is a novel CE finding in SB lesions in CD patients. TSL can be used in the differential diagnosis between CD and other inflammatory bowel diseases in patients with limited distribution of such lesions in the SB during the early stages. Early diagnosis and appropriate optimized treatment may improve prognosis in patients with CD of the SB.

P126
Clinical Predictors at Diagnosis for Disabling Crohn's Disease in Korea : Results from the CONNECT Study

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Background: Identification of Crohn's disease (CD) at high risk of disabling disease would be invaluable guidance for clinicians in making initial therapeutic strategy. The aim of this study was to identify at diagnosis factors predictive for subsequent 5-year disabling course and to validate previously proposed clinical predictors in Korea patients with CD.

Methods: Among the 1,382 CD patients who comprise the retrospective cohort from 32 hospitals in Korea, we excluded patients underwent abdominal surgery within 1 month after diagnosis, received immunosuppressant or biologics therapy within 6 months of diagnosis, and those with shorter follow-up duration. A total of 843 patients with a follow-up of longer than 5 years were enrolled. The definition of disabling CD, which was modified from Saint-Antoine definition, included at least one of the following criteria: further hospitalization for flare-up or complications, need for immunosuppressant or biologics, intestinal resection or perianal surgery.

Results: The rate of disabling CD during subsequent 5-years after diagnosis was 89.4%. An age below 40 years (Odd ratio [OR] : 5.3, 95% confidence interval [CI] : 3.232-8.751), the initial requirement for corticosteroids use (OR: 2.3, 95% CI: 1.116-4.797), and jejunal involvement (OR: 2.4, 95% CI: 1.113-5.169) were independently associated with disabling CD. Meanwhile, presence of perianal disease, which was significant predictor in previous study, was not related with disabling CD. Based on those three predictors, the positive predictive value of the risk factors for disabling disease was 0.62 (zero risk factor), 0.90 (one risk factor), 0.96 (two risk factors), and 1.00 (three risk factors).

Conclusions: Predictors for subsequent 5-year disabling course are an age below 40 years, the initial requirement for corticosteroids, and jejunal involvement in Korean patients with CD. Further prospective validation of these parameters is warranted.

P127
Clinical outcomes of ileocaecal Crohn's disease: Surgery versus pharmacotherapy

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Background: Ileocaecal Crohn's disease (CD) with disease activity confined to the terminal ileum, with or without caecal involvement, can be treated either surgically or medically. However, little is known about the timing of surgery or benefits of surgery compared to medical treatment. The aims of this study were to assess outcomes after medical versus surgical management of ileocaecal CD in the current era.

Methods: Of 885 patients with CD diagnosed and prospectively enrolled in our hospital between 1980 and 2013, 93 (10.5%) ileocaecal CD patients were identified. Those who had a follow-up shorter than 6 months were excluded (n = 5). Patients were assigned to either medical or surgical remission group by initial management strategy that had leaded to remission. Relapse, hospitalization, and surgery rates after medically or surgically induced remission were compared using Kaplan-Meier curve with log-rank test.

Results: Patients assigned to surgical and medical remission groups were 15 (17.0%) and 73 (83.0%), respectively. Median follow up duration was 6.6 years (interquartile range, 3.1 - 9.9 years). In total, relapse occurred in 48 (54.5%) patients, and the median time to relapse was 3.9 years (95% confidence interval, 3.1 - 4.7 years). Surgical remission group showed a lower relapse rate with prolonged maintenance of remission (10.7 vs. 3.7 years; P = 0.017). Hospitalization after first remission tended to be lower in surgical remission group (P = 0.054), and there was no case with repeated intestinal resection after initial surgical remission strategy, whereas 23% and 39% of surgery rates were reported at 5 and 10 years after initial medical treatment (P = 0.037). At multivariate analysis, initial medical management strategy (Hazard ratio [HR] = 3.23, P = 0.039) were strongly associated with relapse in ileocaecal CD, along with a younger age at diagnosis (HR = 1.06, P = 0.003) and a longer time to achieve first remission (HR = 1.04, P = 0.013).

Conclusions: Overall outcomes of ileocaecal CD are excellent with 44.5% of patients remaining symptom-free at 5 years after first remission. In selected cases of localised ileocaecal CD, ileocolic resection might be a good alternative to the long-term medical treatment, with a lower relapse rate and prolonged maintenance of remission.

P128
A new chemiluminescent immunoassay for measurement of Calprotectin in stool

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Background: The interest in calprotectin is constantly increasing due to its potential as a non-invasive, cheap and sensitive marker for intestinal inflammation. Currently, calprotectin is measured with commercially available ELISA and EliA assays. At present, these Methods are time-consuming and used only in clinical laboratories. Determination of calprotectin in stool requires often manual and long pre-analytical processing of the fecal samples, which may lead to long turn-a-round time for the calprotectin Results. We have validated a new chemiluminescent immunoassay for determination of calprotectin in combination with fully automatic system for pre-analytical processing of fecal samples in order to improve efficiency and generate shorter turn-a-round time for the calprotectin Results.

Methods: A new chemiluminescent immunoassay assay (DiaSorin S.p.a.) for determination of calprotectin was validated on LIAISON XL Analyzer (DiaSorin S.p.a.). Pre-analytical processing of fecal samples was performed with a fully automated robotic system (SoniC, S2G Scandinavia), which perform weighing, homogenization and centrifugation of stool samples.

Results: Assay linearity was proven throughout the measuring range from 5 to 800 mg/kg. Samples with higher levels of calprotectin are automatically diluted and reanalyzed. Within-run CVs ranged from 3,8-4,7 %, for concentrations of 40- and 160 mg/kg and total CV was calculated to 5 %.

The LIAISON Calprotectin assay shows good precision between duplicates. 90 samples with the concentrations between 5 mg/kg and 5000 mg/kg were analyzed and CV was calculated to 2%. The assay was compared to the ELISA assay that is currently used in the laboratory (BÜHLMANN Laboratories AG). Results obtained with the chemiluminescent immunoassay showed lower values then Results obtained with ELISA (slope=1,8, R2 = 0,79, n=85 (conc. range 5-5000 mg/kg), slope = 2,8, R2 = 0,81, n=66 (conc. range 5-300 mg/kg)).

Our laboratory yearly analyze 15 000 calprotectin samples. The turn-around-time for calprotectin Results could be significantly decreased, from 2-3 weeks to 2-3 days when using automatic system for processing of stool samples and new LIAISON Calprotectin assay for measurement of calprotectin in stool.

Conclusions: The chemiluminescent immunoassay for measurement of Calprotectin in stool was shown to be precise with proven linearity over the measuring range. The automation of both pre-analytical processing of stool samples and measurement of calprotectin concentration resulted in improved efficiency and significantly shorter turn-around-time for calprotectin Results.

P129
Systematic evaluation of clinical predictors of aggressive ulcerative colitis

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Background: Studies evaluating risk factors associated with an "aggressive" disease course in ulcerative colitis (UC) are scarce. A recent definition of "aggressive" UC incorporated the following characteristics: 1) high relapse rate, 2) need for surgery, 3) development of colorectal cancer, and 4) presence of extraintestinal manifestations (EIM). The following factors for an aggressive / disabling disease course in UC have been identified so far: age < 40 years at

UC diagnosis, pancolitis, concomitant primary sclerosing cholangitis, and deep ulcerations of the colonic mucosa. We aimed to evaluate risk factors for an "aggressive" disease course in UC patients.

Methods: Data from the Swiss IBD cohort study were analyzed. Patients were recruited from university centers (80%), regional hospitals (19%), and private practices (1%). We applied the following definition for "aggressive" UC: 1) patients ever treated with TNF-antagonists or calcineurin inhibitors (tacrolimus / cyclosporine), and 2) need for (procto)-colectomy. Non-normal data are presented as median and interquartile range [IQR].

Results: A total of 1,130 adult UC patients were included. Of these, 422 (37.3%) had an aggressive disease course. UC patients with aggressive disease course were characterized by the following features when compared to UC patients with non-aggressive disease course: more frequently males (59.2% vs. 50.6%, p = 0.005), younger at UC diagnosis (median 28 years vs. 33 years, p < 0.001), more frequently < 40 years at diagnosis (79.8% vs. 72.1%, p = 0.004), more frequently pancolitis at diagnosis (51% vs. 37.1%, p <0.001), younger age at latest follow-up (median 41 years vs. 46 years, p < 0.001), and had more frequently extraintestinal manifestations (52.6% vs. 36.3%, p < 0.001). No difference was found between the two groups when analyzing the length of diagnostic delay, body mass index, NSAID intake at symptom onset, disease duration (both median of 10 years), geographical provenience (urban vs. rural), and education level. UC patients with aggressive disease course were more frequently treated with antibiotics (40.3% vs. 18.6%, p < 0.001), with steroids (92.4% vs. 72.2%, p < 0.001), and immunomodulators (80.6% vs. 47.5%, p <0.001).

Conclusions: Our large cohort study confirmed the following risk factors for "aggressive" disease course: young age at diagnosis, extensive colitis / pancolitis at diagnosis, and presence of extraintestinal manifestations. In addition, our study identified male gender to be a risk factor for "aggressive" disease course. Further studies will have to show if early stepup therapy is beneficial in UC patients fulfilling criteria for "aggressive" disease course.

P130
Persistent Enhancement in Contrast Ultrasound Studies of Severe Crohn's Disease: Stuck Bubbles?

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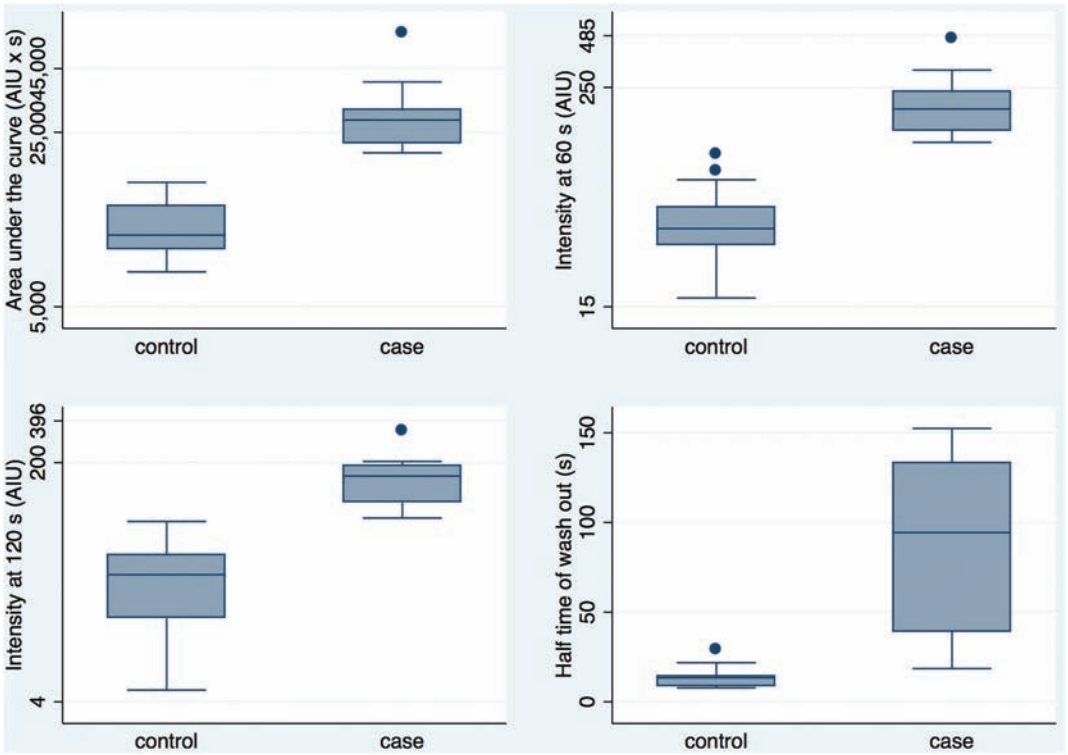
Background: Our aim is to describe a unique observation on contrast-enhanced ultrasound (CEUS), seen in a small population of patients with severe Crohn Disease (CD) in whom contrast enhancement does not show typical decline over time. Clinical significance is assessed. We hypothesize the non-targeted microbubbles adhere to the site of inflammation, [1] as previously shown in animal models with induced inflammation. [2] [3]

Methods: From an existing CD study cohort examined with CEUS for determination of disease extent and activity, 17 patients show high peak enhancement (PE), over 23 dB, consistent with severe active disease, but with minimal decline over a 3 minute interval. From the same cohort, a matching control group of 19 patients with the same PE but typical washout were selected. Original cineloop



"Box plot differences in time intensity curve details between study patients (cases) and control patients."

files were retrieved for detailed time intensity curve (TIC) analysis. Patient outcomes were assessed. Variables were compared between the study and control groups using the Paired T-test, Mann-Whitney U Test and the Fisher Exact Test, where appropriate.

Results: TICs showed similar PE in both groups, but significant higher area under the curve, washout time and intensities at 60s and 120s in the study population, $p<0.0001$.

Study patients had a worse overall outcome and failed biological therapy more often $p<0.001$ and $p<0.05$ respectively. A trend towards higher surgery frequency and change in medication were observed.

Conclusions: Heightened enhancement with a lack of decline on CEUS suggests that microbubbles remain stuck within the inflamed bowel wall for an extended period. This observation occurs in patients with a bad outcome

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P131
High prevalence of Inflammatory Bowel Disease like findings in endoscopic and pathological samples of patients with common variable immunodeficiency

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Background: Common variable immunodeficiency (CVID) is an immunological disorder characterized by a primary deficiency in antibody production. Patients are at risk for recurrent infections but paradoxically may present with autoimmune manifestations some resembling inflammatory bowel disease (IBD).

Our aim was to review endoscopic and pathologic findings in patients with CVID and determine the prevalence of IBD like findings.

Methods: We reviewed patients with CVID followed in our institution. Reasons for endoscopy included dyspepsia (37.0%) and diarrhea (34.2%) and for colonoscopy diarrhea (55.2%) and suspicion of IBD (20.7%).

Results: Out of 82 patients with CVID, 35 (65.7% males, age 43.2 ± 15.2 years) were reviewed including 86 endoscopies and 50 colonoscopies. Biopsies were taken from the esophagus (8), stomach (52), duodenum (48), ileum (14) and colon (25). Endoscopy was normal in 20.9%. Findings included esophageal candidiasis (5), esophagitis (7), varices (5), gastric polyps (12), ulcers (4) and hyperemia (37), duodenal ulcers (11) and atrophy (10). Pathology revealed chronic gastritis in most patients (48), with Helicobacter pylori being frequent (21.2%). Atrophic gastritis (17), complete intestinal metaplasia (20) and lymphoid aggregates (14) were common findings. 2 patients lacked plasmocytes and 3 resembled lymphocytic gastritis. Gastric carcinoma was diagnosed in 5 patients. CMV inclusions were found in 4 patients. Duodenal specimens showed villous atrophy or irregularity (10), chronic duodenitis (22), cryptitis (7), intraepithelial lymphocytosis (13) and lymphoid aggregates (9). 9 patients lacked plasma cells and 4 patients revealed Giardia infection. Colonoscopy showed ileum (5) and colon ulceration (10), diminished vascular pattern (6) and polyps (8). Ileum showed architectural distortion (16), chronic ileitis (13) and focal cryptitis (5). 2 patients had paucity of plasma cells, 3 granulomas and 2 a collagenous and lymphocytic pattern. Giardia and CMV were detected in 1 patient. Colon samples revealed chronic inflammation (24), reaching the submucosa in 5. Crypt distortion was present in 18 patients with cryptitis in 17. A paucity of plasma and goblet cells were found in 7 and 4 patients respectively. Lymphoid aggregates were frequent (11). 2 patients showed a lymphocytic and 1 a collagenous colitis pattern. Paneth cell metaplasia was found in 5 patients and adenocarcinoma in 2. CMV was detected in 2 patients.

Conclusions: CVID may present with a wide spectrum of both endoscopic and pathologic findings. In our series, up to 30% had findings resembling IBD. This has important implications in both therapy, follow-up and cancer surveillance. We alert to the high incidence of gastrointestinal neoplasia in these patients.

P132
Could the cytokines concentration be a marker of IBD activity and be usefull in evaluation of IBD differentiation?

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Background: In inflammatory bowel disease (IBD) the imbalance between cytokines pro- and antinflammatory is observed.

The aim of this study was the assessment of IL10, IL6 and TNF alfa concentration usefulness in the evaluation of the activity of ulcerative colitis (UC) and Cohn's disease (CD).

Methods: 35 patients diagnosed with UC (age 18-55), and 39 with CD (age 21-50) were examined. The control group (CG) consisted of 35 healthy volunteers (age 21-50). Diagnosis of the disease was confirmed by videocolonoscopy and histopathological evaluation of intestinal biopsies. Disease activity of UC was assessed according to the Mayo Scoring System and by the CDAI in CD patients. Among patients with UC 18 (51%) had severe, 14 (40%) moderate and 3 (9%) mild disease. Among patients with CD 7 (18%) was diagnosed with high, 27 (69%) moderate, and 5 (13%) with low activity of the disease. WBC, PLT, serum concentration of TNF alfa, IL-6 i IL-10 were determined. The Results of the study were statistically analyzed using the program R.

Results: The average concentration of TNF alfa in UC patients was: 14,3 (IQR=12,6), in CD: 12,6 (IQR=11,9), in theCG: 3,1 (IQR=1,7). The average concentration of IL6 in UC was: 19,6 (IQR=21), in CD: 10,8 (IQR=7,6), in CG : 3,2 (IQR=1,6). The average level of IL10

in UC was: 14,4 (IQR=5,9), in CD: 10,4 (IQR=9,3), in the CG: 3,3 (IQR=2,5). In the IBD TNF alfa, IL6 and IL10 concentration was significantly higher than in CG. However, IL10 was significantly higher in UC than CD. In patients with UC statistically significant positive correlation between the concentration of TNF alfa, IL-6 and IL-10 and and disease activity was noticed. There were no correlation between TNF alfa, IL6 and IL10 concentration and CD activity.
Conclusions: Determination of TNF alfa, IL6 and IL10 serum concentration can be used for noninvasive evaluation of inflammation activity in patients with UC. IL10 concentration may be helpful in differentiation of UC and CD.

P133
Frequency of fecal incontinence and factors associated with its development in patients with Inflammatory Bowel Disease

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Background: There is little information about the prevalence of fecal incontinence (FI) in patients with inflammatory bowel disease (IBD). Risk factors that have been associated with FI is the presence of perianal fistula and ileo-anal pouch surgery. However, there is no enough evidence if during relapse symptoms such as urgency, frequent watery or loose stools could increase the risk for FI and if pelvic floor disorders by obstetric complications, vaginal delivery and anal sphincter surgery have been associated with FI in patients with IBD.The aim of this study is to determine the frequency of FI and the factors associated with their development in IBD patients.
Methods: A cross-sectional study was conducted in patients with a confirmed diagnosis of IBD. We analyzed 96 patients [78 patients with Ulcerative Colitis (UC) and 18 with Crohn´s disease (CD)]. Demographic and clinical data were collected for the analysis. Current disease activity was reported using the Harvey Bradshaw Index for CD and Mayo score for UC. Risk factors for incontinence (> 3 vaginal deliveries, obstetric complications of pelvic floor, anal sphincter surgery and the presence of perianal fistula) were investigated and Wexner scale to assess the presence of incontinence was applied. Descriptive statistics were used and odds ratios (OR) to determine the strength of association. Data were analyzed using SPSS, a P value <0.05 was considered as significant.
Results: In patients with UC, the mean age was 43 years, 54% female and 46% male. In 56% of the patients the extent of disease was pancolitis and 82% had intermittent clinical course (less than 2 relapses per year), 45% of patients had extraintestinal manifestations and only the 5% had ileo-anal pouch surgery. Thirty-one percent of patients with UC had FI; the factor associated with the presence of FI was the clinical activity of the disease (P= 0.002, OR = 7.5; 95% CI = 2.0 - 28). In patients with CD the mean age was 55 years, 67 % female and 33% male. In 67% the localization was ileocolonic, and the behavior in 50% was non-structuring, non-penetrating and 39% had extraintestinal manifestations. Fourty-four percent of patients with CD had FI; the factor associated with the presence of FI was the inflammatory behaviour of the disease (P= 0.04, OR=1.8; IC95% 1.1 - 2.2).
Conclusions: The frequency of FI in UC was 31% and 44% in CD. The only factor associated in patients with UC was the disease activity and the inflammatory behavior in CD patients.

P134
Clinical, Morphological and Histological Features of X-linked Lymphoproliferative Syndrome Type 2 Enteritis Diagnosed in three Cases with Childhood Onset Inflammatory Bowel Disease

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Background: Inherited immunodeficiency cases are rare, but need to be differentiated from childhood onset inflammatory bowel disease (IBD). X-linked lymphoproliferative syndrome type 2 (XLP2) is a recently recognized immunodeficiency condition. Thirty-seven cases with complicating gastroenteritis resembling IBD have been reported, but there is inadequate knowledge on XLP2 enteritis. We describe clinical course, morphological and histological features of XLP2 diagnosed in cases with childhood onset IBD.
Methods: Case 1, a 7-year-old boy was diagnosed with distal ulcerative colitis (UC), and with Crohn's disease (CD) at the age of 9 based on the appearance of duodenal and longitudinal ulcers in the distal colon refractory to immunosuppressive therapy. Further, haemophagocytotic lymphohistiocytosis (HLH) appeared 4 times during infliximab therapy. Because of his brother's history of HLH, immunodeficiency syndrome was doubted, but genetic analysis revealed XLP2. At the age of 13, ileostomy was done due to his intractable clinical course. He has been well for 2 years. Case 2, a 50-year-old man, the maternal uncle of Case 1. He was diagnosed with UC at the age of 14, and had undergone proctocolectomy due to his intractable clinical course at the age of 16. At the age of 23, he was diagnosed with CD based on anal fistula, and longitudinal ulcers in the small-intestine. He required 6 times surgery due to intractable clinical course, including multiple internal-fistulae, and died of pneumonia, age 50. Case 3, a 13-year-old boy was diagnosed with colonic CD. Immunosuppressive therapy failed to control his enteritis, and HLH occurred after IFX therapy. He was diagnosed with XLP2, and received bone marrow transplantation in 2014. To characterise the features of XLP2 enteritis in these 3 cases, we looked at the clinical course, the distribution of intestinal lesions, endoscopic and pathological findings, and response to medications.
Results: In these 3 cases, the average age at the onset of enteritis was 10 years and a family history of HLH and XLP2 existed. Endoscopy showed fragile rectal mucosa and shallow longitudinal ulcers in the distal colon, but no lesion was found in the right colon. Histologically, granuloma was detected in one case, whereas basal plasmacytosis characterizing IBD was not found in 3 cases. Two cases developed HLH after receiving infliximab.
Conclusions: To our knowledge this is the first report on the clinical features of XLP2 enteritis. The Results suggest that a diagnosis of XLP2 should be considered for severe refractory childhood onset CD, especially those showing predominant appearance in the distal colon and develop HLH during infliximab therapy.

P135
Diagnostic delay in IBD- Evaluation of risk factors

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Background: The diagnosis of IBD is often delayed, however, the underlying causes are unclear and may vary. Therefore, we evaluated reasons and circumstances which lead to a delayed diagnosis of Crohn's disease (CD) or Ulcerative Colitis (UC).
Methods: 386 adult IBD patients (200 CD=51.8%, 186 UC=48.2%, 210 females and 176 males) visiting 3 IBD outpatient clinics of the University hospital Charité and the City Hospital Waldfriede were included. We created a questionnaire to assess patient characteristics like gender, age, residence at diagnosis, intervals from begin of symptoms to first medical contact and determination of diagnosis. Disease characteristics such as disease location, symptom intensity or leading symptoms were assessed. Data were analyzed using the SPSS 20.0.
Results: The mean time from first symptom to diagnosis for all IBD patients was 1.53ys (0-15ys). UC patients were significantly faster diagnosed than CD patients (UC 1.2ys vs. CD 1.9ys, p=0.002). Males were significantly faster diagnosed than females (0.8 vs. 1.2ys; p=0.048). Interestingly, CD patients waited 0.4ys and UC patients about 0.5ys from beginning of symptoms to contact a physician (no significant difference), whereas CD males waited significantly longer than CD females (0.7 vs. 0.4ys, p< 0.05). Female UC patients were significantly faster diagnosed than female CD patients (1.2ys vs. 1.9ys (p=0.02), whereas there was no difference between male CD or UC patients.
Patients under the age of 50 were significantly faster diagnosed compared to patients >50ys (1.4ys vs. 2.7ys, p=0.022).
The diagnosis of CD was fastest determined by gastroenterologists (1.2ys), the diagnosis of UC was fastest established during hospitalization (0.7ys).
Before 1990 patients waited significantly shorter (0.3ys) to contact a physician than after 1990 (0.6ys), (p=0.042). Nevertheless, time from contact a physician to diagnosis did not change over the decades (1.1ys). Interestingly, patients with nausea and vomiting, weight loss or fever contacted significantly faster a physician than without (p< 0.02 each), whereas heartburn delayed correct diagnosis (p=0.04).
Patients, who were residents of a town (20,000-100,000 inhabitants) waited shortest with 0.25ys until they contacted a physician compared to residents of a city (>100,000 inhabitants) (0.9ys; p=0.016) or village (<5,000 inhabitants)(0.7ys; p=0.17). There was no significant difference between time to diagnosis of patients living in a town compared to a city (1.1ys vs. 2.2ys, p=0.062).
Conclusions: The delay of diagnosis of IBD is still an underestimated problem in western industrial countries, especially in female CD patients, indicating the need for a better information system for physicians but also patients.

P136
Usefulness of serum IL-32 and IL-33 as a predictor of clinical course in Crohn's disease

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Background: IL-32 and IL-33 are newly discovered cytokine. IL-32 induces other proinflammatory cytokines including IL-1β , IL-6 and TNF-α, and recent studies demonstrated that IL-32 is overexpressed markedly in the inflamed tissues from patients with Crohn's disease (CD). IL-33 is a new member of the IL-1 superfamily of cytokines and can function as a proinflammatory cytokine inducing T-helper cells type-2 of immune response. We investigated the association with serum IL-32 and IL-33 titer, and clinical activity of patients with CD, and identify whether serum IL-32 and IL-33 test are helpful to predict the clinical course in patients with CD.
Methods: Serial serum samples from 15 patients (12 men and 3women: median age 31 years, range 20-42 years) with CD were collected during follow up period from January 2012 to May 2013. Serum IL-32 and IL-33 with IL-1b, IL-6, IL-10 and TNF-α were measured by commercially available enzyme linked immunosorbent assay kits. Serum C-reactive protein (CRP) and Crohn's disease activity index (CDAI) were also assessed.
Results: Univariate linear regression analysis showed significant positive correlations between IL-32 and CDAI (r[correlation coefficient]=0.002, p=0.013) and significant negative correlation between IL-33 and CDAI (r = -0.002, p=0.015). The correlation between IL-32 and CDAI was remarkable in CD patients involving both small and large intestine (r = 0.003, p=0.000), while in CD patients involving only small intestine, this correlation was disappeared. On the contrary, the correlation between IL-33 and CDAI was maintained in CD patients involving only small intestine (r = -0.003, p=0.022), while this correlation was disappeared in CD patients involving both small and large intestine. Other proinflammatory cytokines didn't show any correlation with CDAI and. Serum IL-32 didn't show the correlation with serum CRP. However, in CD patients with involving only small intestine, serum IL-32 showed significant positive correlation with serum CRP (r = 0.061, p=0.014).
Conclusions: Serum IL-32 and IL-33 can represent CD activity and be helpful to predict in the clinical course in patients with CD. However, prospective large studies are needed to verify the usefulness of serum IL-32 and IL-33 in monitoring of clinical course in CD patients.

P137
5 year budget impact analysis of CT-P13 (Infliximab) for the treatment of Crohn's Disease in UK, Italy and France

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Background: CT-P13 (infliximab) has been approved for the treatment of inflammatory autoimmune disorders including Crohn's disease, ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and psoriasis. Recent studies have shown considerable potential savings through the use of biosimilars for the investigated classes of biological drugs, for instance, the first generation biosimilar filgrastim which decreased the treatment cost by its introduction in oncology field. The market growth of comparator infliximab was reported to grow since the product introduction on EU market.
Methods: We aimed to evaluate the cost benefits of the introduction of CT-P13 (infliximab) in treatment of Crohn's disease from the payer and the patient perspectives by using an Excel based budget-impact model over a five-year time horizon. The model calculated

patients eligible for infliximab treatment based on the prevalence of Crohn's disease, total population, and annual population growth rate in 3 major EU countries; UK, Italy, and France. The acquisition cost of comparator infliximab was assumed not to change after the introduction of biosimilar mAb. The price of the CT-P13 (infliximab) is currently unknown, therefore three different discount scenarios (10%, 20%, and 30%) were applied to evaluate the budget impact. Market uptake growth was also varied in each of the scenarios at 20%, 30%, and 40%, respectively. The market share was assumed to be 25% in the first year in all scenarios

Results: The total budget saving for the 10% price discount scenario for all three countries throughout the years 2015, 2016, 2017, 2018, and 2019 was 10,210,000, 12,240,000, 14,730,000, 17,670,000, and 21,220,000 euros, respectively. The total budget saving for the 20% price discount scenario throughout the years 2015, 2016, 2017, 2018, and 2019 was 20,420,000,26,560,000, 34,570,000, 44,930,000, and 58,440,000 euros, respectively. The total budget saving for the 30% price discount scenario across the years 2015, 2016, 2017, 2018, and 2019 was 30,640,000, 42,900,000, 60,120,000 84,180,000, and 117,890,000 euros, respectively. The total budget saving over the five year period (2015 -2019) for all three countries was 76,070,000, 184,920,000, and 335,730,000 euros for the 10%, 20%, and 30% price discount scenarios, respectively.

Conclusions: The introduction of the CT-P13 (infliximab) as a treatment option for patients with Crohn's disease could achieve substantial cost savings. In the scenarios tested, the total 5 year saving across UK, Italy and France ranged from 76 million to 336 million euros.

P138
Health Quality and Sexual Dysfunction in Turkish IBD Patients

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Background: In Inflammatory Bowel Diseases (IBD) patients, there is an impaired quality of life (QoL) and sexual dysfunction. However, there might be some differences between countries because of different cultures and socio-economical alterations.

In this study, we aimed to evaluate the frequency of sexual dysfunction and the level of QoL in Turkish IBD patients.

Methods: In this study, we evaluated 112 IBD patients (64 patients with Ulcerative colitis: 57%) and 42 control subjects. All patients and control subjects were asked to fill three questionnaires (SF 36, Hospital Anxiety and Depression Scales (HAD-A and HAD-D), Arizona Sexual Experience Scale (ASEX)). Demographic characteristics are collected and disease activity was determined for each patient.

Results: In all evaluated patients, demographic data (age, disease activity, gender, education) was not differ from each other. Inpatient subjects had more severe disease than outpatient subjects as expected. Smokers and ex-smokers were more frequent in Crohn's Disease group whereas there were no difference in alcohol consumption.

HAD-D scores were significantly higher in both Ulcerative colitis (UC) and Crohn's Disease (CD) patients when compared to control group. However, there was no difference between 2 disease groups. HAD-A scores were significantly higher in CD group when compared to UC and control subjects. There was no difference between UC and control group. Female patients had more anxiety scores, there were no correlation between depression scores and gender. Both HAD-D and HAD-A scores are positively correlated with educational status.

When SF-36 scores were evaluated, in both disease groups, scores were worse than control group as expected, whereas there was no difference between UC and CD patients.

Sexual dysfunction frequency was different between three groups, however, patients with more severe disease had more sexual dysfunction.

Conclusions: In conclusion, we found no difference between CD/UC groups and control group for sexual dysfunction scores. However, with the increase in disease activity, both UC and CD patients have more sexual dysfunction than control subjects.

Disease activity was also found to be positively correlated by anxiety and depression score whereas, there was a negative correlation between disease activity and QoL. Anxiety and depression were seen more frequently in highly educated subgroup.

P139
Predictive Factors for Differentiating between Crohn's disease and Intestinal tuberculosis in Korea

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Background: A differential diagnosis of intestinal tuberculosis (ITB) from Crohn's disease (CD) is still challenging and a delayed diagnosis or misdiagnosis has sometimes a big impact on prognosis. The aim of this study was to investigate the value of clinical, endoscopic and histological features which may be helpful in distinguishing between CD and ITB.

Methods: 261 patients, 99 patients with conformed diagnosis of ITB and 162 patients with CD, were recruited from 2005 to 2013 in 7 tertiary centers and reviewed retrospectively. Their clinical, laboratory, endoscopic, and pathologic feature were analyzed.

Results: The clinical feature of age (CD: 28±13 vs ITB: 50±17, P<0.001), sex (CD; M: 70.4%, F: 29.6% vs ITB M: 38.4%, F: 61.6%, P<0.001), hypertension (CD: 2.5% vs ITB: 14.1%, P<0.001), abdominal pain (CD: 82.7% vs ITB: 60.6%, P<0.001), diarrhea (CD: 67.9% vs ITB: 20.2%, P<0.001), hematochezia (CD: 29.6% vs ITB: 14.1%, P=0.004), fever (CD: 24.7% vs ITB: 13.3%, P=0.003), weight loss (CD: 32.1% vs ITB: 15.2%, P=0.002), and perianal disease (CD: 32.1% vs ITB: 0%, <0.001) were significantly difference between both groups. The laboratory feature of platelet (CD: 379.2 x 103 vs Tb: 295.3 x 103/mm3, P<0.001) (CD: 355.2 x 103 vs Tb: 283.1 x 103, P<0.01), ESR (CD: 46.8±33 vs TB: 30.6±27, <0.001) and Quantiferon TB gold test (CD: 9.3% vs ITB: 75.7%, <0.001) were significantly difference between both group. The endoscopic feature of aphthous ulcer (CD: 59.9% vs ITB: 21.2%, P<0.001), ring shape ulcer (CD: 14.2% vs ITB: 71.7%, P<0.001), longitudinal ulcer (CD: 63.0% vs ITB: 7.0%, P<0.001), cobble stone appearance (CD: 40.1% vs ITB: 10.1%, P<0.001), scar change (CD: 16.7% vs ITB: 30.3%, P=0.01), stricture (CD: 27.8% vs ITB: 9.1%, P<0.001), and fistula (CD: 19.4% vs ITB: 0.0%, P<0.001) were significantly difference between both group. The sites of intestinal involvement (CD: 3.4±2.3 vs ITB: 2.2±1.6, P<0.001) were significant larger in CD and transverse, descending, sigmoid, and rectal involvement were more frequent in CD. The pathologic feature of caseous necrosis in granuloma was significantly more frequent in Tb (P<0.001). However, cryptitis and crypt abscess were no significant difference between two groups. On multivariate analysis, ring shape ulcer (odds ratio (OR) 29.1 (confidence interval (CI) 6.29-135.2), P<0.001) was predictor of ITB. Abdominal pain (OR 4.6 (CI 1.0-21.4), p=0.05), diarrhea (OR 6.8 (CI 1.0-21.4), p=0.004), aphthous ulcer (OR 7.6 (CI 1.8-33.4), p=0.008), and longitudinal ulcer were predictors of CD.

Conclusions: Abdominal pain, diarrhea, aphthous ulcer, and longitudinal ulcer were the most important features in differentiating CD from ITB.

P140
Proximity Extension Assay technology identifies novel serum biomarkers for predicting Inflammatory Bowel Disease: IBD Character Consortium

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Background: Technological advances in protein profiling using proximity extension assays (PEA) have transformed our ability to compare concentrations of multiple proteins across biological samples. [1] [2] This technique utilises the high sensitivity and specificity of polymerase chain reaction (PCR) to detect proteins of interest.As part of the European Commission funded IBD Character initiative to discover biomarkers for clinical use using multi-omic technologies (www.ibdcharacter.eu), we performed high-throughput prospective case-control serum profiling to identify protein biomarkers that can predict Inflammatory Bowel Disease (IBD).

Methods: Utilising Proseek Multiplex arrays (Olink Bioscience, Uppsala, Sweden), serum profiling was performed in patients with a new diagnosis of IBD. Our control group consisted of symptomatic individuals. Phenotypic data was captured including age, sex, diagnosis and IBD medications. Statistical analysis was performed using R. Data were normalised and then batch corrected using ComBAT. Linear models were created for each protein including age and sex as covariates. After quality control, data from 186 proteins was available for analysis.

Results: A total of 245 patient serum samples (n=153 newly diagnosed IBD, n=92 symptomatic controls) from 4 IBD centres from Norway, United Kingdom and Sweden were included in the study from December 2012 to June 2014. 70 had Crohn's disease (CD), 70 ulcerative colitis(UC) and 13 Inflammatory Bowel Disease Unclassified (IBDU). The mean age of the entire cohort was 33 years (range 0-79 years) and 54% were female. Multivariable analysis identified a set of 48 protein markers that were significantly associated with IBD. The 5 most significant protein markers were MMP-12 (Holm-adjusted p=3.3×10-13), OSM (p=2.4×10-12), CXCL9 (p=1.7×10-9), MMP10 (p=1.7×10-9) and EGFR (p=1.8×10-9). Of these five, all except EGFR were upregulated in IBD. The top 2 markers, MMP-12 and OSM were able to discriminate IBD from controls with an area under the receiver operator characteristics curve of 0.81 and 0.75 respectively. Using linear discriminant analysis, a combined biomarker consisting of MMP-12 and OSM was able to discriminate IBD from controls with a sensitivity and specificity of 80% and 72% respectively.

Conclusions: We have identified PEA-based serum biomarkers that can predict IBD. These data demonstrate the translational potential

of a PEA based technology in IBD diagnostics and its ability to identify novel proteins that may be relevant in disease pathogenesis.

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P141
Presence of anaemia is an indicator of long-term disease course in Inflammatory Bowel Diseases. Results from a population-based inception cohort

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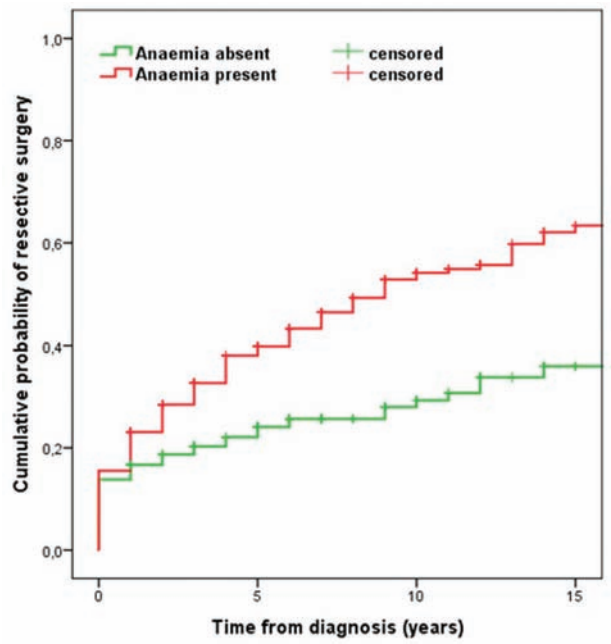
Background: Anaemia is an important extraintestinal manifestation in inflammatory bowel disease (IBD) and it is partly associated to disease activity. Limited data are available on the association between different forms of anaemia and disease outcomes. The aim of this study was to analyze the association between the prevalence of different forms of anaemia and treatment strategy and long-term disease outcomes in the population-based IBD inception cohort from Veszprem province between 1977 and 2012.

Methods: Data of 506 incident CD patients (male/female: 251/255, age at diagnosis: 31.5 years, SD 13.8 years) and 347 incident UC patients (m/f: 200/147, median age at diagnosis: 36, IQR: 26-50 years) diagnosed between January 1, 1977 and December 31, 2010 were analyzed. Both in- and outpatient records were collected and comprehensively reviewed.

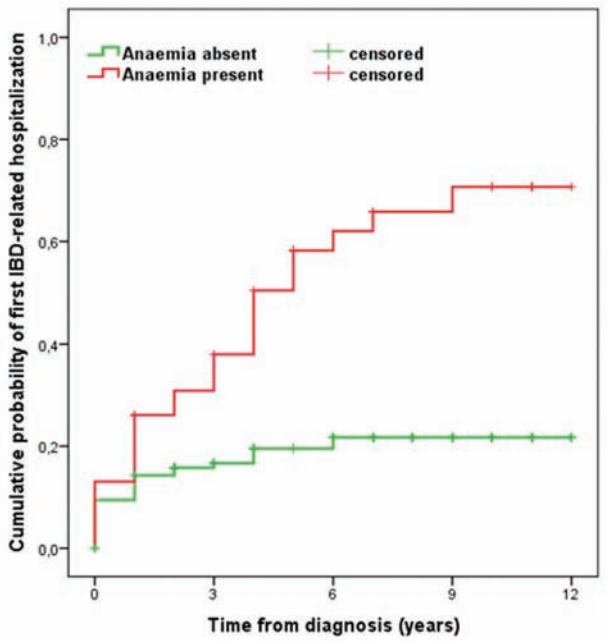
Results: Anaemia (iron deficiency, anaemia of chronic diseases or macrocytic anaemia) was present in 57.5% and 30.2% of CD and UC patients. Anaemia was associated to age at onset (pCD=0.001, pUC=0.026), location/extent (pCD=0.016, pUC<0.001), perianal fistulas (p<0.001) and complicated behavior (p=0.002)/time to behavior change (pLogRank<0.001). In contrast, there was no association with gender and smoking status in either CD or UC. Need for steroids and/or azathioprine was significantly associated to anaemia in both CD and UC (p<0.001 for all both univariate and logistic regression). In addition, anaemia was associated with the need for anti TNF (p=0.002), time to azathioprine (pLogRank<0.001, pCox <0.001), need for (p<0.001) and time to surgery (pLogRank<0.001, pCox <0.001) and time to IBD-related hospitalization (p<0.001) in CD.

In UC, anaemia, was associated with the need for colectomy (p=0.004, OR: 5.57, 95%CI: 1.67–18.54) and time to IBD-related hospitalization (p<0.001, pCox <0.001).

Conclusions: Anaemia is an indicator of long-term disease course, including treatment steps, hospitalizations and surgery requirements in both CD and UC.



"Figure 1. Association between the presence of anaemia and respective surgery in CD"



"Figure 2. Association between presence of anaemia and need for hospitalizations in UC"

P142
Quantification of inflammation in small bowel Crohn's disease (SBCD) patients by videocapsule endoscopy (VCE) and magnetic resonance enterography (MRE)

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Background: Video capsule endoscopy (VCE) and MRE are the prime modalities for the evaluation of SBCD.. Mucosal inflammation on VCE can be quantified using the Lewis score (LS)or the Capsule Endoscopy Crohn's Disease Activity Index (CECDAI), incorporating mucosal edema, ulceration and strictures. Magnetic Resonance Index of Activity (MaRIA) is a novel MRE-based score that incorporates wall thickness, relative contrast enhancement, mucosal ***edema and ulceration in the distal SB and colon The aim of this study was to compare the quantification of distal SB inflammation using VCE and MRE-based diagnostic indices.
Methods: Patients with known SBCD in steroid free clinical remission or with mild symptoms (CDAI<220) for at least 3 months were prospectively recruited and underwent MRE, followed by Agile patency capsule. If patency was proven, VCE was performed. LS, CECDAI and MaRIA scorewere calculated for the distal SB. C-reactive protein (CRP) and fecal calprotectin (FC) levelswere obtained and evaluated for their association with the clinical scores
Results: Fifty patients underwent both VCE and MRE. Active disease was demonstrated in the distal SB in62% of the patients by VCE and 72% by MRE (p=0.4). There was a strong correlation between MaRIA score and both VCE indices (LS-r=0.53, p=0.001; CECDAI-r=0.49, p=0.001), as well as between the CECDAI and LS (r=0.677, p=0.001). LS associated with mucosal healing (<135) correlated with a mean MaRIA score of 13.3 and a mean CECDAI of 4.9 by linear regression. CRP had moderate correlation with MaRIA (r=0.38, p=0.01) but not with VCE scores (LS- r=0.1 p=0.5 CECDAI-r=0.24, p=0.1). FC was significantly correlated with all scores, however the association was somewhat stronger for the VCE scores (MaRIA-r=0.44 p=0.02; LS - r=0.54 p=0.001; CECDAI- r=0.49, p=0.001).
Conclusions: Significant correlation between the quantitative MRE and CE-based indices of inflammation in the distal SB was observed. A significant correlation was also demonstrated between LS and CECDAI. FC levels better correlated with VCE then with MRE score, while CRP had a good correlation with the MaRIA score only. The utility of these indices for prediction of future clinical relapse will be prospectively evaluated in future studies.
UK and EK equally contributed to the study
RE and MM equally contributed to the study

P143
The Usefulness of Ultra-low Dose CT colonography for Assessing Mucosal Inflammation in Patients with Ulcerative Colitis

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Background: Mucosal healing (MH) at endoscopy is a major therapeutic goal in ulcerative colitis (UC). Endoscopy, however, is invasive, time consuming and uncomfortable. Computed tomography colonography (CTC) has emerged as a noninvasive screening procedure for colorectal neoplasia but radiation exposure is a major concern if applied to patients with UC. We aimed to examine ultra-low dose CTC (uCTC) for evaluating mucosal inflammation in patients with UC.
Methods: Patients with UC underwent colonoscopy and uCTC acquired with low dose at 75 mAs or ultra-low dose at 5 mAs levels on the same day. As bowel preparation, patients took low residue diets on the previoursday and 1.8L of isotonic magnesium solution on the day. CTC images were evaluated for UC, in which selected valuables (loss of colonic haustra, luminal narrowing, bowel wall thickness, mural hyper-enhancement and mesenteric hyper-vascularity in both air images or multiplanar reconstruction (MPR) images) were scored from 0 to 1 in the worst affected segment of colon, to create a novel uCTC score from 0 to 5. Endoscopic severity was evaluated by Mayo Clinic endoscopy sub-score (eMCS, 0-3) and the two score were correlated.
Results: In 90 patients the median uCTC score was 3.56 (range 0-5) and eMCS 1.89 (range 0-3). The uCTC score correlated with eMCS ($r = 0.727$, $p< 0.001$). The CTC score for each Mayo e-score were as follows (mean±SD): score 0, 0.77 ± 0.77; 1, 2.56 ± 1.40; 2, 3.69 ± 1.69; 3, 4.83 ± 0.34. The uCTC score showed significant differences between endoscopic activity and MH (eMCS 0 vs 1 P<0.001; 1 vs 2 or 3, P<0.01 and <0.001, respectively). Furthermore, uCTC air images alone revealed a significant relationship with eMCS, even with ultra-low dose CTC at 5 mAs levels.
Conclusions: uCTC may be a non-invasive tool to assess mucosal activity in UC and may be a technique to determine MH. Ultra-low dose CTC resolves concern about radiation exposure.

P144
Characterisation of incident cases of cancer in Inflammatory Bowel Disease: A prospective multicenter nested case-control IG-IBD study

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Background: In a prospective, multicenter, nested case-control study, we aimed to characterize incident cases of cancer in IBD. The role of characteristics of IBD versus immunosuppressants (IS) and/or anti-TNFs use in determining the frequency and histotype of cancer was also investigated.
Methods: From January 2012 to October 2014, all incident cases of cancer in IBD patients (pts.) referring to 15 IBD Units were prospectively recorded. Each IBD pt. with cancer (IBD-K) was matched with 2 IBD controls with no cancer (IBD-C) for: IBD type (CD/UC), gender, age (±5yrs). Statistical analysis: data expressed as median (range), Student T test, chi-square test, multivariate logistic regression analysis, OR.

Results: Incident cases of cancer were observed in 130 IBD pts.: 77 CD (CD-K), 53 UC (UC-K). The frequency of cancer was higher in CD (59%) than in UC (41%)(p=0.004). Gender, age, IBD duration were comparable between the 130 IBD-K and 260 IBD-C (p=ns). Cancer incidence was 3.5/1000 pts., mortality rate 0.4/1000 pts. Among the 130 IBD-K pts., cancer involved: the gastrointestinal (GI) (41%;n=53) or genitourinary tract (21%;n=27;urinary n=17),lung (9.2%;n=12),skin (9.2%;n=12: 4 NMSC, 6 melanoma, 2 Kaposi), breast (6.1%;n=8), lymphoma (4.6%,n=6 only in CD: 4 NHL, IS in 4/6, IS+anti-TNFs 1/6), others (8.4%; n=11). The 53 GI tract cancers included: 35 (66%) colorectal (CRC),6 ileal (11%), 11(23%) others. GI and genitourinary tract cancers were the first and, respectively, the second more frequent cancer in IBD (p<0.0001 vs others). Cancer sites were comparable in UC vs CD: GI (51% vs 34%), genitourinary tract (17% vs 23%), skin (7% vs 10%), lung (11% vs 8%), breast (6% vs 6%), lymphoma (0 vs 10%;p=ns all), respectively. CRC, including 35/53 (66%) GI cancers,were more frequent in UC vs CD (63% vs 37%;p<0.0001). In CD, the percentage of pts. with perforating CD was higher in those developing any cancer (CD-K vs CD-C:29% vs 16%;p=0.01). In UC, the percentage of pts. with pancolitis was higher in those developing any cancer (UC-K vs UC-C: 60% vs 34%;p=0.006). Risk factors for any cancer included perforating behavior in CD (OR 2.94; 95% CI 1.25-7.11), pancolitis in UC (2.95;95% CI 1.35-6.71), but not IS and/or anti-TNFs use (CD:OR 1.77;95% CI 0.95-3.36;UC:OR 0.91; 95% CI 0.31-2.80). Age, active smoking, IBD duration, IS and/or anti-TNFs use did not increase the overall cancer risk.

Conclusions: In a prospective multicenter study, clinical characteristics, severity and phenotype of IBD (but not IS and/or anti-TNFs use) appeared to influence the overall cancer risk in IBD. CD phenotype, pancolitis in UC and penetrating behavior in CD were significant risk factors for any cancer.

P145
Fecal calprotectin correlates with inflammatory disease activity as seen on CT imaging of the small bowel better than clinical assessment

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Background: The Harvey Bradshaw Index (HBI) is a clinical index used to assess disease activity in patients with Crohn's disease (CD). The HBI may not correlate well with more objective assessments of disease activity such as endoscopic, histologic or radiologic evaluations. As a result, biomarkers such as Fecal Calprotectin (FC) have been developed which may correlate better with objective measures of disease activity. However, the validity of FC as a marker of active small bowel inflammation has been questioned. We evaluated the validity of the HBI and FC to assess for active small bowel inflammation in patients undergoing Computed Tomography Enterography (CTE) for investigation of potential CD.

Methods: FC and HBI were evaluated in patients enrolled in a CTE trial undergoing standard and low radiation dose CT scans for patients with CD. Patients referred to a tertiary IBD centre for diagnostic CTE for evaluation of potential CD, underwent a standard exam and a low dose CTE exam in a random sequence on the same day. The HBI was used to determine clinical disease activity and stool samples for FC were processed in standard fashion and analyzed using the Buhlmann Quantum BlueTM device. FC levels were reported with a range from < 100ug/g to >1800 ug/g. De-identified, randomly ordered images were reviewed by 2 experienced radiologists, independently for signs of small bowel CD and an overall assessment of "active" or "inactive" was made.

Results: A total of 103 patients underwent CTE scanning and had HBI and FC Results available for review. 46% of the subjects were male with mean age of 43.6 (± 15.7) years. Average HBI and FC scores are presented in (insert Table here)

Conclusions: Fecal Calprotectin accurately identifies the presence or absence of active inflammation as seen on CTE scanning in patients being evaluated for small bowel Crohn's disease while the Harvey Bradshaw index did not correlate with disease activity.

P146
Detection and characterization of colonic dysplastic lesions in IBD surveillance colonoscopy - a randomised comparison of high definition alone with high definition dye spraying and electronic virtual chromoendoscopy using iSCAN

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Background: The standard of practise for IBD surveillance colonoscopy is now considered dye spraying chromoendoscopy. However, high definition endoscopy has improved in its resolution significantly. Therefore, it is important to determine the best technique for detection of dyspastic lesions (DL) in IBD surveillance colonoscopy. We aimed to determine the frequency of DL during surveillance colonoscopy in IBD and to define the endoscopic features of these lesions by using three different techniques: high definition white light colonoscopy (HD), dye spraying (0.2% indigo carmine) chromoendoscopy (DSC) and electronic virtual chromoendoscopy using i-SCAN (EVC).

Methods: A randomized study (NCT02098798) was conducted to determine the detection rates of DL with HD, DSC or EVC in 95 patients (46 female, median age 52 years, range 22-77 years) with long standing colitis (8 years from diagnosis, including both UC and CD). Patients with inactive disease were enrolled in 1:1:1 ratio into three arms of the study. Colonoscopy was performed using a Pentax EPKi processor and high-resolution video colonoscope (EC-3490Fi; Pentax Tokyo). Endoscopic colonic lesions were classified by size, Kudo pit pattern and Paris classification. Lesions of dysplasia-associated lesion or masses and adenoma-like masses (DALMs/ALMs), sessile serrated adenomas (SSAs), adenoma-like polyps (ALPs), hyperplastic polyps (HPs), and inflammatory polyps (IPs) were identified.

Results: Patients were randomized into three groups, HD (n=32, 33.7%), VEC (n=33, 34.7%) and DSC (n=30, 31.6%). 47 DL were found in total. Thirty (63.8%) were detected in the HD group (8 SSAs, 20 ALPs and 2 DALMs), 6 (12.8%) in the DCE group (6 ALPs) and 11 (23.4%) in the EVD group (7 SSAs, 1 ALP and 3 DALMs). The endoscopic characteristics of SSA were <5mm in size (66.6%), non-polypoid (53.3%) and Kudo pit pattern IIO (93.3%). Similarly, ALPs were <5mm in size (77.7%), polypoid (55.5%) and Kudo pit pattern III (77.7%). Finally, DALMs were <5mm (60%), non-polypoid (60%) and Kudo pit pattern IIIL (40%) and IV (40%). Among the three groups, HD had a sensitivity of 86.67%,

Table 1. Using a cutoff of 150 ug/g with values > 150 ug/g representing active disease, FC had a sensitivity of 0.61, specificity of 0.79, a PPV of 0.76 and an NPV of 0.62 for detecting active disease on CTE.

ASIR	Active	Inactive/Absent	P		Active	Inactive/Absent	P
HBI			0.281	Fecal Calprotectin			<0.001
Median (IQR)	3.0 (1.0, 6.0)	3.0 (2.0, 8.0)			254.5 (100.0, 834.0)	100.0 (100.0, 131.0)	
Mean (SD)	4.4 (4.5)	5.3 (4.9)			556.8 (596.8)	181.6 (222.3)	
Range	(0.0, 19.0)	0.0, 21.0)			(100.0, 800.0)	100.0, 1206.0)	

Average HBI and FC scores compared to CTE assessment

specificity of 89.29%, PPV 89.66% and NPV 86.21% in detecting DL. DSC had a sensitivity of 66.67%, specificity of 88.57%, PPV 50%, NPV 93.94% and EVC had a sensitivity of 100%, specificity of 83.3%, PPV 64.71% and NPV 100%.

Conclusions: DL are frequently detected in long-standing IBD. Our Results indicate that DSC is not more accurate than either HD or VEC in detecting DL. In fact, the majority of dysplastic lesions were detected in the HD group, suggesting that advances in high definition technology may favour this technique as the surveillance method of choice for IBD in future.

P147
Usefulness of fecal S100A12 in defining mucosal healing in Ulcerative Colitis

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Background: Mucosal healing (MH) has been proposed as a therapeutic goal of ulcerative colitis (UC). However, it is still not feasible to perform "invasive" colonoscopy repeatedly to evaluate endoscopic changes and/or MH, therefore, usefulness of non-invasive biomarker has been widely investigated. Fecal S100A12 is reported to be more accurate in distinguishing IBD from non-IBD than fecal calprotectin (Gut 2007), and also believed to correlate with disease activity in UC, however, its clinical applicability in predicting MH is yet to be confirmed.

Methods: Written informed consent was obtained to measure fecal S100A12 from 45 patients with ulcerative colitis who had colonoscopy between November 2013 and June 2014. Mayo score was recorded when the stool sample was collected. Fecal S100A12 was measured by enzyme-linked immunosorbent assay.

Results: Mayo endoscopic subscores (eMayo) were 0/1/2/3 in 9/12/12/12 patients, respectively. eMayo 0 and 1 are defined as MH. Fecal S100A12 was significantly lower in MH (n=21) compared to non-MH patients (n=24) (p<0.0001). Fecal S100A12 was significantly correlated with eMayo (r=0.748), Mayo rectal bleeding subscore (r=0.8068) and partial Mayo score (r=0.8101) (all p<0.0001). Correlation of eMayo with fecal S100A12 was superior compared to that with serum C-reactive protein (r=0.59). Fecal S100A12 very well distinguished MH from non-MH (ROC=0.94, sensitivity 87.5%, specificity 85.71% (cutoff 0.8956 mg/kg)), suggesting its usefulness in evaluating MH. There were 6 patients whose fecal S100A12 positivity did not correlate with MH status - all 3 patients in MH with positive S100A12 had extensive mild colitis (eMayo 1), and 3 patients in non-MH with negative fecal S100A12 had moderately active lesion (eMayo 2) limited to distal colon (<20 cm in length).

Conclusions: Our data suggest that fecal S100A12 well correlates with endoscopic and clinical severity and is useful in defining MH. Furthermore, fecal S100A12 seems to be able to quantitate the inflammation in the entire colon whereas eMayo is defined only by the severity of the most affected area. Therefore, fecal S100A12 could be not only alternative to, but could also be complementary to colonoscopy in assessing disease activity and defining MH in UC.

P148
Immunohistochemical staining of plasma cells and eosinophils in Inflammatory Bowel Disease: a preliminary report.

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Background: The initial histological diagnosis of inflammatory bowel disease (IBD) is often difficult due to the poorly specific morphological signs of the disease. The early appearance (within 2 weeks) of basal plasmacytosis is the most useful sign in differentiating IBD from non IBD colitis within the first two weeks after symptom onset (1,2,3). Moreover, a recent study demonstrated that the presence of eosinophils intermingled with plasma cells are strictly related to a IBD diagnosis (4). On the other hand, the evaluation of these population of inflammatory elements is often limited by the modification of plasma cell nuclear chromatin, due to tissue processing artifacts or to incorrect staining. Purpose of the study was to evaluate the advantages of immunohistochemical (IHC) staining of eosinophils and plasma cells in colonic biopsies in order to improve the detection of basal plasmacytosis.

Methods: 44 cases of naïve patients (first diagnosis, no ongoing treatment), 20 cases with histological diagnosis of IBD and 24 cases with non IBD colitis, with complete mapping of ileocolic segments were recruited for the study. Biopsy samples from each site of the endoscopic mappings were stained with a monoclonal antibody against plasma cells (CD138, clone MI15 - Dako, Denmark 1:700) and against eosinophil granulocytes (CD193 Abcam 1:100)

Results: IHC double staining with the two antibodies demonstrated a basal distribution of plasma cells intermingled with eosinophil granulocytes in 20/20 (100%) of cases of IBD colitis and in 7 out of 24 (29%) cases of non IBD colitis (p < 0.05).

Conclusions: (1) IHC stains allows an easy detection of basal plasmacytosis in all cases of IBD colitis and in a smaller proportion of non IBD cases. The technique demonstrated high sensibility and lower specifity in this preliminary study. (2) the detection

of inflammatory cell populations by IHC markers could provide new insights on the value of basal plasmacytosis in the diagnostic process.
(3) more reliable data about the distribution of the above mentioned cells during the natural history of the disease and in non-IBD colitis could open new perspectives in understanding the pathogenesis of the disease and in surveillance and treatment strategies.

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P149
Clinical Characteristics and Prognosis of Crohn's Disease Patients with Jejunal Involvement in Korea: Results from the CONNECT Study

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Background: The incidence of Crohn's disease (CD) has been increasing in Korea. Despite disease location is associated with complicated disease phenotype and need for surgery, there are few data of large scaled multicenter study for the prognosis of jejunal involvement in Korean CD patients. We investigated the clinical characteristics and prognosis of CD patients with jejunal involvement in nationwide Korean CD cohort.
Methods: This retrospective multicenter cohort study enrolled 1,382 patients diagnosed with CD between 1982 and 2008 from 32 centers in Korea. Clinical characteristics and outcomes of CD patients were evaluated according to jejunal involvement by logistic regression analysis.
Results: Among 1,352 CD patients with complete disease location data, 306 patients (22.6%) had jejunal involvement. Jejunal involvement was significantly associated with ileal location, perianal fistula at diagnosis, and complicated (stricturing and penetrating) behavior. In multivariate analyses, jejunal involvement was independently associated with more common use of steroid at diagnosis and higher operation rates. Remarkably, esophagogastroduodenal (EGD) involvement was more common in patients with jejunal involvement than in those without jejunal involvement (24.8% vs 18.5%, P<0.001).
Conclusions: Jejunal involvement is more common in Korean CD patients compared to western patients. Jejunal disease is a significant risk factor for complicated behavior, common use of steroid at diagnosis, and higher intestinal operation. Upper endoscopy is highly warranted in the evaluation of disease location and prognosis of CD patients.

P150
The influence of different information sources, disease related knowledge and anxiety in patients with IBD

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Background: IBD patient education aims to increase disease related patient knowledge and reduce anxiety and fears about the illness. The advent of social media and the internet has opened new avenues in addition to traditional paper based materials and face to face educational sessions. We aim to investigate which information sources are associated with better patient knowledge and reduced anxiety.
Methods: Ambulatory IBD patients at a large British Teaching hospital were recruited. Data including demographics, disease characteristics, and use of information sources were gathered using structured questionnaires and from medical records. Patient knowledge was assessed by the Crohns and Colitis Knowledge Score (CCKnow; 0-24 points) and anxiety was assessed using the Hospital Anxiety and Depression score (HADS, 0-21 points).
Results: Of 186 participants (57.5% female, mean age 49 years) 95 were suffering from Crohn's disease and 91 from ulcerative colitis. Mean CCKnow and HADS were 10.5 and 6.9 respectively. Women had higher levels of anxiety (7.8 vs 5.7; p<0.001). Better knowledge was associated with higher levels of educational achievement (p<0.001), younger age (pearson correlation -0.3, p<0.001) membership of a patient organisation (12.4 vs 9.6; p<0.001) and general and health related internet use (11 vs 7; p<0.001). Health related internet use was also associated with higher levels of anxiety (8.1 vs 6.3; p=0.015). All information sources (hospital IBD team, information leaflets, general practitioners, official websites, internet news pages and internet patient forums) were associated with better knowledge (p values between 0.015 and <0.001). In contrast to IBD team, information leaflets, and general practitioners the use of internet based information sources was however associated with significantly higher levels of anxiety. Users of patient forums (8.5 vs 6.4; p=0.003) and alternative health sites had the highest levels of anxiety (9.9 vs 6.7; p=0.003).
Conclusions: Patients with IBD gather information from a wide variety of sources and with the exception of alternative health sites all sources are associated with better disease related knowledge. Internet use for health related information - especially the use of unregulated websites such as forums and alternative health sites - is however associated with higher levels of anxiety. Web based materials are associated with better knowledge. However in light of higher anxiety levels patient education should still include paper based written materials and ideally opportunities for face to face information gathering.

P151
Validation of the Inflammatory Bowel Disease Disability Index in a population-based cohort

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Background: Inflammatory bowel diseases (IBD) are chronic disabling conditions influencing physical, psychological, familial and social dimensions of life and may result in disability. Recently, an international collaborative effort led to the development of the first IBD Disability Index (IBD-DI) according to the WHO classification (1). The aims of this prospective study were: 1. To validate the IBD-DI in an independent cohort of IBD patients; 2. To develop a scoring system for the IBD-DI to be used in clinical trials and cohort studies; 3. To assess for the first time disability status among a well-defined population-based cohort of French IBD patients using the IBD-DI and to identify associated factors.

Methods: From February 1st 2012 to 31st March 2014, the questionnaire was administered to a random sample of 200 adult patients with an established diagnosis of IBD for at least 3 months. This random sample was selected among a well-defined population-based registry in France. The IBD-DI consists of 28 items covering the 4 domains of Body Functions, Activity Participation, Body Structures and Environmental Factors. The steps of the quantitative validation included Item quality, factorial validity, internal and external consistency, inter and intra-observer reproducibility. Socio demographic and clinical associated factors were assessed using a multivariate regression. Clinical variables according to the Montreal classification and disease activity according to HBI and partial Mayo scores were recorded at the time of interview.

Results: A total of 150 CD and 50 UC patients completed the validation phase of the IBD-DI. Intraclass correlation was 0.9 and Cronbach's alpha of internal consistency was 0.86. IBD-DI correlated with IBDQ (-0.82; $p<10^{-3}$) and SF36 (-0.61 for physical and -0.71 for Mental; $p<0.05$). IBD-DI score varied from 0 to 100 (higher is the IBD-DI higher is the disability) with a mean at 35.3 ± 20.5 without any difference between CD and UC (33.9 ± 19.5 in CD vs 39.2 ± 23.1 in UC; $p=0.12$). The only factor independently associated with higher IBD-DI in both CD and UC was the female gender. The IBD-DI was associated with increased clinical disease activity ($p<10^{-4}$) in CD, while a trend was observed in UC ($p=0.06$).

Conclusions: The IBD-DI is reliable and reproducible for measuring disability status in IBD. It comprises 19 questions and it ranges from 0 to 100. The mean disability score was 35, it correlated with clinical disease activity and was associated with female gender in this population-based cohort. This validated index and its scoring system can now be used in cohort studies and clinical trials.

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P152
Ultrasound elasticity imaging accurately quantifies ileal fibrosis in patients with Crohn's Disease

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Background: Bowel wall fibrosis is associated with a complicated disease behavior and a reduced efficacy of anti-inflammatory therapies in patients with Crohn's disease (CD). A quantitative assessment of fibrosis severity in CD-affected areas, and their differentiation from inflammatory lesions, can be of great help in clinical decision-making. We have hereby aimed to evaluate the feasibility, reliability and reproducibility of Ultrasound Elasticity Imaging (UEI) in the assessment of ileal fibrosis in patients with CD.

Methods: A group of consecutive patients (n=16) with ileal or ileocolonic CD underwent bowel ultrasound (US) and UEI as well as surgical resection of the terminal ileum. Bowel wall stiffness was evaluated with UEI by means of both a color scale and a quantitative strain ratio measurement. Bowel wall thickness, stratification pattern and vascularization were evaluated at bowel US. The severity of bowel wall fibrosis and that of acute and chronic inflammation were evaluated on histological sections by both semi-quantitative and quantitative image analysis, and used as a reference standard.

Results: Both UEI color scale and strain ratio measurements were characterized by an excellent inter-rater agreement. A highly significant correlation was found between strain ratio values and severity of bowel fibrosis at both semi-quantitative and quantitative histological image analysis. At variance, UEI Results were not influenced by the severity of acute and chronic intestinal inflammation. A degree of mucosal vascularization at bowel US was associated with more severe ileal fibrosis and with higher strain ratio values at UEI.

Conclusions: The Results show that UEI is a reliable highly reproducible technique, which can be complementary to bowel US examination in CD patients, as it can accurately identify small bowel segments affected by advanced fibrosis, without being influenced by the severity of intestinal inflammation.

P153
Small bowel cleansing does not improve quality of wireless capsule endoscopy

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Background: Wireless capsule endoscopy (WCE) is the most important tool for investigating obscure gastrointestinal bleeding in the small bowel and is superior to cross sectional imaging in detecting early and subtle inflammation of the small intestine in Crohn's Disease (CD). [1] With increasing demand of early diagnosis, WCE becomes more important. However, a drawback is the limited visualization of the mucosa in patients with poor cleansing quality. The aim of our study was to determine the benefit of preparation with Picoprep prior to examination with WCE and evaluate two different Methods for cleansing quality.

Methods: This prospective cluster trial examined all patients from two Danish centres, who underwent WCE with PillCam SB based on either known or suspected small bowel CD or obscure bleeding from August 2013

to July 2014. Our local ethics committee waived the necessity of informed consent. Both Centres used the same instructions for preparation; the day before examination, normal breakfast and lunch was allowed until 2 pm, hereafter patients were instructed to go on a liquid diet. Only water was allowed the last two hours before the procedure. Site A, in addition to Site B, instructed patients to ingest one sachet of Picoprep powder, at 9 pm the day before examination, followed by 1.5 litres of liquid diet, as per standard of care at Site A. Patients were matched between centres based on indication, sex and age. Cleansing quality was assessed by two different Methods described by Park et al. 2010 [2] with a 3 grade subjective assessment every 5 minutes and Weyenberg et al. 2011 [3] with a computer assessment of cleansing using the colour bar in the capsule reading software. Mean overall score between groups were compared using students t-test.

Results: We enrolled 135 consecutive patients allowing matching of 92 patients with a mean age of 45 years (16-83), 67 % women. CD was the indication in 69.6 %. Both scoring systems correlated well (rho = 0.80). Using both scoring systems, cleansing quality decreased significantly throughout the small bowel when comparing each third individually, $p < 0.01$. There were no overall difference in quality between groups.

Conclusions: Small bowel cleansing prior to WCE does not improve mucosal visualization of the small bowel in patients with suspected CD or obscure bleeding.

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P154
Identifying predictors of low adherence in patients with Inflammatory Bowel Disease

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Background: Inflammatory Bowel Diseases (IBD) are chronic gastrointestinal conditions that often require medical therapy. However, medication can be costly, difficult to take or associated with unpleasant side effects. This may result into less optimal adherence and, consequently, poorer disease outcome. Therefore, identifying predictors of low adherence is paramount to effectively intervene and increase the adherence and outcome of IBD patients.

Methods: Between November 2013 and March 2014, 471 ambulatory IBD patients in our tertiary referral center were requested to complete the Morisky 8-Item medication adherence questionnaire (MMAS-8) as well as a survey containing socio-demographic data (smoking, educational level, marital status and occupation). Based on the self-reported MMAS-8, adherence was categorized as low (MMAS-8 score >2), medium (1-2) or high (0). Using SPSS 22.0, we looked for factors independently associated with low adherence.

Results: Data were collected for 466 IBD patients (50% male, median age 41 years, 71% Crohn's disease, 29% ulcerative colitis), giving a participation rate of 99%. Univariate analysis in the IBD group showed that mesalamine was the only therapy associated with low compliance [1.572 (1.032-2.395), p=0.035]. As regards occupation, low adherence was most frequently observed in students (47.6%) and employees (42.0%), and less frequently in the self-employed (20.0%). Other significant predictors of low adherence were higher educational level and being single. In multivariate analysis, factors independently associated with low adherence were higher educational level [1.867 (1.315-2.650), p<0.001], being single [1.724 (1.147-2.590), p=0.009], and being self-employed [0.348 (0.156-0.774), p=0.010]. IBD patients who felt worse had more difficulty sticking to the treatment plan [39.1% vs. 19.5%, OR 2.652 (1.092-6.437), p=0.026] and they concealed their doctor about this [21.7% vs. 8.7%, OR 2.911 (0.996-8.507), p=0.042].Patients with a higher educational level reported that they forgot more often to take their medication [35.2% vs. 17.8%, OR 2.513 (1.638-3.855), p<0.001] and they stopped the intake of their medication more often when they felt well [20.9% vs. 12.6%, OR 1.836 (1.116-3.020), p=0.016]. As regards occupation, students had more difficulties sticking to the treatment plan [35.9% vs. 21.5%, OR 2.047 (1.030-4.067), p=0.037].

Conclusions: Approximately one third of the IBD patients were low adherers. Predictors of low adherence in this group were higher educational level, being single, and not being self-employed. More data are warranted to define a well-validated profile for IBD patients with low medication adherence requiring a tailored intervention.

P155
Comparison of video capsule endoscopy and faecal calprotectin as diagnostic tools in patients with abdominal symptoms suggestive of small bowel Crohn's Disease

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Background: Faecal calprotectin (FC) is a widely agreed non-invasive marker of gastrointestinal (GI) inflammation. There is a dearth of evidence comparing FC levels to findings of video capsule endoscopy (VCE). Particularly, there is a scarcity of data investigating the suitability of FC as a screening tool to select individuals requiring VCE in the investigation of patients with abdominal symptoms suggestive of small bowel Crohn's Disease (CD). We studied the correlation between FC levels and VCE findings and analysed their combined utility in detecting small bowel CD.

Methods: We retrospectively compared VCE findings and FC levels in adult patients referred with GI symptoms (abdominal pain, diarrhoea, weight loss, anaemia and bloating). Where multiple FC were measured, the value closest to the date of VCE was used. History of non-steroidal anti-inflammatory drugs, aspirin, clopidogrel and prednisolone use in the six weeks prior to VCE were identified. Findings of relevant investigations (GI endoscopy, MRI, CT, coeliac serology, histology, haemoglobin, C-reactive protein and platelet count) were also reviewed. FC and VCE findings were analysed against final diagnosis.

Results: 62 patients were studied (21 males, mean age 41). One study was excluded due to capsule retention in the stomach. The median time between FC and VCE was 92 days. 29 had a normal FC (< 60mg/g, mean 18mg/g) of whom 5 had abnormal VCE findings (17.2%). 32 had a raised FC (>60mg/g, mean 263mg/g) of whom 7 had abnormal VCE findings (21.9%). Two-tailed Fisher's exact test revealed that the difference between the two groups was not statistically significant (p=0.75).

In the normal FC/abnormal VCE group 3 out of 5 patients were diagnosed with CD (one had CD confirmed on colonoscopy). One case had mild patchy terminal ileal (TI) erythema. Another had non-specific TI aphthous ulcers. In the raised FC/abnormal VCE group 3 out of 7 patients were diagnosed with CD (all 3 had active CD on

colonoscopy). Two cases had jejunal apthous ulcers, and there was one case each of mild patchy TI erythema and TI apthous ulcers. Two-tailed Fisher's exact test revealed that the difference between these two groups was also not statistically significant (p=1).

Conclusions: The utility of FC to diagnose small bowel CD remains debatable, with previous studies showing differing outcomes. In our cohort, FC levels did not reliably correlate with VCE findings. The correlation of FC level with the diagnosis of small bowel CD by VCE was also not statistically significant. Based on our findings, the decision to proceed to VCE should be based on clinical symptoms, and not on abnormal FC levels.

P156
Comparison of fetal risks in pregnancy before and after diagnosis of Inflammatory Bowel Disease: A prospective study

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Background: Inflammatory bowel disease (IBD) commonly affect young women during the reproductive years. The fetal prognosis of pregnancy occurring in IBD is generally considered as good.

Methods: To evaluate the impact of IBD on pregnancy (P), we studied the fetal outcome in 112 patients suffering from ulcerative colitis (UC) and 112 with Crohn's disease (CD), who have been pregnant before and / or after onset of disease.

In this prospective study we have compared during a 5 year period (1/1/2005 to 31/12/2009) outcome of the pregnancy which occurred before or after onset of disease.

Statistic study used Student Fisher's t test and Mann Whitney's U test

Results: - We recorded 303 pregnancies including 95 before diagnosis of UC and 208 after the disease, and 294 pregnancies including 88 before diagnosis of CD and 206 after the disease.

- Mean number of pregnancy was 0,84 and 1,85 in UC and 0,76 and et 1,84 in CD before and after the disease respectively.

- There was no statistical significant difference (SSD) as regards to fetal risk in UC considered before and after pregnancy.

- In CD, the rate of caesarean (10,7% Vs 4,5%), spontaneous abortion (6,8% Vs 2,5%), Stillborn (1,9% Vs 0%) were significantly higher after the diagnosis of the disease, than before.

- Comparing UC to CD , we found no statistical significant difference (SSD) as regards to fetal risk in UC and CD before the disease ; however, the rate of caesarean (10,7% Vs 4,9%) was higher in patients with CD after diagnosis.

- After diagnosis, the rate of caesarean (UC : 19,2% Vs 2,7% ; p<0,001 ; CD : 35,7% Vs 6,7% ; p<0,001), stillborn (UC : 3,8% Vs 1% ; p<0,8034 ; CD : 3,6% Vs 1,6% ; p<0,9426) and congenital abnormalities (UC : 3,8% Vs 0% ; p<0,2664 ; CD : 3,6% Vs 0,5% ; p<0,6505) were higher in primiparous than in multiparous patients.

Conclusions: However, CD in the post diagnosis phase and a primiparous statute have some negative influence on outcome of pregnancy; thus pregnancy in those IBD patients should be closely monitored.

P157
A randomised, assessor-blinded, multicentre trial (OPTIMA) investigating the efficacy, safety and tolerability of a novel tailored split-dosing schedule for colon cleansing in preparation for colonoscopy

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Background: An effective, well-tolerated bowel cleansing schedule is instrumental in ensuring safe and successful colonoscopy, as well as in improving detection rates of dysplastic lesions as precursors of colorectal cancer. Some currently approved bowel cleansers recommend an intake on the day before the scheduled colonoscopy. The European Society of Gastrointestinal Endoscopy and recent consensus guidelines,[1] suggest 4 h and 3-8 h, respectively, between last dose of the bowel preparation and colonoscopy procedure to improve quality of bowel preparation. There is a broad consensus of a need for improvement in both cleansing regimen efficacy, but also patient convenience. Herein we report the design of an ongoing trial to assess the efficacy and safety of a novel tailored PICOPREP® (sodium picosulphate, magnesium oxide, citric acid) versus the day-before PICOPREP® dosing schedule. The dose timing will be determined by the timing of the colonoscopy instead of a fixed recommendation. This will allow split dosing for morning colonoscopies and even same-day dosing for afternoon procedures.

Methods: 198 eligible subjects (≥18 years; scheduled for elective colonoscopy; ≥3 spontaneous bowel movements/week for preceding month) will be enrolled in this phase 3, assessor-blinded, multicentre trial across 10-15 sites (Germany, France and the Netherlands) and randomised (2:1) to tailored and day-before dosing schedules.

In the tailored dosing schedule the first and second doses are administered 10-18 and 4-6 h, respectively, before the colonoscopy (Figure 1). In the day-before dosing schedule the first dose is administered on the day prior to colonoscopy, before 08.00 h, and the second dose 6-8 h later.

The primary endpoint assesses the overall colon cleansing efficacy using the total Ottawa scale score. The key secondary endpoint is the ascending colon cleansing by percentage of subjects classified as successful (excellent or good scores). Both endpoints are evaluated per site by a colonoscopist blinded to the dosing schedules. Safety signals include the frequency and intensity of adverse events, clinically significant changes in vital signs and laboratory values.

Results: Patients are currently being recruited.

Conclusions: It is anticipated that this tailored PICOPREP® dosing schedule may improve the quality of bowel preparation, as well as offer increased convenience to patients by minimising the impact on work schedules and daily activities.

clinicaltrials.gov identifier: NCT02239692

References

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P158
Short-term MRE predictors of need in Crohn's disease related surgery

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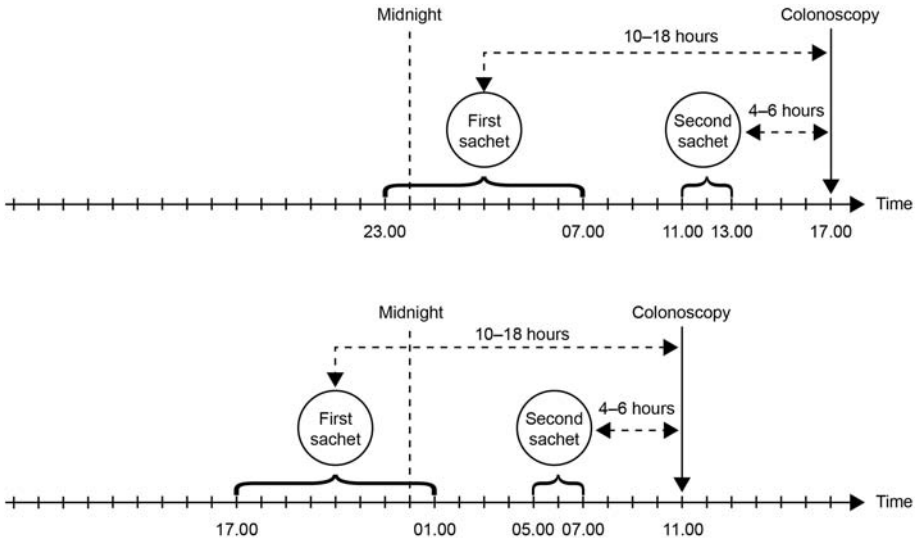

"Figure 1. Examples of tailored PICOPREP® dosing schedules"

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Background: Most patients with Crohn's disease (CD) during follow-up period and at diagnosis require surgery. Verification of predictors that can estimate the risk of need for surgical treatment is important to optimize the treatment policy. MRE signs may act as the predictors of the need for CD surgical treatment during the short-term observation and an unfavorable outcome.

The aim of the study was determine specific MRE signs that can help to predict the risk of the need for surgical treatment in the following year-long clinical observation.

Methods: Patients with CD were chosen from prospective and maintained registry of City IBD centre (St.-Petersburg) from May 2007 to May 2014. They underwent MR enterografy on magnetic resonance tomograph with a capacity of 1.5 T magnetic field. Each segment of the small and large bowel were evaluated.

The need for CD- related surgical resection, 1 month after the MRE during 12 month follow-up period was an endpoint. Specific MRE signs correlated with the endpoint. Acceptance of anti-TNF was an exclusion criterion .

In the frames of statistical analysis Methods of variance analysis, Student's t-test and the tabulation of conjugation with the counting statistics Chi-square were used. The regression analysis was used to determine the probability of surgery.

Results: During the MRE observation was conducted for 134 CD patients. Among them 10 patients were operated during the year (average time before surgery 5,5 month). The need for surgical treatment was considered as unfavorable CD outcome.

More common features for operated patients in the analysis of the overall MRE significantly are: dilated small bowel loops (p=0,0001, OR: 12,78, CI 3,11-52,5), fibro-fatty proliferation (p=0,0023, OR: 8,00 CI 1,94 - 32,98), inflammatory reaction of mesentery (p=0,0004, OR: 15,84; CI3,16 - 79,27 engorged mesenteric vessels (p=0,0143,OR: 11,29; CI 1,39 - 91,85), stricture (p=0,0466, OR: 5,08 CI 1,25 - 20.72) , fistulas (p=0,0005, OR: 14,5 CI 3,47 - 60,7), abscess in ileo-cecum (p=0,0002, OR: 11 78 CI 2,96 - 46,94), lesions of the colon (p=0,0126, OR: 5,24; CI).

More than that MRE signs were connected with the risk of resection obtained during evaluating of the terminal ileum and the ascending portion of the colon/

Odds ratio for corresponding MRI features are shown in figure 1, 2.

*p<0.05 **p<0.01 ***p<0.001

Conclusions: MRE signs may act as the predictors of the need for CD surgical treatment during the short-term observation and an unfavorable outcome.

P159
Transabdominal ultrasound has high negative predictive value for short-term complications of Inflammatory Bowel Disease

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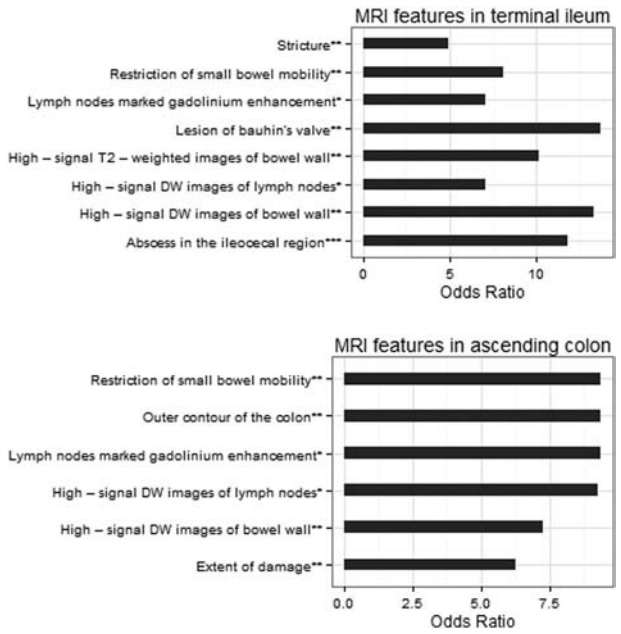
Background: Transabdominal ultrasound (US) is a non-invasive, easily accessible cross-sectional imaging technique for bowel examination. It has been shown to have high specificity but traditionally lower sensitivity compared with other cross-sectional techniques and/or endoscopy in depiction of inflammatory bowel disease (IBD) activity. The data available provide comparison of transabdominal US with endoscopy and other cross-sectional imaging but the predictive value of IBD complications is unknown for US. Therefore, the aim of this study was first, to determine the negative predictive value of US in a setting of IBD patients with clinical suspicion of flare and second, to establish the rate of agreement between US and endoscopic and magnetic resonance enterography (MRE) findings.

Methods: Between July and October 2014, all consecutive IBD patients with clinical suspicion of IBD flare were referred for transabdominal US at one referral IBD centre. The activity of IBD on US was determined according to standard criteria for each small and large



*p<0.05**p<0.01***p<0.001

bowel segment. Negative predictive value for short-term complications of IBD, i.e. flare or surgery occurring within 1 to 4 months of US, was calculated. Endoscopic and MRE findings were categorized for each bowel segment and the agreement between US and other techniques was considered only if the agreement on presence of disease activity was achieved for all segments.

Results: In total, 80 US were performed in 79 patients; 62 (78%) with Crohn`s disease, 16 (20%) with ulcerative colitis, 1 pts with IBD unclassified; 52 (65%) women; mean age 35 years, range 19-79. Overall, there were 44 (55%) cases of US findings of active disease, in 6 patients fistula or abscess were found on US. From 36 cases with negative US findings, 35 were in remission without any changes in therapy at the median follow-up of 3 months (range 1 to 5 month); resulting in negative predictive value of 97% (95%CI 85.42 % to 99.54 %). During the follow-up period, 32 (40%) patients underwent MRE and 21 (26%) ileocolonoscopy, with agreement of US findings in 84% and 73% of cases for MRE and ileocolonoscopy, respectively.

Conclusions: Transabdominal ultrasound has high negative predictive value for short-term complications of inflammatory bowel disease and seems to be a promising tool for rapid and non-invasive triage of IBD patients who do not necessitate further diagnostic work-up.

P160
Need for Recurrent Resection and Complex Phenotype are Associated with a Specific Antibody Signature in Crohn's Disease Patients undergoing Resection. Smoking is Not Associated with Prevalent Antibodies. Prognostic and Mechanistic Implications.

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Background: Patients with Crohn's disease develop antibodies to microbial antigens as a result of an atypical immune response to the intestinal microbiota. There are limited data on the serologic profile of patients with Crohn's disease who progress to surgery. We assessed the baseline serologic profile of a prospective cohort of patients from the POCER (Post-operative Crohn's Endoscopic Recurrence) Study, prior to surgery for luminal Crohn's disease.

Methods: 160 Crohn's disease patients undergoing intestinal resection were prospectively evaluated. Disease phenotype (Montreal Classification), smoking status, surgical history and length of disease history were assessed. Patients were high risk if ≥1 of risk factors for disease recurrence were present (≥1 previous intestinal resection, perforating disease, current smoking). Serological testing was undertaken immediately prior to, or within 4 weeks of, surgery for presence and titre of antibodies: ANCA, pANCA, ASCA IgA/IgG and the bacterial antibodies anti-OmpC, anti-CBir1, anti-A4-Fla2, anti-Fla-X. Positivity and titre magnitude were assessed in relation to phenotype.

Results: 160 patients (85% high risk) were assessed. 22 patients (14%) were positive for all and 32 (20%) negative for all bacterial markers (OmpC, CBir1, A4-Fla2, Fla-X). On univariate analysis, positivity for ASCA IgA and anti-OmpC were associated with complex disease (B2/B3) (ASCA: B1 69% v B2/3 93%, P=0.02; anti-OmpC: B1 31% vs B2/3 65%, P=0.018). Current or past smokers were less likely than non smokers to be ASCA IgG positive (27% vs 49%, P= 0.004), anti-OmpC (56% vs 71%, P=0.04) and anti-Fla-X (42% vs 64%, P=0.006). Anti-OmpC was associated with a history of ≥2 previous operation (59% <2 vs 94%; P=0.006). There were no differences between high and low risk patients for any antibodies.

Conclusions: ASCA IgA and anti-OmpC are associated with complex stricturing or fistulising phenotype and anti-OmpC with repeated surgery, suggesting a possible predictive role in managing Crohn's disease. The lower serological antibody prevalence in smokers suggests that smoking exerts its deleterious effect in Crohn's disease through a different mechanism.

P161
Validation of a risk score predicting post-surgical complications in patients with inflammatory bowel diseases

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Background: Predicting surgical complications is extremely important when deciding which therapeutic strategy is best. There is not a validated surgical risk score for IBD patients. This analysis provides external validation to an IBD-specific risk score previously developed at another Center by Yarur, et al. [1]

Methods: Patients at the University of Chicago who underwent a non-emergent intra-abdominal IBD-related surgery between January 2011 and September of 2014 were included. Patients who had diverting ostomies or with no available laboratories before the surgery were excluded. Variables described in the predictive model are shown in Figure 1. The primary outcome was development of a

post-operative medical or surgical complication, defined as wound infection or dehiscence, intra-abdominal abscess, anastomotic leak, urinary tract infection (UTI), acute kidney injury (AKI), pneumonia, deep venous thrombosis (DVT) or death. The secondary outcome was length of post-operative stay (LOS). The risk score was calculated for each patient (Figure 1).

Receiver operating characteristic (ROC) curves were done to assess the performance of the original model in the validation cohort.

Results: 75 patients met inclusion criteria. 63% (47) had Crohn's disease (CD) and 37% (28) had ulcerative colitis (UC). The median LOS was 6 days (range: 3-36). 11 (14.7%) of the patients had one or more complications: 2 (2.7%) had a UTI, 3 (4%= had a DVT, 1 (1.3%) had an AKI, 4 (5.3%) had a wound infection or dehiscence, 6 (had an abscess), 2 (2.7%) had a bowel obstruction, while no patients developed a pneumonia or sepsis. The ROC for any type of complication was 0.78 (p=0.0002) and is shown in Figure 2.

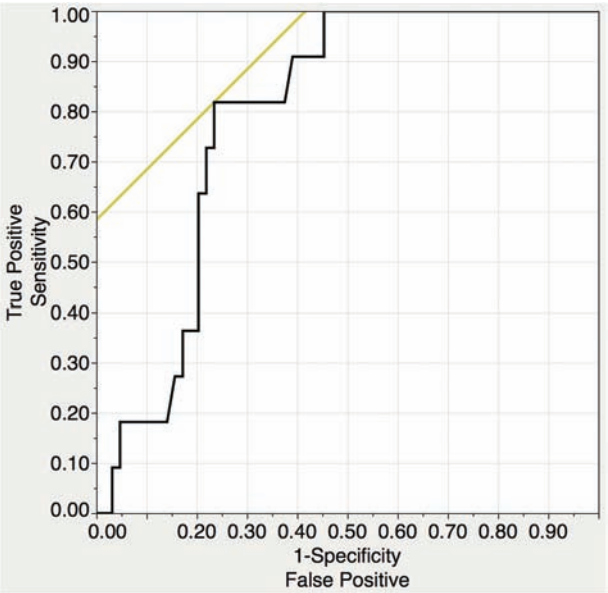
There was a positive correlation between LOS and the risk score (rho: 0.3, p=0.009). Patients with a score of 100 had almost 8 fold the risk of developing a complication when compared to those with 99 or less (OR: 7.5 {95% CI: 1.5–37.7], p=0.006).

Conclusions: The previously developed risk score performed well in an external validation group and correlated with LOS.

C-reactive protein	x 0.72
Age	x 0.14
(Abs neutrophil /Abs lymphocyte)	x 0.09
(BUN/Serum Creatinine)	x 0.14
BUN	x -0.17
Serum Sodium	x -0.47
Serum Potassium	x -2.46
Smoker	+ 2.76
+ Patient with diagnosis of Ulcerative Colitis?	+ 5
TOTAL SCORE	Risk Score

$$\text{Predictive risk of a post-surgical complication} = \frac{1}{(1+e^{-(\text{Risk Score}+58)})}$$

Figure 1 "Variables and calculation of the predictive score"



"Figure 2 Area under the curve plotting the performance of the score in predicting a post-surgical correlation."

References:

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P162
Is Sensorineural Hearing Loss Frequent in Patients With Inflammatory Bowel Disease? Preliminary Results Of Ongoing Study

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Background: Sensorineural hearing loss (SHS) has been reported in many autoimmune diseases before. Inflammatory bowel diseases (IBD) have a lot of characteristics of autoimmune diseases. But there are little data about SHS frequency in these patient population.

Methods: We conducted a prospective blinded comparative study to be continued over a 2 year period in three large medical centers in Kocaeli. IBD patients and controls underwent a complete otorhinolaryngeal examination include an eudiometry test. Any participant who has current use or history of take an ototoxic medication or recurrent either existent ear infections was excluded from the study.

Results: Up to the present 84 participants (63 patients and 21 controls) were included. 36 (57.1%) had Crohn's disease (CD) and 27 (42.9%) had ulcerative colitis (UC). Mean age was 33 ± 16. 52.4% were males and 63.5% of the patients were presently hospitalized due to IBD exacerbation. 11/63 of the IBD patients complained of hearing loss since first IBD diagnosis and 5 had current hearing disabilities. Audiometric examination revealed that any hearing loss (mild to severe) was found in 13 (20.1%) of the IBD population, compared to 1 (4.7%) of the control group (p=0.05). was Major hearing deficiency type was sensironeural ones. Hearing loss was present in 5/15 (30%) of patients with extra intestinal manifestation(s) (EIM), compared to 2/36 who did not have EIM (p<0.01).

Conclusions: Sensironeural type hearing loss may be another EIM of IBD. Early complete hearing evaluation should be recommended to IBD patients especially one's who have other EIM's.

P163
Where do patients go for information on Inflammatory Bowel Disease (IBD)?

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Background: Patient education is an important part in the management of patients with IBD. Information on IBD can be gathered from many sources including alternative information sources such as social media and the internet. We aim to investigate which information sources IBD patients use and trust.

Methods: Ambulatory IBD patients at a large British Teaching hospital were recruited. Data including demographics, disease characteristics, and use of information sources were gathered using structured questionnaires and from medical records.
Results: Of 186 participants (57.5% female, mean age 49 years) 95 were suffering from Crohn's disease and 91 from ulcerative colitis. Highest educational achievement was secondary school (39%), college (26%) and university (35%). Only 65 patients were current or previous members of the patient organisation CCUK. 88% had access to the internet (75% using it daily), but only 27% used it frequently to search for health related information. Patients reported using official information leaflets (89%) and their hospital IBD team (75%) frequently to gather information. Fewer (25%) used their general practitioner and only 10% attended CCUK meetings. Internet based sources included official information sites (CCUK, NHS; used by 50%), news sites (28%) and patient discussion forums (27%). Very few patients used alternative health sites (9%), random links on search engines (17%) or patient supports sites from pharmaceutical companies (6%). Patients trusted information from the IBD team (89%) and official leaflets (77%) the most. Web based information was less trusted (official information sites 66%, patients forums 28%, random links 21%, alternative health sites 11%).
Conclusions: Despite the advent of social media and a host of health information on the internet patients turn to official paper based leaflets and their IBD team for information. When searching online most patients tend to use official websites with regulated information. The use of sites with unregulated and potentially misleading information is currently low. For the time being face to face education and paper based educational materials remain the cornerstone of patient education.

P164
Evaluation of an interim Crohn's disease outcome measure (PRO-2) based on two patient-reported components (stool frequency, abdominal pain) of the Crohn's Disease Activity Index (CDAI) in the ustekinumab CERTIFI Study

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Background: The CDAI has been the standard outcome measure in CD trials for ~40 years, but its complexity, high PBO response, and inconsistency with FDA guidance on patient-reported outcome (PRO) measures are disadvantages. This has generated interest in exploring a PRO based on the stool frequency(SF) and abdominal pain(AP) components of the CDAI, known as PRO-2. A potential PRO-2 definition for remission (mean daily score of AP ≤ 1 AND[also] SF ≤ 1.5) was proposed based on data from two CD populations, one with mild-moderate disease and one with steroid-dependent disease. Whether this PRO-2 definition is optimal in patients with moderate-to-severe disease, and/or refractory to TNF α antagonists is unknown.
Methods: Using the previously reported 8-week induction data from the ustekinumab(UST) Phase 2 CERTIFI study (in patients previously failing and/or intolerant to TNF-antagonists; mean baseline CDAI=324), the contributions of SF/AP to baseline CDAI and subsequent improvements post-treatment were assessed. Sensitivity(SENS)/specificity(SPEC) analyses that defined optimal cutoffs for detecting remission(CDAI<150) at week 8 were used to generate remission definitions based on unweighted mean daily scores for AP alone, SF alone, or both: Either requiring maximums for each(e.g. AP ≤ 1 AND SF ≤ 1.5)or, applying maximum thresholds to the sum of AP+SF, using standard CDAI weightings. The treatment effects of UST in CERTIFI were then evaluated and compared using the selected definitions.
Results: The unweighted mean daily score cutoffs of AP ≤ 1/SF ≤ 3/ combined AP ≤ 1 AND SF ≤ 3,respectively, provided better balance of SENS(87.1%;84.7%;72.9%)and SPEC(77.1%;73.9%;94.1%) compared with the previously proposed cutoff of combined AP ≤ 1 AND SF ≤ 1.5(55.3% SENS;96.8% SPEC) in the detection of remission at week 8. A weighted total AP+SF score cutoff of <75 best optimized SENS(91.8%)&SPEC(85.3%) compared with the unweighted mean daily AP/SF cutoffs. Candidate remission definitions all demonstrated significant treatment effects(UST vs. PBO):total AP+SF<75 (29.4% vs.16.7%, p=0.004),combined AP ≤ 1 AND SF ≤ 3(19.3% vs.9.1%, p=0.007), combined AP ≤ 1 AND SF ≤ 1.5(13.7% vs.5.3%, p=0.009).
Conclusions: Definitions of PRO-2 remission based on SF&AP CDAI components are sensitive and specific in an anti-TNF refractory/ intolerant population with high CD activity. In this population,the PRO-2 definition of AP ≤ 1 AND SF ≤ 3 better reflects clinical remission than the previously proposed AP ≤ 1 AND SF ≤ 1.5 threshold, identified in the mild-to-moderate patient populations. A weighted total AP+SF score <75 may be a good PRO-2 definition of remission, because it provides the best overall balance of SENS/SPEC and facilitates comparisons with studies utilizing the full CDAI.

P165
The distribution and severity of small bowel inflammatory activity forecast the emergence of anemia and nutricional deficits in Crohn's Disease

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Background: Crohn's Disease (CD) affects the small bowel in over 80% of the patients, and may result, among others, in anemia and nutritional deficiencies, in consequence of malabsorption and inflammatory bowel activity.
We aimed to analyze and correlate the presence of anemia and nutritional deficiencies (iron, folic acid, Vitamin B12, albumin and total proteins) with both the extent and severity in small bowel inflammatory activity, using small bowel capsule endoscopy (SBCE), through the Lewis Score (LS).
Methods: Retrospective single-center study, including patients with exclusively small bowel CD undergoing SBCE between January/2007 and June/2014. Exclusion criteria: patients with small bowel resection surgery as well as patients with red blood cell transfusions or nutritional supplements (iron, folic acid, Vitamin B12) in the 3 months prior to SBCE.
We assessed hemoglobin, iron, iron binding capacity, ferritin, folic acid, Vitamin B12, albumin and total protein serum levels at the moment of the SBCE procedure. Small bowel inflammatory activity was assessed, according to LS, in each tertile (< 135 - no

inflammatory activity; 135-790 - mild inflammatory activity; ≥ 790 - moderated to severe inflammatory activity).

Results: Included 69 patients, 62% (n=43) were female, with mean age 33 years (range 18-75); inflammatory activity was observed in 41 (59%) patients, and was moderate to severe in 28 (41%).

Eighteen patients (26%) presented with anemia, and 74% (n=51) with iron deficit (defined as ferritin levels < 100 ng/mL or transferrin saturation < 16%); nutritional deficits of albumin, folic acid and Vitamin B12 were encountered in 4 patients each (8,7%). Proximal small bowel disease was significantly correlated with lower acid folic serum levels (p=0,004). LS superior to 790, independently of disease location, was significantly associated with anemia (p=0,039) and low serum proteins (p=0,002).

Conclusions: In our series, we observed an important prevalence of both anemia and iron deficit. Proximal inflammatory activity in the small bowel was significantly associated with lower folic acid levels, while anemia and low serum proteins were correlated with the severity of the inflammatory lesions, assessed through Lewis Score, regardless of their distribution.

P166
Upper gastrointestinal involvement in asymptomatic Crohn's disease patients in two countries of emerging disease: Asia and Eastern Europe

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Background: The incidence of inflammatory bowel disease (IBD) is still increasing in Asia and Eastern Europe. Disease phenotype may differ when compared the East and the West. However, limited studies have reported on the frequency of upper gastrointestinal (GI) involvement in patients with Crohn's disease (CD) in non-Western countries. In this prospective, international, multicenter study we compared the prevalence of macroscopic and microscopic upper GI manifestations and Helicobacter pylori positivity in asymptomatic CD patients in Asia and Eastern Europe in comparison with sex- and age-matched non-IBD controls.

Methods: Consecutive asymptomatic CD patients were prospectively recruited for upper GI endoscopy between 2013 and 2014 in Hong Kong and in Hungary. Endoscopy and biopsy findings were recorded and histology was performed to assess for Helicobacter pylori and microscopic signs characteristic for CD.

Results: One hundred and thirteen CD patients (50 Hong Kong; 63 Hungary; 66.4% male; median age, 35 years) and 114 controls (49 Hong Kong; 65 Hungary) were included. CD patients in Hungary (median age, 33 years, range 18-76) were younger than those in Hong Kong (median age 39 years, range 19-73; p=0.027). There was no difference in the presence of macroscopic inflammation (30% vs. 47.6%; p=0.059), microscopic inflammation (92% vs. 74.6%; p=0.075), gastroduodenal erosions (22% vs. 11%; p=0.122) or Helicobacter pylori positivity (6% vs 9.5%; p=0.376) in CD patients in Hong Kong and in Hungary. Peptic ulcer or duodenal strictures were found in 1.6% of patients in Hungary and none in Hong Kong. Granulomas were detected in 4% in Hong Kong and 9.5% in Hungary (p=0.135). Two CD cases (3.2%) in Hungary were diagnosed with celiac disease. Overall CD subjects had a significantly lower Helicobacter pylori positivity as compared to controls (8.0% vs 20.2%; p=0.010).

Conclusions: The rate of upper GI lesions in CD patients in Asia was similar to that of Hungary, and comparable to Western countries. CD patients had a significantly lower Helicobacter pylori positivity rate as compared to controls. The convincingly high frequency of macroscopic and especially microscopic inflammation observed in our study justifies the need of upper GI endoscopy in asymptomatic CD patients independently of ethnicity.

P167
Prolonged Small Intestinal Transit in Crohn's Disease is associated with a history of stricturing and penetrating disease.

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Background: Gastrointestinal motor disorders may complicate Crohn's disease (CD) and make clinical evaluation difficult. In spite of this, little is known about gastrointestinal motor disorders in CD. Moreover, it is not clear which clinical characteristics of CD are associated with abnormal transit patterns. This is relevant to the clinician, especially when symptoms are present in otherwise quiescent CD. Our aim was to investigate which clinical characteristics of CD are associated with abnormal small intestinal transit time (SITT).

Methods: This retrospective study includes data from capsule endoscopy examinations and medical reports of 118 patients with CD and 43 controls without CD performed at Aarhus University Hospital, Denmark from 2002 to 2011. Cases with capsule retention were excluded. Data were analysed using regression models.

Results: Gastric emptying (GE) and SITT did not differ between patients with CD (median GE: 27 min (range 1 - 592), SITT 295 min (range 78 - 481)) and controls (median GE: 16 min (range 1 - 138), SITT 285 min (range 114 - 481)). Among patients with CD, prolonged SITT was associated with stricturing (p = 0.012) and penetrating disease behaviour (p = 0.003). No statistically significant difference was found between stricturing and penetrating disease (p = 0.51). Age, gender, duration of disease, smoking, disease localization, active disease, level of faecal calprotectin, and specific findings on capsule endoscopy were not associated with significant changes in SITT.

Conclusions: This study indicates that prolonged SITT is associated with the behaviour or phenotype of CD. Furthermore, our findings imply that changes in small intestinal motility causing prolonged SITT are chronic rather than a transitory phenomenon since disease location and signs of inflammation present at the time of CE did not significantly affect SITT.

P168
Diffusion-weighted magnetic resonance imaging in ileocolonic Crohn's disease

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Table 1 ADC (x 10^{-3} mm^2/s) in bowel segments with and without Crohn's disease.

		Normal	Crohn's disease	*P*-value
All segments	- Buscopan	1.48 (1.37-1.58)	1.43 (1.18-1.69)	0.08
	+ Buscopan	1.40 (1.27-1.53)	1.36 (1.51-1.59)	0.49
Terminal ileum	- Buscopan	1.22 (0.81-1.63)	1.09 (0.82-1.35)	0.30
	+ Buscopan	1.47 (0.73-2.21)	1.20 (0.68-1.72)	0.61
Ascending colon	- Buscopan	1.60 (1.21-1.99)	1.82 (0.86-2.78)	0.65
	+ Buscopan	1.34 (1.02-1.67)	1.54 (1.09-1.98)	0.29
Transverse colon	- Buscopan	1.58 (1.37-1.79)	1.18 (0.96-1.40)	0.01
	+ Buscopan	1.52 (1.17-1.87)	1.10 (0.74-1.46)	0.09
Descending colon	- Buscopan	1.45 (1.24-1.66)	1.27 (0.93-1.61)	0.29
	+ Buscopan	1.34 (1.01-1.66)	1.28 (1.07-1.50)	0.83
Rectum	- Buscopan	1.43 (1.29-1.58)	1.94 (1.07-2.80)	0.25
	+ Buscopan	1.38 (1.22-1.54)	1.73 (1.04-2.42)	0.46

95% confidence intervals are displayed in parenthesis.

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Background: Diffusion-weighted magnetic resonance imaging (dw-MRI) utilizes differences in the motion of water molecules between tissues for image formation without administration of contrast materials. Inflammation in the bowel wall slows water transit resulting in lower apparent diffusions coefficients (ADC). Previous studies have shown that dw-MRI combined with conventional MR sequences can be useful for detection of Crohn's disease in the terminal ileum and colon. The present feasibility study examined the diagnostic performance of free-breathing dw-MRI without fasting, bowel preparation or contrast administration in ileocolonic Crohn's disease.

Methods: A total of 10 patients with known Crohn's disease were included in this prospective and blinded study. dw-MRI was performed with a Philips Achieva 1.5T MR system and body coil (Philips Medical Systems, Eindhoven, The Netherlands). The MR protocol contained coronal e-thrive and SShT2 with free-breathing and a factor b fixed at 800 s/mm2. Patients were examined in the prone position before and after intravenous administration of 20 mg Hyoscin Butylbromide (Buscopan®, Boehringer Ingelheim, Basel, Switzerland). Ileocolonoscopy with Simple Endoscopic Score for Crohn's disease (SES-CD) served as gold standard. Active Crohn's disease was defined as a segmental score ≥ 1.

Results: A total of 46 bowel segments were assessed with ileocolonoscopy and dw-MRI of which 22 (48%) were inflamed according to the gold standard (median SES-CD segmental score 4, range 2-8). ADC obtained with and without Buscopan correlated with a Spearman's rho of 0.64 ($P < 0.001$). Without Buscopan, there was a trend towards lower ADC in segments with Crohn's disease compared to segments without inflammation (1.43 x 10 – ^{3}3 mm2/s vs. 1.48 x 10 – ^{3} mm2/s, P = 0.08, Table 1). However, this difference was not observed with Buscopan (P = 0.49). ROC-analysis revealed an area under the curve (AUC) of 0.56 and 0.64 with and without Buscopan, respectively (P = 0.3). In the transverse colon, dw-MRI significantly discriminated active from inactive Crohn's disease (1.58 x 10 – ^{3} mm2/s vs. 1.18 x 10 – ^{3} mm2/s, P = 0.01).

Conclusions: The ability of dw-MRI to discriminate Crohn's disease from normal bowel segments is inadequate. Large variations of ADC in normal and diseased bowel segments emphasize the importance of optimal anatomical distinction for obtaining precise measurements.

P169
Exhaled volatile organic compound breath analysis in Inflammatory Bowel Disease

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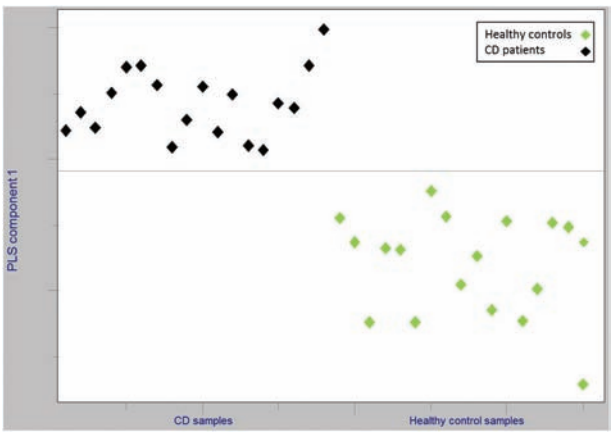
Background: Distinguishing between Crohn's disease (CD) and ulcerative colitis (UC) is important for determining management and prognosis. Selected ion flow tube mass spectrometry (SIFT-MS) may be used to analyse volatile organic compounds (VOCs) in exhaled breath: these may be altered in disease states, and distinguishing breath VOC profiles can be identified [1]. A recent paediatric study used SIFT-MS to distinguish IBD patients from healthy controls [2]. The aim of this pilot study was to identify, quantify and analyse VOCs present in the breath of adult IBD patients and controls, potentially providing insights into disease pathogenesis and complementing current diagnostic algorithms.

Methods: SIFT-MS breath profiling of 56 individuals (20 UC, 18 CD and 18 healthy controls) was undertaken. Multivariate analysis included principal components analysis and partial least squares discriminant analysis with orthogonal signal correction (OSC-PLS-DA). Receiver Operator Characteristic (ROC) analysis was performed for each comparison using statistically significant (as calculated by Mann Whitney U test $p \geq 0.05$) VOCs.

Results: OSC-PLS-DA modelling was able to distinguish both CD and UC from healthy controls and from one other with good sensitivity and specificity.

ROC analysis using combinations of statistically significant VOCs (dimethyl sulphide, hydrogen sulphide, hydrogen cyanide, ammonia, butanal and nonanal) gave integrated areas under the curve (AUC) of 0.86 (CD vs healthy controls), 0.74 (UC vs healthy controls) and 0.83 (CD vs UC).

Conclusions: SIFT-MS breath profiling was able to distinguish IBD patients from controls, as well as separate UC from CD, using both multivariate and univariate statistical techniques. The specific VOCs characterising the breath in IBD relate to bacterial dysbiosis and oxidative stress [3] - both mechanisms implicated in disease pathogenesis.



"Figure 1. Cross-validated OSC-PLS-DA score plot for 18 CD patients and 20 healthy controls showing the separation achieved with the one-component model"

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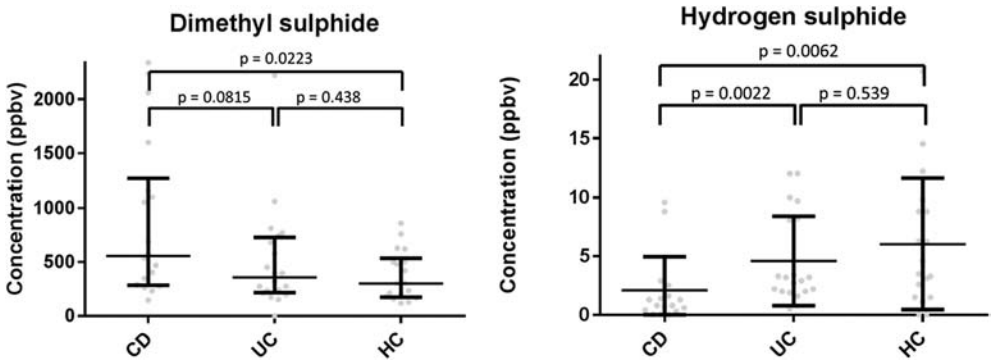
Predictive abilities of OSC-PCS-DA models created

	Sensitivity (%)	Specificity (%)	Q2 (cross validation parameter) value
CD vs HC	94.4	94.4	0.78
UC vs HC	90.5	94.4	0.66
CD vs UC	88.9	90.0	0.69

ROC analysis using significant VOCs

	AUC	95% confidence limits
CD vs HC	0.864	0.749–0.980
UC vs HC	0.742	0.581–0.902
CD vs UC	0.828	0.699–0.956



"Figure 2. Concentrations of (a) dimethyl sulphide and (b) hydrogen sulphide; median concentration and inter-quartile ranges are shown."

P170
Comparison between elderly onset and adult onset inflammatory bowel disease

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Background: As the population ages the incidence of elderly onset inflammatory bowel disease (IBD) is expected to increase. In this study we compared clinical presentation and disease behaviour of IBD diagnosed in geriatric age (65 ≥ yrs) vs adulthood (40-64 years).

Methods: From January 2000 to May 2014 all patients diagnosed with IBD after the age of 65 were enrolled (elderly-onset IBD), each case was matched 1:1 by disease (UC or CD), gender and year of diagnosis with a control with IBD onset from 40 to 64 years (adult-onset IBD).

Results: Table 1 shows characteristics of UC and CD by age.

Symptoms at the presentation of UC and CD where similar between elderly and adults except for weight loss which was more common in elderly-onset UC and for constipation which was more frequent in elderly-onset CD. At the diagnosis of UC, higher proportion of elderly were classified as E2 and less as E1 according to Montreal Classification (65% vs 43%, p=0.02), while disease progression at maximum follow up was similar. For CD there were no differences between extension, phenotypes and histological activity between elderly and adults; disease progression was negligible. Therapy at the diagnosis and clinical behavior of UC and CD were similar between groups . Kaplan Meier analysis for time to first relapse showed no differences between elderly and adults neither for UC, nor for CD. Elderly onset UC, had a tendency to higher surgical approach (18% vs 8%, p=0.07). For CD, in both groups, about 50% of patients received surgical intervention but elderly onset CD were more likely to be operated early in the course of the disease; mean time to the surgical intervention was 1.5±1.9 months and 18.5 ±22.8 months, p=0.02 in elderly and adults respectively. Complications were more likely to occur among elderly-onset UC, we recorded an higher number of systemic infections (28% elderly VS 9% adults, p=0.027), deep vein thrombosis (14% elderly vs 1.5% adults, p= 0.003), intestinal complication (17% elderly vs 5% adults, p=0.022). Iatrogenic complications like steroidal diabetes, hypertension and osteoporosis occurred more frequently among elderly (17% vs 8%, p=0.029)

Conclusions: Elderly-onset IBD seems to have similar presentation and clinical behaviour when compared to adult-onset IBD. Elderly IBD patients presents more comorbidities and are more likely to develop complications; these aspects needs to be taken into account when treating these patients

P171
Smoking is associated with watery diarrhea and decreased likelihood to achieve clinical remission in collagenous colitis

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Background: Smoking seems to be a risk factor for microscopic colitis and smokers develop the disease more than 10 years earlier than non-smokers. However, the impact of smoking on clinical activity and outcome has not been elucidated.

Methods: In a post-hoc analysis from pooled data of two randomized controlled trials (BUC-60/COC and BUC-63/COC) we assessed the association of demographical (gender, age, smoking habits, previous and/or concomitant medication, family history of inflammatory bowel disease) and clinical variables (duration of symptoms, mean number of stools/watery stools per day, abdominal pain, clinical remission). Moreover, we analyzed the predictive value of baseline parameters on clinical outcome in a logistic regression model.

Results: Pooled data from 202 patients with active collagenous colitis (CC) were available thereof 36% current smokers, 29% former smokers and 35% non-smokers. Current smokers had an increased number of watery stools at baseline compared to non-smokers (p=0.05). 20/137 (15%) patients treated with budesonide did not achieve clinical remission. The majority of these (85%) were either smokers or former smokers. An association was found between smoking status (current smokers vs. non smokers: OR 0.37, 95% CI: 0.14-0.96, p=0.041; former smokers vs. non smokers: OR 0.21, 95% CI: 0.07-0.60, p=0.004), mean number of watery stools per day (OR 0.77, 95% CI: 0.66-0.90, p=0.001) and decreased likelihood to obtain clinical remission. All other variables showed no significant association.

Conclusions: Smoking is associated with increased number of watery stools and decreased likelihood to achieve clinical remission in collagenous colitis. Smoking seems to have an impact on disease activity and treatment outcome in patients with CC.

Table 1 shows characteristics of UC and CD by age.

	elderly UC	adults UC	elderly CD	adults CD
Patients, N°=178	65	65	24	24
Mean age at diagnosis yrs (SD)	71.3(5)	48.6(6)	71.6(4.9)	47.1(6.5)
Female N(%)	35(54)	35(54)	15 (62.5)	15 (62.5)
Follow up length, yrs mean(SD)	4.9(3.3)	5.4(3.6)	6.1(3.2)	6.4 (3.4)
Time from symptoms onset to diagnosis yrs, mean (SD)	0.7(1.5)	0.5(1.2)	2.7(4.6)	3.0(4.8)
Comorbidity Index (CIRS), mean (SD)	3.7(2)	1.5(0.9)	4(2)	1.5(0.6)

Characteristics of UC and CD by age

P172
Clinical and biological predictors of fatigue in Inflammatory Bowel Disease patients

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Background: Fatigue is a common and bothersome symptom that inflammatory bowel disease (IBD) patients have to face even in remission. Many psychological and biological factors have been related to fatigue. The aim of the study is to determine the role of different biological and psychological factors in IBD-related fatigue.
Methods: All IBD patients followed at our Gastroenterology Day Hospital between January and December 2013 were included. Patients complete Functional Assessment of Chronic Illness Therapy-Fatigue score (FACITC-F) as well as psychological scores (Beck for depression, Stai for anxiety, Epworth for sleep disturbances and IBDQ-9 for quality of life) and IBD activity scores. Biological parameters (Interleukin 5, 8, 12, complete blood count, ferritin, C-reactive protein, erythrocyte sedimentation rate and micronutrients) were tested by appropriate blood tests.
Results: A total of 219 were studied and at the end of the study 177 patients (mean age, 39 ± 12 years, 28% ulcerative colitis and 72% crohn's disease) were included for the analysis. The median Fatigue score (38, range (1-52)) was lower that than in general population. Twenty-eight (16%) patients had moderate-to-severe fatigue determined as fatigue score of 22 or lower. In the univariate analysis, fatigue differed significatively with gender, type of IBD, Harvey and Mayo score, articular disease, body mass Index (BMI), psychological tests, thiopurine and biological treatment. All these variables were included in the multivariate analysis. Female gender (ß -6.61, p<0.001), BMI (ß -0.61, p<0.001) and higher depression (ß -0.43, p<0.001) and anxiety (ß -0.18, p<0.001) scores were predictors of increased fatigue. IBDQ-9 (ß 0.51, p<0.001) was independently related to lower fatigue.
Conclusions: Fatigue was prevalent in our IBD patients and was related to high levels of anxiety and depression and low quality of life. None of the biological factors evaluated including pro-inflammatory interleukins or micronutrient deficiencies was associated with fatigue.

P173
Contrast-enhancement at magnetic resonance enterography does not differentiate between fibrosis and inflammation in Crohn's disease: a prospective cohort study

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Background: Contrast-enhancement (CE), measured at magnetic resonance enterography (MRE), is one of the established parameters of inflammation in Crohn's disease. No studies at the best of our knowledge has quantified fibrosis and correlated with MRI parameters. Therefore, we aimed to investigate the correlation the relative CE (RCE) seen at MRI prior to surgical ileo-colonic resection for complicated Crohn's disease (CD) and the quantity (measured as the actual percentage) of fibrosis and inflammation.
Methods: We prospectively enrolled CD subjects with planned ileo-colonic surgery for complicated CD. They underwent MRE not earlier than 4 weeks prior to surgery. RCE was calculated at the level of 1 cm above the ileo-ciecal valve or anastomosis to be resected. After surgery, surgical samples were cut and processed. All the histological sections were digitized using a computer-aided image analysis system at 10x objective magnification. Ad-hoc software automatically selected the total CD45+ immunoreactive surface (IRA, %) as a marker of inflammation, or Sirius red stained surface (SS, %) as a marker of fibrosis, on the basis of RGB (Red, Green, Blue) color segmentation. Spearman's correlation test was used to assess the correlation between RCE values and the percentage of inflammation and fibrosis, as well as the pattern of inflammation (dispersed/aggregated). Statistical significance was set as $p<0.05$.
Results: Thirty-six subjects were enrolled, 27 subjects were included into the final analysis. Ten subjects (37%), underwent surgery for stricturing disease 5 subjects (18.5%) for stricturing and penetrating disease, 12 subjects (44.5%)for penetrating disease. In all subjects, fibrosis and inflammation were found coexisting. In the entire cohort, median RCE ranged from 0.18 to 2.33 (median 0.99), inflammation ranged from 2% to 20% (median 8.86%), fibrosis from 2% to 32% (median 10.23%) No correlation was found between RCE and the percentage of inflammation (R^2= 0.0036, p=0.77), and with fibrosis (R^2= 0.008, p=0.15). Also no correlation was found between RCE and patterns of inflammation, both dispersed and aggregated (R^2= 0.0014, p=0.19).
Conclusions: In CD RCE was found not to correlate with the grade of inflammation and fibrosis. RCE may not be able to discriminate fibrosis and inflammation in CD in the preoperative settings.

P174
Diagnostic value of a novel combination score of disease activity in a real-life IBD cohort.

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Background: Monitoring of mucosal inflammation in inflammatory bowel disease (IBD) is of major importance to improve the long term outcome. Clinical activity indices however have shown insufficient correlation with endoscopic disease activity in Crohn's disease (CD). Fecal calprotectin (FC) is a better predictor of endoscopic activity but values between 100-250 µg/g are difficult to interpret. Therefore, the aim of our present study was to evaluate the role of FC and the additional value of a combination of non-invasive markers,

especially in patients with indefinite FC values, for assessment of disease activity in a real-life IBD cohort.

Methods: Three hundred and three consecutive IBD patients were enrolled and participated in a 1 year prospective follow-up study. Patients were assessed during routine outpatient clinic visits or when a flare occurred. Clinical disease activity was scored by Harvey Bradshaw index or Simple Clinical Colitis Activity Index, also C-reactive protein (CRP) and FC were determined. We defined FC levels between 100-250 μg/g as inconclusive. Endoscopic evaluation was performed when indicated. Endoscopic disease activity was determined by the Simple Endoscopic Score-CD and Mayo endoscopic subscore in ulcerative colitis (UC). Clinical activity index, CRP and FC were combined into a new combination score and evaluated in the cohort of patients who underwent an endoscopy. Patients with inconclusive FC values were re-classified with the combination score.

Results: Inconclusive FC values were present in 24% (CD) and 15% (UC) of the patients. In both CD and UC more patients had active disease according to the combination score (47% and 39%) than with assessment of FC alone (26% and 32%). In CD, the combination score could predict endoscopic disease activity with sensitivity of 79%, specificity of 58% (positive predictive value (PPV) 54%, negative predictive value (NPV) 82%). In UC this was 85% and 57% (PPV 88%, NPV 50%). All patients with inconclusive FC values could be classified with the new combination score.

Conclusions: In our real-life cohort of IBD patients, a substantial part of patients has inconclusive FC values. The combination of FC with clinical activity indices or CRP helped to classify disease activity in these patients. We think that the concept of combining non-invasive markers is an interesting new tool in the search for reliable and easy to use surrogate markers for endoscopy in daily clinical practice.

P175
Clinical outcome of ulcerative colitis with mucosal healing demonstrated by white light endoscopy but with subtle abnormalities detected by high definition iSCAN endoscopy

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Background: Current practice is to assess mucosal inflammation in patients with ulcerative colitis (UC) with white light endoscopy (WLE). However, novel endoscopic techniques such as high definition (HD) iSCAN endoscopy can demonstrate inflammation by showing changes in mucosal and vascular pattern in the apparently healed mucosa on WLE. However, the clinical significance of these subtle abnormalities is still unknown. We aimed to monitor the clinical outcome of patients with Mayo subscore of 0 and to determine if abnormalities detected on HD iSCAN endoscopy is associated with a worse prognosis of the disease

Methods: 41 patients (16 female, median age 49) with quiescent UC Mayo subscore of 0 were followed during a median period of 20.3 months. All patients were previously endoscopically assessed by WLE and HD iSCAN (Pentax EPKi processor (EC-3490Fi; Pentax Tokyo) and Mayo endoscopic subscore was assigned to patients according to WLE findings. Mucosal pattern on iSCAN was graded as 1=normal, 2=mosaic pattern, 3=tubular-gyrus, 4=nodular rosette. The vascular pattern was graded as 1= normal, 2=spiral isolated vessels, 3=crowded tortuous vessels, 4=Irregular vessels. The validated New York Mount Sinai score was used to assess the grading of inflammation on histology. The clinical outcome was assessed by monitoring CRP levels, Mayo clinical score, further endoscopic evaluation, changes in treatment, use of steroids, introduction of new medication, admission to hospital and colectomy rate. Statistical analysis was performed with Chi Square test and compared the endoscopic findings between patients that flared and patients that remained stable.

Results: Six patients (14.6%) out of 41 developed a relapse of UC during follow up. The initial endoscopic assessment of these six patients showed an abnormal mucosal pattern in 2 patients (33.3%) and an abnormal vascular pattern in 4 patients (66.6%). Among 35 patients that remained stable, 27 (77.1%) presented an abnormal vascular pattern and 5 (14.3%) had an abnormal mucosal pattern on HD iSCAN colonoscopy. Histologic assessment showed quiescent colitis in all patients. There was no statistical significance between patients that relapsed and those that did not relapse when comparing the distribution of normal and abnormal iSCAN scoring.

Conclusions: A high proportion of patients with mucosal healing on WLE have residual changes detected by HD iSCAN endoscopy. However, we could not demonstrate that this is associated with increased frequency of relapse or worse outcome of the disease. In addition, 14.6% of patients with Mayo endoscopic subscore of 0 relapsed during the follow up period. A more precise endoscopic score is needed to better describe the endoscopic features of mucosal healing in patients with UC.

P176
Irritable bowel syndrome frequency in Inflammatory Bowel Disease during both clinical and deep remission and its association with fecal calprotectin

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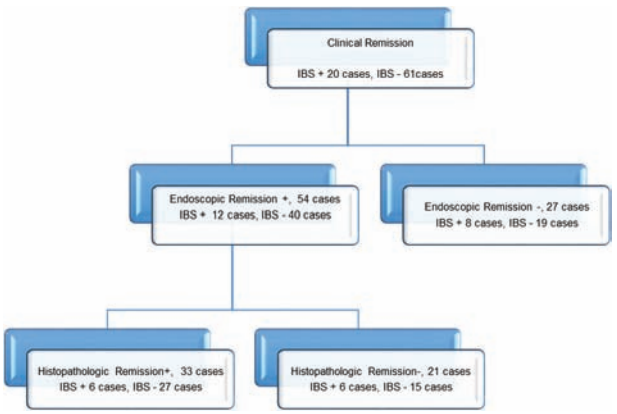
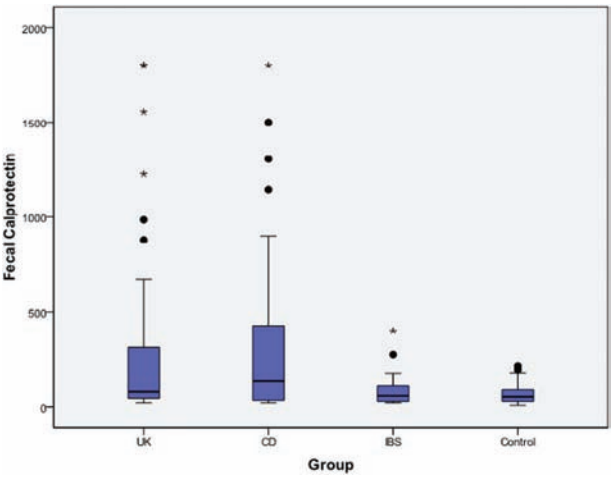
Background: Inflammatory bowel diseases (IBD) are chronic inflammatory diseases that may involve any part of the gastrointestinal tract and have a clinical course of remissions and exacerbations.



"Figure 1. Clinical, endoscopic, and histopathologic remissions and number of IBS cases"



"Figure 2. Fecal calprotectin levels in UC, CD in clinical remission, IBS, and control groups"

Abdominal pain occurs in 20-50% of the IBD patients that are in clinical and/or endoscopic remission [1]. Irritable bowel syndrome (IBS) is among the causes [2]. IBS patients even if in clinical remission, may not be in endoscopic and histopathologic remission, and these symptoms that appear in cases in remission may be indicators of randomly occurring IBS or clinically undetectable low-grade inflammation [3]. The aim of this study was to identify the frequency of IBS in patients with IBD in remission, to investigate the association of clinical remission with endoscopic and histopathologic remission and the association of these with IBS and fecal calprotectin.

Methods: A total of 163 cases were included in this study, among who were 43 ulcerative colitis (UC) cases, 38 Crohn's Disease (CD) cases clinically in remission for at least 6 months, 42 IBS patients and 41 healthy control subjects. All of the UC and CD patients in remission underwent colonoscopy and biopsy specimens were taken to evaluate histopathologic remission. All of the cases were administered a questionnaire questioning Roma III criteria for IBS and fecal samples were obtain to measure fecal calprotectin.

Results: IBS frequency was 20.9% among UC cases and 28.9% in CD cases in clinical remission, and this rate did not vary by the presence of endoscopic or histopathologic remission (Figure 1).

Fecal calprotectin, while found to be higher in UC and CD groups compared to IBS cases and control subjects,its levels did not vary by the presence of IBS(Figure 2).

In this study, fecal calprotectin at levels >150 µ /g was found to be a better predictive factor in identifying inflammation.

Conclusions: IBS frequency was 21-29% among IBD patients in remission, which did not vary by the presence of endoscopic or histopathologic remission or by fecal calprotectin levels. This suggests that IBS may not be associated with the subclinical inflammation that continues in IBD during remission and that other factors may have a role in the pathogenesis.

Keywords: inflammatory bowel disease, irritable bowel syndrome, fecal calprotectin

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P177
Patency capsule in patients with established Crohn's disease undergoing videocapsule endoscopy of the small bowel

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Background: Video capsule endoscopy (VCE) is invaluable in diagnosis of small bowel (SB) pathology . Capsule retention is a major concern in patients with Crohn's disease (CD) . Patency capsule (PC) was designed to evaluate SB patency before VCE. However, the actual benefit of PC in CD is unclear. The aim of this study was to evaluate the impact of PC administration on capsule retention risk in patients with established CD

Methods: A retrospective multicenter study of CD patients undergoing VCE for established CD. PC utilization strategy was classified as selective (only in patients with obstructive symptoms , history of intestinal obstruction and surgery or per treating physician's request) or non-selective (in all patients). The main outcome was capsule retention in the entire cohort and each study arm.

Results: A total of 406 patients were included. VCE was performed in 132/406 (32.5%) cases without a prior PC. PC was performed in 274/406 (67.5%) and was negative in 193 patients. The risk of retention was 2.3% after VCE without PC and 2.1% after negative PC (p=0.9); 18/ 81 underwent VCE after positive PC with a retention rate of 11.1% (p=0.001). PC failure was associated with an increased risk of capsule retention on a multivariate analysis. However, PC administration strategy was not associated with retention risk.

Conclusions: Capsule retention is a rare event in patients with established CD. The risk of capsule retention was not decreased by routine use of PC in all CD patients. VCE in CD patients after positive PC is associated with a high risk of capsule retention.

AN and UK have equally contributed to the study

P178
Association between eleven thiopurine metabolites and mucosal healing in patients with Crohn's disease

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Background: Thiopurine-related drug response in treatment of patients with Crohn's disease (CD) is still incompletely understood. Thus, therapeutic monitoring of thioguanine nucleotides (TGN) and methylthioinosine derivatives (MMPR) has been suggested to

improve thiopurine therapy, however with limited success. The comprehensive assessment of thiopurine metabolite pattern instead of determination of total TGN and MMPR levels has been suggested to be beneficial for prediction of thiopurine response.

Methods: Patients with CD on maintenance treatment with azathioprine (AZA) and a stable dose for at least 4 weeks were eligible. We established a novel highly sensitive liquid chromatography-tandem mass spectrometry method for simultaneous quantitation of eleven thiopurine metabolites including mono-, di-, and triphosphates of thioguanosine (TGMP, TGDP, TGTP), methylthioinosine (meTIMP, meTIDP, meTITP), methylthioguanosine (meTGMP, meTGDP, meTGTP), and thioinosine (TIMP, TIDP, TITP). Furthermore, thiopurine S-methyltransferase (TPMT) activity in red blood cell concentrations (RBC) was determined. Blood collection was performed on day of the ileocolonoscopy. Mucosal healing was defined as the absence of any ulcerated lesions.

Results: In total 101 patients (f/m=54/47, median age: 25 years) were included. The median AZA dosage was 2.12 mg/kg/d (range: 0.28-3.13 mg/kg/d) which was stable for median 26 months (range: 1-111 months) before blood collection. Patients without achievement of mucosal healing (non-responder) showed significantly higher concentrations of meTIDP (p= 0.04) and meTITP (p=0.02) in RBC. After stratification of patients in normal and intermediate metabolizers for TPMT the association between non-response and higher RBC concentrations of meTIDP (p= 0.008) and meTITP (p=0.004) held true in patients with normal TPMT activities (n=91). No significant differences between responders and non-responders were found for the isolated thioguanosine phosphate levels (TGMP, TGDP, TGTP).

Conclusions: There was no significant correlation of isolated thioguanosine phosphate levels (e.g. TGDP, TGTP) and mucosal healing. Higher concentrations of methylthioinosine levels in non-responders support the impact of the TPMT metabolizer phenotype regarding thiopurine response.

P179
Serum amyloid A level correlated with endoscopic findings in patients with Crohn's disease - possible biomarker for evaluating mucosal healing

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Background: Mucosal healing (MH) has been proposed as an essential therapeutic goal for treatment of Crohn's disease (CD). Although serum amyloid A (SAA), a major acute-phase inflammatory protein, is a known clinical biomarker of CD, other non-invasive biomarkers for prediction of MH in these patients are lacking. Furthermore, the correlation of SAA in serum with endoscopic disease activity in CD has not been elucidated.

Methods: In this single-center retrospective study, conducted from June 2011 to March 2013 at Shimane University Hospital, Japan, we investigated the correlation of serum SAA level with clinical and endoscopic evidence of CD. Serum samples were obtained at the first visit during the study period and SAA level was assessed in relation to CD activity index (CDAI), defined as 151 or more active phases, as previously reported. SAA was also measured on the day or within 1 week of ileocolonoscopy procedures, with those patients scored according to a simple endoscopic score for CD (SES-CD; inactive 0-3, active >3). MH was defined as an inactive phase of SES-CD. We then assessed the correlation of serum SAA with CDAI and SES-CD findings, and the diagnostic ability of MH correlated with SAA level was evaluated using receiver operating characteristic (ROC) curve analysis.

Results: Sixty-two patients with CD (mean age 36.7 ± 8.8 years; 44 males, 18 females) were enrolled. Mean serum SAA level was significantly higher in the active (n=20, 280.6 ± 491.6 ug/dl) as compared to inactive (n=42, 23.2 ± 34.7 ug/dl) phase (p<0.001) and also significantly correlated with CDAI (Spearman's rank correlation coefficient r=0.45, p<0.001). In addition, the utility of serum SAA level for assessment of MH during the study period was investigated. Mean serum SAA level was significantly higher in the endoscopic active (254.7 ± 481.0ug/dl) as compared to the inactive (8.0 ± 5.2ug/dl) phase (p<0.001), and also significantly correlated with SES-CD (Spearman's rank correlation coefficient r=0.71, p<0.001). The area under the ROC curve for SAA level was 0.83 and the optimal cut-off value for SAA to predict MH was 6.0 ug/dl. SAA level was shown to be associated with MH, with a sensitivity of 93% specificity of 67%.

Conclusions: Our Results demonstrate that serum SAA is elevated during active CD and has a significant correlation with ileocolonoscopy findings. Furthermore, a low concentration of SAA exhibited high sensitivity for MH. Thus, SAA may be a possible biomarker for evaluating MH in CD patients.

P180
The new faecal marker matrix metalloprotease-9 is more sensitive for postoperative endoscopic recurrence than fecal calprotectin in Crohn's disease

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Background: Faecal calprotectin (FC) has been published to predict endoscopic postoperative recurrence in Crohn's disease (CD) patients. The role of the new faecal activity marker, matrix metalloprotease (MMP)-9 has not been examined in postoperative CD. The aim of this study was to assess the diagnostic accuracy of faecal MMP-9 and to compare it with FC in patients with CD who underwent bowel resection or colectomy.

Methods: FC and faecal MMP-9 were determined simultaneously by enzyme-linked immunoassay test in patients with postoperative CD undergoing colonoscopy. Clinical disease activity was assessed according to the Crohn's Disease Activity Index (CDAI). Postoperative recurrence was determined according to the Rutgeerts' score.

Results: Ileocolonoscopy was performed in 24 patients with postoperative CD (12 patients with bowel resection and 12 patients with colectomy or hemicolectomy). FC levels did not correlate with the Rutgeerts' score (R=0.25; p=0.3012). Faecal MMP-9 showed a stronger, but statistically not significant correlation with the Rutgeerts' score (R=0.356, p=0.095). However, the prediction of postoperative recurrence presented an AUC of 0.87 with a cut-off value of 0.15 ng/mL (p=0.049), the sensitivity of 64% and the

specificity of 83% in case of MMP-9. In case of FC, due to the low value of AUC, cut-off value, sensitivity and specificity could not be determined. Median faecal MMP-9 levels discriminated Rutgeerts' score 0-1 from 2-4 were 0.19 vs. 0.75 ng/mL respectively.

Conclusions: This is the first study assessing the diagnostic accuracy of MMP-9 in postoperative CD. Our Results showed that faecal MMP-9 has higher sensitivity and specificity in the detection of postoperative recurrence in CD compared to FC.

P181
Diagnostic performance of Diffusion-Weighted Magnetic Resonance Imaging (DW-MRI) in the evaluation of stenosis and endoscopic recurrence in Crohn's disease

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Acute Inflammatory Score evaluation

Parameter	Score
Mucosal ulceration	0 - None 1 - Apthous ulcer (<7 mm) 2 - Linear ulcer 3 - Confluent-large ulcer
Edema	0 - None 1 - Mild 2 - Moderate 3 - Severe
Neutrophils	0 - No increase 1 - Mild increase 2 - Moderate increase 3 - Marked increase
Depth of neutrophilic penetration	0 - None 1 - Mucosa 2 - Submucosa 3 - Muscularis 4 - Serosa and/or extramural fat

Fibrostenosis evaluation

Grade 0 (none)	Absence of fibrosis or minimal fibrosis limited to the mucosa (<25%)
Grade 1 (mild to moderate)	Mild stricture with nondilated lumen with submucosal fibrosis (>25%) and/or muscular hyperplasia with preserved layers
Grade 2 (severe)	Massive transmural fibrosis and/or effacement of normal layers and/or severe stricture

"Fig1"

Tab 1	*Pearson's* [a] *P <0,01*				
	AIS	***Ulcer***	***Edema***	***Neutr***	***Deep infilt.***
ADC	-0,91[a]	-0,92 [a]	-0,15	-0,93 [a]	-0,85 [a]
DWI	0.66	0,71	0,14	0,57	0,77

Tab 2	*Spearman's rho*		[a] *p < 0,01*
ADC	2 ≤ RS > 2	RS 3G (mild,moderate,severe)	RS 5G (i0,i1,i2,i3,i4)
	-0,85 [a]	-0,53 [b]	-0,73 [b] *p < 0,05*

"tab1,2"

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Background: In active Crohn's disease (CD) the high viscosity and cellularity of inflamed tissue reduce the extracellular space, restricting water diffusion. DWI represents a new application of MRI to study the diffusion of water molecules. ADC (Apparent Diffusion Coefficient) is a quantitative parameter of this phenomenon. We aimed to verify the correlation between DWI findings both with pathological evaluation of fibrosis in surgical specimen (Fig.1) and severity of endoscopic recurrence.

Methods: 21 pts undergoing ileocolonic resection for fibrostenosing CD were submitted to MRI-DWI; 6 pts within 2 months before surgery; 15 pts before follow-up ileocolonoscopy. Conventional MRI findings of terminal or neo-terminal ileum were recorded together with a semiquantitative evaluation of DWI signal intensity using a 3-point scale. To obtain ADC, images were magnified and a ROI was placed on neo-terminal ileum. For the first aim, Acute Inflammatory and Fibrostenosis Score (AIS) was correlated by Pearson's r to ADC values and DWI grading of matched ileo-cecal segment. For the second purpose, patients were divided in three and two classes of endoscopic recurrence based on Rutgeerts' score (Rs) (Rs i0-i1, Rs i2-i3, Rs i4 and Rs ≤ i2, Rs >i2). The correlation was studied by Spearman's rho or Persons'r. ROC curves analysis was used to find out an ADC cut-off value able to distinguish "low and high grade" severity of post-operative recurrence.

Results: Comparison of DWI findings with surgical specimens pathologic evaluation showed a very good correlation, inverse and statistically significant, between ADC and AIS total (r=-0.91, p=0.013). There was a good correlation, not statistically significant, between the qualitative assessment of DWI and total AIS, tab1. The mean ADC value of the 3 pts with mild/moderate fibrosis was not statistically different from the 3 pts without fibrosis. The comparison between ADC and Rs (i0-i4) showed a good correlation, inverse and statistically significant (rho=-0.73, P=0.002), as well as between ADC and the other criteria of division, tab2.

ROC curves analysis highlighted that a value of ADC ≤ 1.82 x10^{-3} mm^2/s could predict a severe recurrence (Rs >i2) with a sensitivity of 88.9% (51.8 to 99.7, CI 95%) and a specificity of 83.3% (35.9 to 99.6, CI 95%).

Conclusions: The Results of this study showed the ability of DWI sequences to provide quantitative measures, allowing a more objective assessment of the CD, bringing out a new "imaging biomarker" capable to monitor the progress/regress of the disease and the effectiveness of therapies. The limitation of our study is mainly the small number of patients that did not allow us to understand whether ADC evaluation could predict the presence of fibrosis in surgical specimens.

P182
New risk score for prediction of relapse in patients with Ulcerative Colitis, Results of a prospective cohort study

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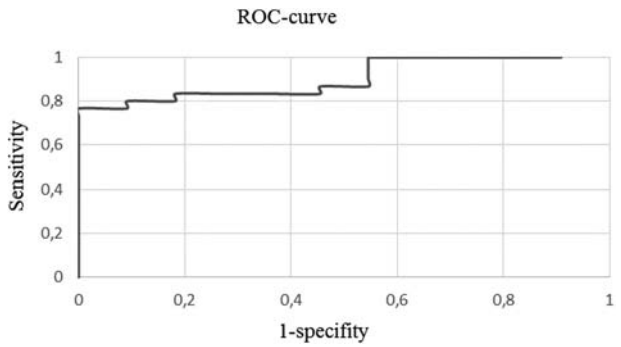
Background: The natural clinical course of Ulcerative Colitis (UC) is characterized by episodes of relapses and remissions. The aims of this study were to develop a new risk score formula for prediction of relapses in UC patients.

Methods: One hundred fifty seven patients with diagnosis of clinically UC, in remission, were followed for 12 months or shorter if they had relapsed. Hemoglobin (Hb), erythrocyte sedimentation rate (ESR), albumin (Alb), iron, platelet, white blood cells (WBC), fecal calprotectin (FC) and Seo activity index were evaluated for each patient every 3 months. Multiple logistic regression was applied to find regression coefficients of significant predictors. Receiver operating characteristics (ROC) curve analysis was performed to find the cut of points of the variables and accuracy of new risk score to prediction of relapse.

Results: A total 157 ulcerative colitis patients were followed between Oct 2012 and Oct 2013 in periods of three month. One hundred fifty four patients were completed the study. They were 48.7% female (mean age: 42.48 ± 11.22 years, range: 20-69 years) and 51.3% male (mean age: 41.81 ± 10.82, range: 21-83 years) with no significant differences (P=0.70). The main consume medication in 64 non-relapsing (80%) and 62 relapsing (83.8%) patients was Mesalasin (P=0.65). Mean age was 42 years, mean number of previous relapses before study, mean duration of disease and mean duration of remission before study were 3.7, 99, 46 months, respectively. Seventy four patients (33 males and 41 females, 48.1%) relapsed during 12 months follow up. Final multiple logistic regression analysis demonstrated that fecal calprotectin level, number of previous relapses (NPR), age and Seo activity index can significantly predict the relapse (p=0.001, 0.024, 0.002 and <0.001, respectively). Regression coefficients of these variables (2, 2, 1 and 4, respectively) were used to develop a new risk score formula. ROC curve analysis revealed that patients with scores equal or greater than 6.5 (from total 9 scores) are the cases with high risk of relapse in the coming one year (sensitivity=73%, specificity=98%, and AUC=0.957). Finally, the following formula was obtained:

Risk Score = (2 × FC) + (2 × NPR) + (1 × age) + (4 × Seo index)

Conclusions: Four predictor variables which were used in the risk score formula are simple and calculate easily. These findings help to physicians for prediction of relapse risk. High score patients must be have restricted observation, treatments and follow up.



"ROC-curve"

P183
Diagnostic value of fecal gelatinase-associated lipocalin as a surrogate marker of inflammation in Inflammatory Bowel Diseases

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Background: Nowadays, there is a need for the use of non-invasive laboratory surrogate markers of intestinal inflammation in inflammatory bowel diseases (IBD). Fecal gelatinase-associated lipocalin (NGAL) secreted by neutrophils and epithelial cells during inflammation and possibly can be used as a marker of inflammation. Aim: to evaluate the diagnostic value of fecal NGAL as a surrogate marker of inflammation in IBD.

Methods: 30 patients with active IBD (9 pts with Crohn's disease, 21 - ulcerative colitis) and 11 healthy controls were included into the study. Fecal NGAL was determined by ELISA in fecal specimens. We used a set of Human Lipocalin-2 / NGAL ELISA, production BioVendor, Czech Republic. ROC-analysis was done to determine the diagnostic value of fecal NGAL - to define the cut point, sensitivity, specificity, and area under the curve (AUC). Also positive predictive value (+PV), negative predictive value (-PV), positive likelihood ratio (LR +) and negative likelihood ratio (LR-) were calculated.

Results: Fecal NGAL was significantly higher in patients with active IBD [4892,5 ng/ml (2730 ng/ml; 9424 ng/ml) compared with healthy controls [433 ng/ml (169 ng/ml; 850 ng/ml) (p<0,01). ROC-analysis (Figure 1) defined the threshold of fecal NGAL as a marker for determining an active phase of inflammation in IBD - 1029 ng/ml, to which were empirically determined sensitivity of 80%, specificity of 90,9%, and AUC - 0,9. Further we constructed 2x2 Table to determine the diagnostic values: +PV - 96%, -PV - 62,5%, LR+ - 8,8 and LR- - 0,22. Thus, the findings suggest that studied indicator have high resolution in identifying IBD.

Conclusions: Fecal NGAL is a novel non-invasive marker to distinguish active IBD from healthy individuals with a high sensitivity, specificity and AUC. Fecal NGAL might be used as one of the non-invasive biomarkers of intestinal inflammation.

P184
Simplifying the meaning of small bowel thickening

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Background: Small bowel thickening (SBT) is a frequent finding. In its presence, we are often faced with a long list of differential diagnoses and the classic recommendation of "clinical- laboratory correlation." The aim of this study was to identify the frequency of the various etiologies for SBT, in order to minimize the gap in radiological literature and provide a better therapeutic strategy for these patients.

Methods: Retrospective study including all patients admitted for clarification of SBT, in the time period between January 2010 - July 2013. Evaluation of the epidemiological, clinical, imaging, endoscopic, histological and microbiological data and the final diagnosis.
Results: 119 patients were included with SBT documented on abdominal ultrasound and / or CT performed in the emergency department: 63.9% female; mean age 46.7 years (15-85 years); 87.4% with abdominal pain. Most common location of SBT: ileum in 58.8%. Investigations: total colonoscopy with / without ileoscopy terminal in 54.6%; enteroscopy in 4 cases; stool cultures in 29.9% of patients. Etiologies: 24.3% infectious; 20.8% primary inflammatory (1 Behçet's disease, other - Crohn's disease); ischemic 5.8%; 5.8% reactive inflammatory (acute appendicitis); 5.8% neoplastic; 5.0% iatrogenic (5 radiation enteritis; 1ACEi angioedema); 1.6% obstruction bowel (hernia). In 31.0% cases it was not possible to reach a final diagnosis. 96 patients underwent radiological reevaluation with enteroCT, 41.6 % of which had no longer any changes in control. In the remaining patients, the enteroCT findings were in agreement with those suggested at admission.
Conclusions: The SBT is a relatively nonspecific feature associated with a wide spectrum of clinical conditions, most of which are acute. The most common etiology for the SBT is infectious. The enteroCT findings were consistent with those at admission. Epidemiological information from this study can be used as an additional tool in the management of SBT and in narrowing its differential diagnosis.

P185
Multidisciplinary approach in IBD patients with arthralgias: Usefulness of a combined reumatologic and gastroenterologic assessment in a prospective study

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Background: The real prevalence of rheumatologic abnormalities in patients with Inflammatory Bowel Disease (IBD) may be underestimated by gastroenterologists. In a prospective study, we evaluated the prevalence and characteristics of articular manifestations in IBD patients, as assessed by a dedicated rheumatologist. Therapeutic changes after the combined assessment were evaluated.
Methods: From December 2012 to November 2013, all IBD patients referring articular pain to the IBD-dedicated gastroenterologist were referred to an experienced rheumatologist. Assessment was made according to current guidelines. Statistical analysis: Data were recorded in a common database expressed as median (range), Student's T test, chi-square test.
Results: During the 12 months follow up, 1275 IBD outpatients were assessed. Arthralgias occurred in 93/1275 (7.3%) IBD patients referred to the rheumatologist. Ulcerative Colitis (UC) group included 38 patients (11M): age 46 years (18-77), UC duration 10 years (0-47), all inactive (Mayo score<3), pancolitis in 18 (47%), left-sided in 15 (40%), distal in 5 (13%), active smokers (n=8; 21%), ex- smokers (n=11;29%), family history of IBD in 4 (11%).Crohn's Disease(CD) group included 55 patients: 18M; age 49 years (20-89),CD duration 17 years (range 1-40), active CD in 49 (89%), mildly active 6 (11%), 19 smokers (35%), family history of IBD in 5 (9%). Montreal classification: B1 in 31 (56%), B2 in 22 (40%), B3 in 2 (4%), P in 5 (9%); L1 in 24 (44%), L2 in 8 (14%), L3 in 23 (42%), L4 in 2 (4%). Among the 93 IBD patients with arthralgias, rheumatologists diagnosed rheumatologic diseases in 33 (88%) UC and in 44 (80%) CD, including: enteropathic-related Spondyloarthritis (SpAe) in 50 (54%) IBD (54% peripheral SpA, 24%, axial SpA, 22% both), osteoarthritis in 24 (26%), fybromialgia in 6 (7%), gout in 3 (3%), rheumatoid arthritis in 3 (3%), psoriatic arthritis in 2 (2%). Diagnosis was inconclusive in 5 (6%) patients. After rheumatological assessment, a higher percentage of IBD patients were treated with disease-modifying anti-rheumatic drugs (including anti-TNFs)(5.3% vs 15%, p=0.03, RR 1.6) and/or with anti-COX2 (6.4% vs 27%; p<0.0001; RR 2.3). Anti-TNFs use also significantly increased (19% vs 34%, p=0.009;RR 1.8).
Conclusions: Multidisciplinary IBD care including IBD-dedicated gastroenterologists and rheumatologists allows a proper diagnosis, management and treatments of arthralgias in IBD.

P186
Pregnancy and natural history of Inflammatory Bowel Disease

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Background: Inflammatory bowel disease (IBD) concern young women in age to procreate. The aim of this longterm and comparative study was to assess the influence of pregnancy on the outcome of IBD.
Methods: 261 patients suffering from IBD were enrolled in the study from 1st January 2005 to 31 December 2009. They were divided in 2 groups according to their gestationnal statute: the 1first group (GI) included 224 pregnant patients at inclusion or already having had pregnancies (112 UC and 112 CD); the second group (GII) comprised 37 patients (17 UC and 20 CD) in age to procreate but never having had pregnancies. Statistical studies: Student Fisher's t test and Mann Whitney's U test.
Results: - The comparison of GI and GII didn't show any statistically significant difference (SSD) on baseline or anatomoclinical characters as well in UC as in CD.
-During the course of the last pregnancy or in the post partum:
1/ in UC, when the disease was in remission at conception, the disease remained quiescent in 82% of the patients; relapses were noted in 18% of cases more often in the 1first quarter (64,3%) ; 78,6% of them were mild and healed under treatment. When pregnancy was concomitant to an active disease: a remission was observed in 77,7% of mild disease and 88,8% in moderate flares. Of the 6 severe cases recorded, one needed colectomy (16,7%).
2/ In CD, remission was maintened in 77, 3% of quiescent disease; 79,7% of the mild flares and 91% of moderate flares evolves towards complete remission; a surgical resection was necessary in 2 out of 8 severe colitis (25 %).
-Long term outcome was studied according to 4 items: Unchanged statute, improvement, worsening and need for surgery. The comparison of GI and GII didn't show any SSD in the outcome of UC; in CD a more favourable outcome in patients of the GII was observed.
Conclusions: The Results of this study show that the effect of pregnancy on the outcome of IBD depends, in UC as well as in CD, on

the evolutive statute of the disease at conception. At long term, pregnancy had not a pejorative influence on the evolution of UC; CD's outcome has been worsened by gestations.

P187
Hearing loss in patients with Inflammatory Bowel Disease

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Background: Inflammatory bowel disease (IBD) has many characteristics of autoimmune diseases. Sensorineural hearing loss has been reported in many autoimmune diseases. Little is known about hearing loss in patients with IBD.
Methods: A prospective blinded comparative study was conducted over a 3 year period. IBD patients and controls underwent a complete otorhinolaryngeal examination and eudiometry test. Any participant with current or past use of an ototoxic medication or recurrent ear infections was excluded from the study.
Results: Altogether 105 participants (76 patients and 29 controls) took part in this study. 59 (77%) had Crohn's disease (CD) and 17 (23%) had ulcerative colitis (UC). Mean age was 36 ± 13, 51% were males and 40% of the patients were presently hospitalized due to IBD exacerbation. 16/76(21%) of the IBD patients complained of any hearing loss since IBD diagnosis and 13% had current hearing disabilities. Audiometric examination revealed that any hearing loss (mild to severe) was found in 23 (30%) of the IBD population, compared to 3 (10%) of the control group ($p<0.05$). Sensironeural was the hearing deficiency type in 93% of them. Out of 46 patients, whose extraintestinal manifestation (EIM) status was clearly documented, 43% (n=20) had EIMs. Hearing loss was present in 5/20 (25%) of these patients, compared to 0/23 who did not have EIMs ($p<0.01$). IBD phenotype (inflammatory vs. obstructive/fistulary), current hospitalization and disease type (CD vs. UC) was not significantly different between these groups.
Conclusions: Sensironeural hearing loss may be another EIM of IBD. It is found in 30% of IBD patients, and in up to 43% of patients who have other EIMs. Early hearing evaluation should be recommended to IBD patients who have other EIMs. Ototoxic hazards should be avoided in IBD patients.

P188
Diagnostic yield of MR enterography versus Wireless Video Capsule Endoscopy in suspected small bowel paediatric Crohn's disease

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Background: MR enterography (MRE) and wireless video capsule endoscopy (VCE) are both used as diagnostic tools in the evaluation of small bowel paediatric Crohn's disease (pCD). Both are safe, well tolerated, avoid the use of radiation and have minimal adverse consequences. The aim of this study was to assess the diagnostic yield of MRE versus VCE in pCD and to establish any differences between findings.
Methods: This was a retrospective, observational study based at a tertiary centre. Results of a paediatric database of patients with known or suspected pCD who had both MRE and VCE within 12 months were collated. A total of 41 patients were identified as having had both tests. Information on age, gender, symptoms, diagnosis and relevant findings on MRE and VCE were collected from electronic patient records.
Results: 41 patients were included in this study; 21 female and 20 male. The median age of the patients was 14 years (age range 6 to 21 years). 16/41 patients (39%) had both a normal MRE and VCE, while 11/41 (26.8%) had similarly abnormal findings (small bowel ulceration and inflammation) in a distribution that matched both on MRE and VCE.
In the remainder 14 patients (34.2%) there was a difference in the findings reported on MRE when compared to VCE particularly when disease distribution was considered. 7 of the 14 patients (50%) had a normal VCE but early terminal ileitis noted on MRE. Conversely, 2 (14.3%) patients had a normal MRE though proximal small bowel ulceration was reported on VCE. 4 (28.6%) patients had diffuse small bowel ulceration on VCE but MRE revealed just limited ileal disease. Finally, 1 (7.1%) patient had limited ileal ulceration on VCE but more extensive ileal and jejunal inflammation on MRE.
Extraluminal pathology was detected in 3/41 patients through MRE (2 with sacroileitis, 1 with ascites).
Conclusions: One third of patients undergoing both MRE and VCE had differences in the abnormalities and distribution of small bowel disease. MRE seemed a more sensitive tool for detecting early terminal ileitis while proximal small bowel disease may be more frequently identified through VCE. The use of both modalities in combination will significantly improve the identification of abnormalities in diagnosing small bowel Crohn's disease and help in treatment escalation decisions in patients with established disease.

P189
Latent tuberculosis: Diagnostic value of QuantiFERON and genetic association to the SNP INFG+874 T/A

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Background: This study was conducted in patients with inflammatory bowel diseases (IBD) to evaluate the performance of Mycobacterium tuberculosis (Mtb) antigen-specific interferon gamma releasing assay (QuantiFERON®-TB Gold In-Tube) for the diagnosis of latent tuberculosis infection (LTBI) comparing to tuberculin skin test (TST), to assess the impact of immunomodulator (IM) treatment in their performances and to analyze whether IGRA positivity is related to genetic susceptibility by screening for INFG +874 (T/A) SNP.
Methods: TST by Mantoux method and QuantiFERON®-TB Gold In-Tube (QFT-GIT) in accordance with manufacturer's instructions, were prospectively performed in 100 consecutive IBD patients and

54 healthy individuals. The SNP genotyping was done by an ARMS-PCR technique.

Results: A better agreement was observed between test's Results in controls (k = 0.40) than in patients (k = 0.16). Results found by TST were more positive than those obtained by QFT-GIT and this was the case for both groups: controls [24.1% versus7.5%] and patients [14.3% versus 9.9%], respectively. Although QFT-GIT Results were unaffected by IM therapy, the mean mitogen response was reduced in immunosuppressed patients (8.06 UI/ml) when compared to the rest of patients and controls (12.70 UI/ml). Similarly, lesser TST positivity was observed in those under IM (9.8% versus 20.5%). Among the 12 QFT+ subjects, 10 (88.3%) had the susceptibility allele (A). Additionally, 6 of them were homozygote for this allele (AA).

Conclusions: Although IM weakens the immunity strength, QFT-GIT seems to be as previously described, more accurate for detecting LTBI's cases that would otherwise be missed using solely TST. In a large vaccinated population, QFT-GIT appears more reliable for excluding a false positive TST. Even though, the (INFG +874T/A) SNP has been frequently associated with active tuberculosis, it seems that this SNP can also be associated with the latent form. All these preliminary Results will be ascertained as long as the size of both groups is enlarged.

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Computed tomography enterography and biomarkers in detecting active and complicated small bowel Crohn's Disease

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Background: Computed tomography enterography (CTE) is one of the modalities in the evaluation of small bowel (SB) Crohn`s disease (CD). It can provide assessment of disease activity, extramural abnormalities and SB complications in patients with CD. This procedure is however associated with radiation exposure. In this group of patients SB investigation by capsule endoscopy may be complicated by capsule retention. Magnetic resonance enterography (MRE) is another alternative. However, it is far from perfect due to patient claustrophobia, long scanning times and movement artifacts. The aim of this retrospective study was to determine the clinical indications and findings on CTE as well as to determine if any biochemical biomarkers (CRP, ESR, platelets, haemoglobin and Red cell distribution width) can predict significant pathologies.

Methods: This was a retrospective analysis on all CTE performed on CD patients in our centre over a 1 year period (October 2013 to September 2014). The clinical indications, biochemical markers and CTE findings in these patients were analysed.

Results: 40 CD patients (26 females, mean age: 30.8 years, range: 18-75) underwent CTE. The main indications for CTE were abdominal pain/discomfort and/or symptoms suggestive of SB obstruction. 25% of CD patients had active inflammation and SB stricture and 2.5% had active inflammation, SB stricturing and fistulating disease. All of these patients had 1 or more raised inflammatory biomarkers. 30% of patients with active SB inflammation on CTE had a rise in 1 or more of the inflammatory biomarkers. Two patients with SB inflammation (5%) had normal biomarkers. The latter were also raised in those patients with normal SB but other intra-abdominal pathology. These patients had active colitis (5%), aortitis (2.5%), colonic fistulating disease (2.5%) and splenomegaly (2.5%). All patients with normal SB (25%) on CTE had normal inflammatory markers

Conclusions: CTE is useful in detecting active and complicated SB disease. It is less useful with quiescent disease. In CD patients, due to their young age and risk of radiation exposure, the presence of normal biomarkers should alert the clinician to question the real need for CTE. CE with patency capsule and/or MRE should be considered as alternatives.

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Effects of CT reconstruction algorithm on the quantitative assessment of Crohn's Disease: A comparison of standard and low dose CT enterography

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Background: Traditional Computed tomography (CT) imaging relies on filtered back projection (FBP) for image reconstruction. Newer iterative reconstruction (IR) techniques use computer modeling to generate CT images with lower radiation exposure while retaining sufficient quality for accurate interpretation. CT Enterography (CTE) is the preferred imaging modality for assessing small bowel Crohn's Disease (CD). We report here preliminary findings comparing the validity of 2 low dose CTE techniques for evaluating inflammatory changes in patients suspected of having CD.

Methods: In total, 163 patients referred for diagnostic CTE to evaluate CD will undergo a standard exam and a low dose CTE exam in a random sequence on the same day. The standard exam was used to obtain FBP and adaptive statistical IR (ASIR) images and the low dose scans, Model based IR (MBIR) images. Demographics, historic data and fecal calprotectin were collected from each patient. The Harvey Bradshaw Index (HBI) was used to determine clinical disease activity. De-identified, randomly ordered images were reviewed by 2 experienced radiologists, independently for signs of small bowel CD and an overall assessment of "active" or "inactive" was made. All available clinical data including fecal calprotectin was reviewed by an experienced Gastroenterologist to determine the presence or absence of disease activity which served as the gold standard for comparison with the CT findings.

Results: As of Nov. 2014, a total of 124 patients had been enrolled and underwent CTE scanning. 46% of the subjects were male with a mean age of 43.6 (SD15.7 yrs). The mean HBI was 4.5, 48.4% were clinically assessed to have active disease by the gastroenterologist. The Generalized estimating equations (GEE) method was used to compare the validity of the reconstruction algorithms (Table 1).

These values all suggest non-inferiority, 95% confidence intervals cross the pre-specified non-inferiority margin of 0.1. Completion of enrolment is expected to produce narrower confidence intervals demonstrating no significant difference between the 3 techniques. Standard dose radiation exposure was 6.7 ± 3.8 mSv and low dose

"Comparison of the validity of CTE Reconstruction Techniques"

	Pooled estimate based on GEE			Difference (95% CI)		
	MBIR	FBP	ASIR	FBP vs. MBIR	ASIR vs. MBIR	FBP vs. ASIR
Sensitivity	0.67	0.72	0.72	0.04 (-0.03, 0.11)	0.05 (-0.02, 0.12)	-0.01 (-0.06, 0.05)
Specificity	0.59	0.60	0.64	0.01 (-0.04, 0.06)	0.04 (-0.02, 0.11)	-0.03 (-0.09, 0.02)
PPV	0.60	0.57	0.66	-0.03 (-0.11, 0.05)	0.06 (0.01, 0.11)	-0.09 (-0.16, -0.02)
NPV	0.68	0.75	0.72	0.07 (-0.02, 0.16)	0.04 (-0.03, 0.11)	0.03 (-0.05, 0.12)

exposure was 2.9 ± 2.4 mSv (p<0.001). More frequently, image noise was rated moderate or higher (28.4 - 84.7%) for MBIR compared to only 2.6 - 4.5% for ASIR and FBP.

Conclusions: Iterative reconstruction techniques for CTE have similar validity to traditional CTE techniques, at much lower radiation doses, for the identification of active small bowel inflammation in patients with Crohn's disease.

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Prevalence and causes of anaemia in patients with Inflammatory Bowel Diseases in Southern Italy

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Background: Anaemia (AN) is frequently associated with inflammatory bowel diseases (IBD) with a prevalence varying from 17% to 68%. In recent years, the management of AN in IBD has became a major issue as it negatively affects both the underlying disease and the quality of life of affected patients. Our aim was to evaluate the prevalence and causes of AN in patients with IBD living in a region of Southern Italy.

Methods: We prospectively performed a one-year multicentre study in Campania (Italy) including all consecutive IBD cases attending 5 Units. AN was defined in presence of haemoglobin values Hb <13 g/dl for males and Hb <12 g/dl for females; severe AN was defined in case of Hb <10 g/dl. To explore the causes of AN, all anaemic patients underwent a second-line haematological assessment including ferritin, transferrin, vitamin B12, folic acid and homocysteine levels and screening for celiac disease (total IgA and anti-transglutaminase antibodies). Furthermore, in all IBD cases CRP and ESR were evaluated. Iron deficiency AN (IDA) was diagnosed in case of ferritin <30 ng/ml and transferrin saturation (TSAT) <16%. AN of chronic disease (ACD) was diagnosed when elevated CRP/ESR values coexisted with TSAT < 16% and ferritin >100 ng/ml; mixed type AN was considered in case of TSAT <16% and 30 ng/ml < ferritin < 100 ng/ml.

Results: The study population included 965 IBD patients (582 CD; 383 UC) of whom 142 in- and 823 out-patients. AN was diagnosed in 134 out 965 IBD patients (14%). No significant difference was seen between CD and UC groups (81 CD vs 53 UC; 13.9% vs 13.8%; p=n.s.). The prevalence of AN was more frequent in the admitted IBD group (26% in- vs 11.7% out-patients; p<0.01; O.R. 2.2) and in patients with active disease (CD: 34% active vs 16% in remission; p<0.01; OR 2.1 - UC: 26% active vs 19% in remission; p=0.03; O.R. 1.3). Furthermore, AN appeared to be more frequent in patients with ileo-colic CD and in those with extensive UC (p<0.01). Regarding the causes of AN, IDA was present in 72 patients (53.7%), ACD in 12 patients (8.2%), 11 patients (8.2%) had mixed type AN, 9 had thalassemia (6.7%), 8 (5.9%) had macrocytic AN, while in 18 patients (13.4%) the causes remained unclassifiable. Vitamin B12 deficiency was observed in 7.4% of CD patients and in no case of UC. Folic acid deficiency was detected in 6.1 % of CD and in none of the patients with UC. There was no evidence of celiac disease.

Conclusions: AN is common among patients with IBD in Southern Italy and is more frequent in IBD patients with active and extensive disease and in whom needing hospitalization. Iron deficiency still remains the major cause of AN in IBD population.

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Temporal change in phenotypic behaviour in patients with Crohn's Disease

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Background: Studies from the West suggest that one-third patients have aggressive disease behaviour at presentation and half of all patients will progress to complicated disease behavior in 20 years

Methods: Data of patients with Crohn's disease were taken from Inflammatory Bowel Disease database. Their baseline details were recorded and Montreal class was entered. The patients' baseline phenotype was compared to the disease phenotype at 5, 10 and 15 years to look for the temporal change in disease behaviour

Results: One hundred and seventy-eight patients (Median age 35 years, 97 Men,81 women) were included for analysis.

(Surgery refers to bowel surgery; surgery for perianal disease is not included)

At 5 years 7% patients, at 10 year 13.1% and at 15 years 16.6% patients changed to aggressive disease behaviour (B2 or B3).

In the cohort of 105 patients with 5 years follow up, 17(16.1%) and 21(20%) patients underwent intestinal surgery at baseline and at 5 years respectively. Seven (6.6%) patients underwent more than one surgery.

In 10 year cohort of 38 patients, 8 (21%), 12 (31.5%) and 13 (34.2%) underwent surgery at diagnosis, at 5 years and at 10 years with 7(18.4%) patients undergoing more than one surgery.

"Table showing the temporal change in phenotype of Crohn's disease"

Disease Behaviour	B0 N(%)	B1 N (%)	B2 N (%)	B3 N (%)	Perianal disease N(%)	Surgery* N (%)
Baseline (N=178)		133(74.7)	38(21.3)	7(3.9)	21 (11.8)	19(10.7)
5 years (n=105)				(p= 0.14)	(p= 0.09)	(p= 0.51)
At presentation	0	77(73.3)	24(22.8)	4(3.8)	9 (8.6)	17 (16.1)
5 years	1(0.9)	69(65.7)	23(21.9)	12(11.4)	17 (16.2)	21 (20)
10 year (N=38)				(p= 0.58)	(p= 0.15)	(p= 0.40)
At presentation	0	24(63.1)	11(28.9)	3(7.8)	3 (7.8)	8 (21)
5 years	0	21(55.2)	11(28.9)	6(15.7)	8 (21)	12 (31.5)
10 years	0	19(50)	11(28.9)	8(21)	9 (23.6)	13 (34.2)
15 yrs(N=18)				(p=0.61)	(p=0.5)	(p= 0.58)
At presentation	0	12(66.6)	6(33.3)	0	0	6 (33.3)
5 years	0	11(61.1)	6(33.3)	1(5.5)	2 (11.1)	8 (44.4)
10 years	0	10(55.5)	6(33.3)	2(11.1)	2 (11.1)	9 (50)
15 years	1 (5.5)	8(44.4)	6 (33.3)	3(16.6)	1 (5.5)	10 (55.5)

In 15 year cohort of 18 patients; 6(33.3%), 8(44.4%), 9(50%), 10(55.5%) underwent surgery at diagnosis, at 5 years, at 10 years and at 15 years respectively.
Eighty six patients received Azathioprine and 21(11%) patients received TNF α inhibitors.
Conclusions: In Indian patients with Crohn's disease, one fourth of patients showed aggressive disease at diagnosis but tendency to change their behavior towards more aggressive disease over period of time (15 years) was less than that in western patients.

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The Assessment of Disease Activity by Quantitative Fecal Immunochemical Test in Ulcerative Colitis

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Background: Ulcerative colitis (UC) is a chronic inflammatory bowel disease. The assessment of inflammation performed by invasive colonoscopy. Fecal calprotectin seems to be alternative nowadays, and quantitative fecal immunochemical test (FIT) could potentially be used as a marker for mucosal inflammation. We evaluated the efficacy of quantitative FIT as biomarker for endoscopic inflammation in patients with UC.
Methods: Collected feces were examined quantative fecal blood with automated equipment. Endoscopic disease severity were assessed using the Mayo endoscopic subscore classification, and extent of disease were grouped by proctitis, left-side colitis and pancolitis. Clinical activity were classified by remission or active.
Results: A total of 82 FIT Results in conjunction with colonoscopies were evaluated in 63 UC patients. Colonoscopy findings revealed that endoscopic subscore was Mayo 0 in 21 (25.6%), Mayo 1 in 39 (47.6%), Mayo 2 in 15 (18.3%), and Mayo 3 in 7 (8.5%). Extent of disease was proctitis in 20 (24.4%), left-side colitis in 30 (36.6%) and pancolitis in 32 (39.0%). All of patients with a Mayo 0 endoscopic subscore had no hemoglobin (negative FIT, 0 ng/ml). Quantitative FIT was statistically significant positively correlated with endoscopic activity ($r = 0.626$, $P < 0.01$) and clinical remission ($r = 0.496$, $P < 0.01$). But quantitative FIT was not correlated with extent of disease ($r = - 0.047$, $P = 0.676$).
Conclusions: Qauntitative FIT can use as less invasive and economic biomarker for the presence of endoscopic inflammation in UC patients, although we do not know the extent of disease.

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Bone metabolic disease in Inflammatory Bowel Disease patients with past or current corticosteroid treatment

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Background: Bone metabolic disease (BMD) is a well-known complication of inflammatory bowel disease (IBD) The aim of this study is to analyse the prevalence of BMD in a large sample of Southern European patients with IBD with past or current corticosteroid treatment, and secondary studying the clinical, metabolic and pharmacological factors that are associated with osteoporosis in this population.
Methods: We have conducted an observational, retrospective and cross-sectional study of BMD based on the first bone densitometry (DXA) in patients with IBD and previous corticosteroid therapy from our institution. Clinical charts have been systematically reviewed and the data obtained have been included. The medium T-score on hip and spine was compared with the possible factors involved in the development of osteoporosis in IBD patients.
Results: From our IBD data base we selected patients with past or current corticosteroid treatment and bone densitometry, and finally 412 were included. The average age was 47.8 (SD 14.7), with 42.5% of males. 61.2% had Crohn's Disease (CD), 36.2% Ulcerative colitis (UC), and 2.7% had Indeterminate Colitis (IC). Concerning additional previous treatments, 47% received immunomodulators (IMM), 24.6% biological therapies, 20.4% Proton Pump Inhibitors (PPI). Prior surgery was performed in 30.6% of patients. Bone metabolic disease (i. e. Hip and/or spine T score < -1 SD) was present 66% of patients, while osteoporosis (i. e. Hip and/or spine T score < -2.5 SD) was present in 21.8%. Univariate analysis was performed, and factors correlated with BMD were identified: age ($p<0.000$), not previous treatment with IMM ($p=0.028$). Factors related with osteoporosis were: age ($p<.0000$), type of IBD (suggesting relationship between UC and osteoporosis, $p=0.017$).
Conclusions: BMD is a frequent complication in IBD patients with past or current corticosteroid treatment. Special attention must be paid in early evaluation of bone density in these patients.

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Fatigue Severity and Factors Associated with High Fatigue Levels in Tunisian Patients with Inflammatory Bowel Disease

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Background: The prevalence of fatigue in the outpatient IBD population is not well described. To date, only a few studies in Western countries have focused on fatigue related to IBD, and fatigue has never been specifically studied in African IBD patients. The aim of the present study was to investigate the fatigue level among Tunisian IBD patients, to compare their scores with healthy controls, and to identify demographic and clinical factors that influence fatigue.
Methods: Patients with previously diagnosed IBD, >18 years of age, and who were in remission were eligible for inclusion in this study. Patients were not included if they had cognitive impairment and were judged by the investigator to be unlikely to comply with the study procedures.Fatigue was assessed using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) in itss Arabic version. Corresponding healthy controls (HCs) also completed the fatigue questionnaire. Clinical and socio-demographic data was verified with chart review.FACIT-F scores range from 0 to 52, with lower scores indicating more fatigue and a score of less than 30 indicates severe fatigue. Tow patients were excluded because they did not complete the questionnaire.The study was performed according to the principles of Declaration of Helsinki, and informed consent was obtained from all participants.
Results: Sixty one patients with Crohn's disease and 37 patients with ulcerative colitis (UC) were eligible for analysis, with a mean age of 32.8 years, male/female 68/30. The comparison group consisted of 200 HCs.There were no significant differences between patients with

IBD and HCs with regard to sex, mean age and socio-economic conditions. When comparing UC patients and CD patients, there were no differences in FACIT-F and in all sub-dimensions between the IBDs. However, IBD patients had a mean FACIT-F score of 33.4, significantly lower than the HCs score of 42.1 (p<0.001). In all sub-dimensions of FACIT-F, both UC and CD patients showed significantly increased fatigue symptoms compared to HCs (all p<0.001). The prevalence of severe fatigue in IBD patients (FACIT-F<30) was 38.1% with females having more severe fatigue than males (p<0.001). Factors influencing the fatigue score included anemia and a high C-reactive protein.

Conclusions: Mean FACIT-F scores of Tunisian IBD patients are significantly lower than in HCs, indicating greater levels of fatigue in the IBD patients. Female patients have more fatigue. Anemia and CRP were determinants of fatigue in IBD patients. Physicians need to be aware of fatigue as one of the important symptoms of IBD to better understand the impact of fatigue on health-related quality of life.

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Retrospective Analysis of Enterocutaneous Fistula Management in IBD

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Background: One third of patients with Crohn's disease develop at least one fistula episode during the course of their disease. 6% of these fistulas are enterocutaneous fistulas (ECF).

The objectives of this study was to describe the characteristics, management and outcomes of disease-related ECFs in Crohn's disease in a well-defined cohort

Methods: Patients with a history of enterocutaneous fistulae were identified from a prospectively maintained database of 3,200 patients with IBD. Pathology, radiology and laboratory reports were analysed and data extracted retrospectively.

Results: 41 CD patients were identified who were treated for ECF (22% post-op; 78% spontaneous) over a 36 year period. Median duration of disease was 19 years. Two thirds involved the small bowel. 17% had distal obstruction. 27% (n=11: 9 spontaneous, 2 post-op) had evidence of infection: 55% associated abscess; 46% positive blood cultures; 91% positive wound swabs. Most had active luminal disease. 76% received nutritional support (62% TPN, 38% enteral). 29% (n=12) were treated with biologics with 50% (n=6) treated pre-operatively. 25% (n=3) achieved fistula control. The mean time from surgery to biologic in those treated post-operatively was 3.5 years. Overall, 14% of our cohort was managed medically while 86% proceeded to surgery. There were no cases of fistula recurrence in surgically treated patients. The overall fistula healing rate at 6 months was 73%.

Conclusions: In this cohort, the majority of ECFs occurred in patients with long-standing, small bowel CD. Biologic therapy has a role to play is selected cases, but he majority of patients required surgical resection with excellent outcomes when combined with appropriate nutritional support.

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Ionizing radiation exposure in patients with inflammatory bowel disease: Are we overexposing our patients?

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Background: Crohn's disease (CD) is a lifelong condition. Multiple imaging investigations are often performed during follow-up. This could cause overexposure to radiation. The aim of our study was to determine mean radiation dose in patients with at least a 5-year course of CD and to determine possible risk factors associated with exposure to high doses of radiation

Methods: We conducted a retrospective study including patients who's CD. Epidemiologic features of patients, characteristics of the disease, and types of imaging investigations that were performed during follow-up and cumulative radiation effective dose were determined. Risk factors associated with exposure to high doses of radiation were then, determined.

Results: One hundred sixty seven patients were included. There were 92 males (55.1%) and 75 females (44.9%) with mean age at diagnosis of 31.4 years (11 - 75 years). Global radiation dose was 18.81 mSv (0.02 - 120.02). Twenty seven patients (16.2%) were exposed to more than 35 mSv and 4 patients (2.4%) had an exposure of more than 75 mSv. Use of Infliximab, age at disease onset < 24 years old and number of flares > 8 were independent risk factors of radiation exposure more than 35 mSv with Odds ratios (OR) 2.543 ; 1.631 and 3.158 respectively. Similarly, use of Infliximab and number of flares > 8 were independent risk factors of radiation exposure more than 75 mSv with OR 4.256 and 7.012 respectively.

Conclusions: Radiation risk seems to be increased with severe course of CD. Both referring physicians and radiologists have the responsibility to minimize radiation exposure. Entero-magnetic resonance imaging (Entero-MRI) may reduce this risk.

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Identification of risk factors of colitis-associated carcinoma in Japanese patients with Ulcerative Colitis: Results from a retrospective multicenter study in a Kyoto-Shiga cohort

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Background: The number of patient with ulcerative colitis (UC) has increasing in Japan. Patients with UC are at particularly risk of developing colitis-associated cancer (CAC). Therefore, to validate risk factors for CAC is helpful to stratify the individual UC patient's risk. The aim of the present study is to evaluate the risk factors for development of dysplasia and CAC as well as to determine protective measure in a large cohort of UC patients (-CAPITAL (Cohort and Practice for IBD total management in Kyoto-Shiga Links) study-).

Methods: Data were obtained from the twelve hospitals in Kyoto-Shiga regions during 2003-2013. We performed a retrospective cohort study with a total of 2137 UC patients.

Results: Dysplasia and CAC (total 63 lesions) were detected in 44 patients (2.96%) out of 2137 patients. The mean age of these 44 patients was 53 years old. With regard to disease extension, 79.5% (35/44) of these patients had pancolitis and 18.2% had left-sided colitis. The mean duration of disease was 13.5 years (0-40 years), and 68.2% of those patients had disease duration of more than 10 years. The mean dose of corticosteroids (CS) was 8.34g, and three patients had been treated with a total of more than 10g of CS. 38.6 % (11/44) of these patients had experienced more than one year CS treatment. Primary sclerosing cholangitis was found in two patients (4.5%). 44 (69.8%) of all 63 CAC was located at distal colon. 37 (58.7%) of 63 CAC was detected as superficial type.

Conclusions: Our data demonstrated that disease duration of more than 10 years, long-term and high dose of CS use and pancolitis are predictive factors of CAC. Most of CAC were located at distal colon and detected as superficial type. Further investigations will be required for establishment of CAC surveillance in Japanese UC patients.

P200
Definitions of the endoscopic lesions in Crohn's disease: reproductibility study and GETAID expert consensus.

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Background: Emergence of new therapeutic goals in Crohn's disease (CD), such as mucosal healing, has highlighted the need for endoscopic scores. Although other scores are available, the Crohn's Disease Endoscopic Index of Severity (CDEIS) [1] remains, to date, the most validated score to assess the severity of endoscopic lesions in CD. Clarifying the definition of the endoscopic lesions composing this score appeared as a keypoint to optimize the CDEIS use.

Methods: This expert consensus was performed according to the Delphi process to define aphtoid erosions (AE), superficial ulcerations (SU), deep ulcerations (DU), stenosis and fistulas.

These definitions were then submitted to 30 independent IBD physicians from the GETAID, to calculate an acceptance rate (AR).

We conducted a reproductibility study assessing the intra and inter-observers agreements to recognize AE, SU or DU during endoscopy using these validated definitions. It was performed from 100 short films (selected by AB) focusing on AE, SU, DU or a sham lesion (25/100 for each lesion).

Overall 15 GETAID members performed this study independently and individually. Among them, 9 did not participate to the definitions step. The intra-observer agreement study was performed one month later with the same 100 films in a randomized order.

Results: AE in endoscopy is defined as an ulceration with a white center whose the diameter is less than 5millimetres with red halo (AR=29/30). DU in endoscopy is defined as: a frank depression compared to the surrounding mucosa OR striated bottom of the ulceration OR mucosal detachments OR well-like ulcerations (AR=24/29). A superficial ulceration is defined in endoscopy as: an ulceration whose features fit neither with that of AE nor with that of DU, as previously defined (AR=24/29). A digestive stenosis is defined in endoscopy as a narrowing of the intestinal lumen making impossible or difficult to pass with an adult colonoscope (AR=25/29). A fistula is defined in endoscopy as a deep and well-limited hole whose the bottom cannot be seen, with leaking faecal or purulent material OR with a suspected communication with another organ (AR=27/29). The Results of the reproductibility study will be available at the time of the congress.

Conclusions: The definitions of CD endoscopic lesions retrieved from this GETAID expert panel, if their reproductibility was confirmed, should improve the standardisation and the use of the CDEIS.

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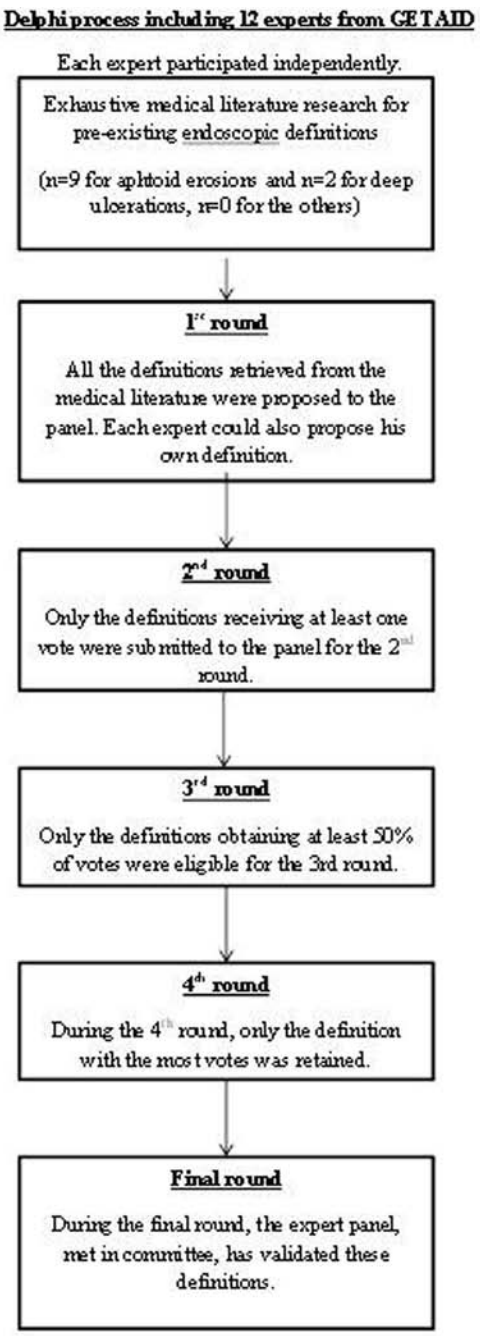

"Delphi process including 12 experts from GETAID"

P201
Reproducibility of magnetic resonance enterography assessment of disease activity in Crohn's Disease using central readers

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Background: Reproducibility is a critical property of magnetic resonance enterography (MRE) Crohn's disease activity indices if they are to be used as outcome measures in clinical trials. We evaluated the reproducibility of two MRE disease activity instruments, the MaRIA and London indices, when centrally read by expert gastrointestinal body imaging radiologist readers in a multi-center trial setting.

Methods: Four central reader radiologists at centers in Europe and North America reviewed 50 MRE sequences of patients with a spectrum of Crohn's disease activity and location. Readers assessed the MaRIA and London indices, pre-specified individual MRE findings, and a global rating of severity based on a visual analogue scale (VAS). Intraclass correlation coefficients (ICCs) for intra- and inter-rater agreement were calculated for each assessment.

Results: Intra-rater ICCs (95% confidence intervals) for the MaRIA, London, London Extended indices and the VAS were 0.89 (0.84 to 0.91), 0.84 (0.76 to 0.88), 0.81 (0.71 to 0.85) and 0.86 (0.81 to 0.90). Corresponding inter-rater ICCs were 0.71 (0.61 to 0.77), 0.50 (0.32 to 0.62), 0.56 (0.40 to 0.64), and 0.71 (0.62 to 0.77) (Table 1).

The correlation between each reader's VAS and the MaRIA, London, and London Extended indices were 0.79 (0.71 to 0.85), 0.68 (0.58 to 0.77) and 0.67 (0.58 to 0.76), respectively.

Conclusions: These Results indicate that there was "almost perfect" intra-rater reproducibility of centrally read MaRIA and London indices. Inter-rater agreement was "substantial" for the MaRIA and "moderate" for the London indices. The MaRIA index appears to

"Table 1. Reproducibility of magnetic resonance enterography indices for Crohn's disease"

Instrument	Variance Components				ICC (95% CI)	
	Image	Central Reader	Interaction	Residual	Inter-rater	Intra-Rater
MaRIA	8.526	0.329	1.813	1.358	0.71 (0.61 to 0.77)	0.89 (0.84 to 0.91)
London	0.200	0.019	0.117	0.066	0.50 (0.32 to 0.62)	0.84 (0.76 to 0.88)
London Extended	1.018	0.040	0.411	0.353	0.56 (0.40 to 0.64)	0.81 (0.71 to 0.85)
VAS Global Rating	426.8	30.9	60.7	83.7	0.71 (0.62 to 0.77)	0.86 (0.81 to 0.90)

have the best operating characteristics and is thus the currently preferred instrument for use in clinical trials.

P202
Outcomes of a large cohort of children with IBDU compared to other IBD subtypes and treatment options- a longitudinal report from the Porto pediatric IBD group of ESPGHAN

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Background: Inflammatory bowel disease unclassified (IBDU) is the rarest subtype of IBD and as such treatment options for patients are based mainly on extrapolation from ulcerative colitis (UC) and Crohn's disease (CD) studies. We aimed to look at treatment choices for IBDU compared to other patients with colonic IBD and to compare patient outcomes at 3 years.

Methods: This was a multicentre retrospective longitudinal study including 23 centres affiliated with the Porto IBD-working group of ESPGHAN. Data on 797 children with colonic IBD were collected on a standard proforma at diagnosis and follow up with strict diagnostic (Porto) criteria [mean age 10.5 ± 3.9, 46% females]: 250 with CD, 287 with UC and 260 with IBDU. Disease severity was assessed by Physician Global Assessment (PGA).

Results: IBDU treatment significantly differed from that of UC for lower use of corticosteroids (CS) [154 (59%) vs. 204 (71%), p=0.004] but higher use of exclusive enteral nutrition (EEN) [26 (10%) vs. 2 (0.6%), p<0.0001]. Compared to CD, IBDU patients received less EEN and immunomodulators [26 (10%) vs. 93 (37%), p<0.0001 and 67 (26%) vs. 129 (52%) p<0.0001, respectively] but more aminosalicylates [228 (88%) vs. 159 (64%), p<0.0001]. At 3-year follow-up, 135 (69%) IBDU patients had a remission or a mild disease compared to 100 with CD (46%, p<0.0001), and 174 with UC (64%, p=0.3). CD patients were more commonly treated with biologics than those with IBDU and UC [82 (34%) vs. 24 (12%) IBDU and 47 (17%) UC; p<0.0001, vs IBDU and UC]. Four patients with IBDU (1%) underwent surgery during follow up, vs. 22 (5%) with UC (p=0.009) and 20 (5%) with CD (p=0.008 vs. IBDU), while no significant differences for time for surgery were reported among the three groups. A significantly higher proportion of IBDU patients treated with CS at the diagnosis required biologics and cyclosporine at follow-up, compared to those treated with other therapies (p=0.04 and p=0.05, respectively).

Conclusions: Children with IBDU receive less 5ASA/steroids than UC but more than CD yet receive less EEN and immunomodulators than CD but more than UC. The need for biologics and surgery at follow up is lower in IBDU than CD. CS use at the diagnosis in IBDU patients is related to worse clinical outcomes. Despite these differences a mild disease course in IBDU patients at follow-up is common.

P203
Contrast-enhanced ultrasonography in the evaluation of Crohn's disease activity: correlation with ileocolonoscopy

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Background: The role of contrast-enhanced ultrasonography (CEUS) for assessing CD activity remains unclear. Our aim was to determine the performance of conventional US and CEUS to detect CD activity assessed by ileocolonoscopy taken as the reference.

Methods: Twenty patients with small bowel CD were prospectively studied. Clinical disease activity was assessed by the Harvey-Bradshaw Index (HBI). All patients underwent ileocolonoscopy and also a conventional US followed by a CEUS using a microbubble contrast agent (SonoVue®). US examinations was performed using a Hitachi HI VISION Avius®, employing a multi frequency convex abdominal transducer. Disease small bowel activity was assessed by ileocolonoscopy (reference) and patients were graded, for the purpose of statistical analysis, as inactive (normal or mild disease) or active (moderate or severe inflammation). Qualitative and quantitative parameters from the sonographic analysis included maximum wall thickness, vascularity by Doppler US, contrast intraparietal and transparietal enhancements, including the time to the peak enhancement, quantitative contrast enhancement at baseline and at maximum enhancement. Statistics were performed with SPSS v.20.0.

Results: Disease severity was as follow: no disease in 5 patients (40%), mild in 2 patients (10%), moderate in 1 patient (5%) and severe in 12 patients (60%). Five patients (25%) had been submitted to bowel resection. Among the 18 patients in clinical remission (HBI ≥ 4 points), 10 patients (56%) had evident signs of inflammatory activity on ileocolonoscopy and 14 patients (78%) in US (bowel wall thickness>4mm). Classic ultrasound parameters (wall thickness>4mm and colour Doppler flow moderate and marked) correlated with disease activity (p=0,01 and p= 0,04). For CEUS, the value of maximum enhancement was related with disease severity (7,25 vs 12,67, p=0,024 and an area under the ROC curve 0,77). There was no correlation with baseline enhancement and time to peak enhancement (p=0,09 and p=0,43).

Conclusions: Wall bowel thickness, Doppler US and CEUS are valuable parameters for an accurate detection of small bowel inflammatory activity in CD. Contrast-enhanced US could be a useful technique to monitor disease activity in the era where mucosal healing is the treatment goal in CD.

P204
Small bowel mucosal healing and deep remission in patients with known small bowel Crohn's disease.

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Background: Mucosal healing (MH) and deep remission (DR) are associated with improved long- and short-term outcomes in Crohn's disease. The vast majority of the available data pertains to colonic MH ***and DR, while the evidence regarding the prevalence and impact of small bowel mucosal healing (SBMH) is scarce.

The aims of the study were to evaluate the prevalence of active inflammation, SBMH and DR in small bowel Crohn's disease (SBCD) patients in clinical remission (CR) or clinically mild disease using biomarkers, video capsule endoscopy (VCE) and magnetic resonance enterography (MRE).

Methods: Patients with known SBCD in CR or with mild symptoms (CDAI<220) for at least 3 months were prospectively recruited and underwent MRE, followed by Agile patency capsule. If patency was ***proven, VCE was performed. The Lewis score (LS) was calculated for each tertile. C-reactive protein (CRP) and fecal calprotectin (FC) were evaluated for their association with clinical activity, MRE and VCE findings. Clinical remission was defined as CDAI < 150. FC >100 µg/g and CRP >5mg/ml were considered abnormal. SBMH was defined as LS< 135; significant SB inflammation was defined as LS >790. Biomarker remission (BR) was defined as a combination of CR (CDAI<150) and normal biomarkers. Deep remission (DR) was defined as a combination of BR and SBMH.

Results: Seventy nine patients were recruited and underwent MRE; 51 with proven patency underwent VCE studies. FC levels were elevated in 47.5% of patients, CRP levels in 29.4% and either biomarker- in 56.5% of the cases. SBMH was observed in 26% of the patients, and MRE did not demonstrate active disease in 23.7% of the patients. In patients with clinica and biomarker remission , SBMH was observed in 47.4% and MRE was normal in 56% of the patients. Deep remission was observed in 22.5% of the patients. The prevalence of deep remission was 50% in patients treated with anti-TNFs, whereas it was 20% in patients treated with thiopurines, 11% in patients not receiving any treatment and 0% in patients treated with 5-aminosalycilates (p=0.045 for treated vs not treated with anti-TNFs). There was a significant correlation between normal FC levels and SBMH (r=0.48, p=0.001). CRP did not significantly correlate with SBMH (r=0.54 p=0.1). The combination of both biomarkers did not improve the diagnostic accuracy.

Conclusions: SB inflammation is detected in the majority of CD patients in CR and BR. DR was achieved in 22.5% of the patients in clinical remission and was more frequent in patients ***treated with anti-TNFs. FC was significantly more accurate in prediction of MH than CRP. Our findings emphasize the true inflammatory burden in quiescent patients with SBCD.

UK and DY- equal contribution ; RE and SBH- equal contibution

P205
Ionizing radiation throughout the duration of immunosuppression therapy in Crohn's disease: should it remain a concern?

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Background: Crohn's disease (CD) patients undergo many radiological studies employing ionizing radiation for diagnosis and management purposes. Our aim was to assess the total radiation exposure of our patients over the years, to estimate risk factors for exposure to high doses and to correlate radiation exposure to immunosuppression.

Methods: The cumulative effective dose of radiation (CEDR) was calculated multiplying the number of imaging studies by the effective dose of each exam. Radiation dose data was collected prospectively.

Results: Four hundred and fifty-one patients with CD (226 female) were followed during 11.0 years (IQR: 6.0-16.0), with 52.1% of the patients being B3-classified patients and 38.6% being steroid dependent. Thirty nine percent of the patients were under combo therapy and 41% had previous abdominal surgery. Sixteen percent were exposed to high radiation dose levels (CEDR>50 mSv) and 4% to CEDR>100 mSv. The mean CEDR between 26-35 years old was 12.539 mSv and a significant dose of radiation (over 50 mSv) was achieved at a median age of 40 (IQR: 29.0-47.0). Abdominal-pelvic computed tomography (CT) scan was the examination that contributed the most for CEDR.

High CEDR (β value; 95% CI) were found for penetrating disease phenotype (22.785, 17.139;28.431), steroid resistance or dependence (8.860, 3.050;14.670), abdominal surgery (18.673, 13.217;24.129), azathioprine (14.739, 6.875; 22.603) and anti-TNF therapy (17.141, 11.564; 22.716). Patients with penetrating phenotype (B3), previous surgery, azathioprine and anti-TNF α therapy were exposed earlier on the course of the disease to CEDR above 50 mSv (p<0.001). The value of CEDR in the patients under immunosuppression mainly increased in the first year of immunosuppression.

Conclusions: Penetrating phenotype, abdominal surgery, steroid resistance or steroid dependence and treatment with anti-TNF α and azathioprine were predictive factors for high CEDR. It was also demonstrated that immunosuppression and anti-TNF α treatment were followed by a sustained increment of radiation exposure.

P206
Prevalence and risk factors for thromboembolic complications in IBD patients

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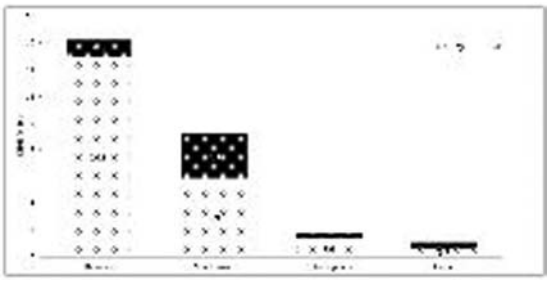

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Background: Inflammatory bowel disease (IBD) patients have an increased risk of venous thromboembolic complications (VTEC) such as deep vein thrombosis (DVT) and pulmonary embolism when compared to the non-IBD population. However, studies assessing VTEC prevalence in IBD as well as analyses of VTEC associated risk factors are scarce. We aimed to assess VTEC prevalence in IBD patients and to identify associated risk factors.

Methods: Data from patients enrolled in the Swiss IBD Cohort Study (SIBDCS) were analyzed. Since 2006 the SIBDCS collects data on a large sample of IBD patients from hospitals and private practices across Switzerland.

Results: A total of 90/2284 (3.94%) IBD patients suffered from VTEC. Of these, 45/1324 (3.4% overall; 2.42% with DVT, 1.51% with PE) had CD, and 45/960 (4.7% overall; 3.23% with DVT, 2.40% with PE) presented with UC.

In CD patients, median disease duration was 12 years in the VTEC group compared to 8 years in the CD group without VTEC (p=0.001). IBD-related intestinal surgery was more often performed in CD patients with VTEC compared to patients without VTEC (53.3% vs. 35.8%, p=0.016). No differences among the two groups were observed for perianal surgery (26.7% vs. 19.2%, p=0.216) or for disease location (p=0.596). UC-related intestinal surgery was more frequently encountered in the VTEC group compared to the one without VTEC (22.2% vs. 5.0%, p<0.001). Perianal surgery was not identified as risk factor for VTEC in CD patients (VTEC prevalence 4.4% in CD patients having undergone perianal surgery vs. 2.0% VTEC prevalence in CD patients not having undergone perianal surgery, p=0.240). UC patients with VTEC were found to suffer more frequently from pancolitis when compared to UC patients without VTEC (53.3% vs 40.3%, p=0.003). IBD treatment, including immunomodulators and anti-TNF agents, was used in similar frequencies in CD and UC patients with and without VTEC. Ciclosporin use was more prevalent in UC patients group with VTEC (15.6% vs. 6.0%, p=0.021). Logistic regression modeling found no significant association of VTEC with the following factors: age, gender, use of oral contraception, body mass index, smoking status, age at time of IBD diagnosis, and IBD family history.

Conclusions: IBD is associated with an important number of VTEC. VTEC were more prevalent in UC patients compared to CD patients. Intestinal surgery is a risk factor for VTEC in both UC and CD patients. Disease duration was identified as risk factor for VTEC in CD patients whereas pancolitis was significantly associated with VTEC in UC patients.

P207
Serological Antibodies for the Prediction of Post-operative Recurrent Crohn's Disease. Results from the POCER study

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Background: Disease recurrence after Crohn's disease resection occurs in up to up to 80% of patients, with two thirds ultimately requiring further surgery. Although clinical risk factors help in assessing the risk of relapse, a test that identifies patients at higher risk of recurrence would be clinically valuable. We investigated the value of serological antimicrobial antibodies to predict disease recurrence after surgery in a large prospective cohort of patients.

Methods: 171 patients had 525 samples tested peri-operatively, and 6, 12 and 18 months post-operatively as part of a structured study ("POCER") designed to diminish post-operative recurrence. Two-thirds of patients underwent colonoscopy at 6 months and all underwent colonoscopy at 18 months post-operatively. Serologic markers (ANCA, pANCA, ASCA IgA/IgG, anti-OmpC, anti-CBir1, anti-A4-Fla2, anti-Fla-X) were tested at each time point. Univariate analysis was performed for each (positive/negative) at all time points for endoscopic recurrence (Rutgeert's score ≥i2). Antibody titre was investigated using quartile sum score (QSS) method (range 7-28) and logistic regression analysis.

Results: Patients with recurrence at 18 months were more likely to be positive for anti-Fla-X than those without recurrence, when measured at baseline (64% v 45%; P=0.049), 6 months (65% v 43%, P=0.021) and 18 months (53% v 33%, P=0.038) post operatively. Patients negative for anti-Fla-X at 6 months had a lower risk of recurrence at 18 months (OR 0.38, 95%CI 0.17-0.84, P=0.018), when adjusted for age, gender, disease behaviour and smoking. A negative ANCA titre at 6 months was associated with recurrence at 6 months (ANCA -ve v +ve: recurrence 87% v 13%, P=0.002). Adjusted for baseline characteristics (age, gender disease location, smoking, pANCA) the total antibody titre for all antibodies combined was not predictive of endoscopic recurrence at 6 or 18 months.

Conclusions: The presence of the serological antibody anti-Fla-X identifies patients at higher risk of developing early disease recurrence, while the presence of positive ANCA predicts patients at lower risk of post-operative recurrence. Fla-X is an immunogenic bacterial antigen, arising from subunits of bacterial flagella (flagellin) from Clostridium subphylum cluster XIVa. Serologic screening of patients prior to surgery may assist in selecting patients at elevated risk of post-operative recurrence. The role of Fla-X in relation to microbiota that may be linked to recurrence requires evaluation.

P208
Patient-reported outcomes in biologic and thiopurine treatment of IBD measured as HRQoL and symptoms

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Background: Biological and thiopurine drugs are these days considered to be first line long-term treatment for severe or 5-ASA non-responding cases of IBD. Treatment strategies can be either single or combination therapy. The monitoring of these treatments tend to vary depending on which treatment strategy is chosen. Patients with biological treatment as either mono- or combination therapy tend to be more frequently monitored, but the frequency and extent of monitoring varies between different IBD clinics. At Danderyd Hospital,

all IBD patients also have regular yearly follow-ups with an IBD nurse, regardless of disease activity.

The aim of this study was to compare treatment outcomes in terms of patient-reported symptoms (stool frequency, consistency, urgency, blood and abdominal pain) and health-related quality of life (HRQoL) measured with the Short Health Scale (SHS) between patients treated with either thiopurines (azathioprin or mercaptopurin), biologics (infliximab) or a combination of both.

Methods: Data was collected from patients with ongoing stable (>3 months) treatment during 2013 using patient files and SWIBREG, a Swedish national quality registry. The study was cross-sectional, and the data was collected by IBD nurses during routine follow-ups.

A total of 79 patients were included, 35 % female, and 60 % had Crohn's disease (CD) vs 40 % with ulcerative colitis (UC). The mean age was 43 years old. The treatment groups were divided in infliximab only (n=20), thiopurines only (n=33) and combination therapy infliximab + thiopurines (n=26).

Results: There were no significant differences in HRQoL or patient reported symptoms between the different treatment groups. When comparing diagnosis groups, the patients with CD reported overall more symptoms, especially more loose stools. Comparison between genders showed that women, regardless of diagnosis and treatment had significantly lower function scores related to their disease and more overall symptoms (SHS), specifically more bowel moments, more urgency and bloody stools, as well as more fecal incontinence.

Conclusions: This study indicates that regardless of treatment, patients with CD and female patients had more symptoms and that the female IBD patients also had lower function scores related to their disease, even during periods of supposed remission. These Results shows the importance of individualized treatment in IBD care, and that regular routine follow-ups with an IBD nurse with registration of self-reported symptoms and quality of life help to identify patient groups with a need for optimized treatment, both to detect early warning signs of flares or increased disease activity, as well as identifying patients with persisting functional symptoms despite aggressive treatment.

P209
Impact of perineal fistulization on behavior characteristics of intestinal crohn's disease

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Background: Fistulization, either intra abdominal or perianal is one of the most prominent characteristics of Crohn's Disease (CD); relationships between these two sites of penetrating disease need to be evaluated.

Methods: To assess the influence of fistulizing perianal CD phenotypical characteristics and long term outcome of abdominal disease we have studied a cohort of 169 consecutive cases of CD enrolled at diagnosis from 01/01/2005 to 31/12/2008 and prospectively followed-up until 31/12/2013 (mean duration of follow-up 6,9 years). All patients underwent initial complete investigation. A systematic clinical control with endoscopy or radiology when needed was performed every 6 or 12 months, and on demand. Statistical study : Students Fisher's t test and Mann Whitney's U test

Results: 59 patients presented with perianal fistulizing disease (GI=34,9%), 18 at diagnosis and 41 during the follow-up and 110 had no anal disease (GII : 65,2%). Comparison of those 2 groups of patients didn't show any Statistical Significant Difference (SS as regards to : 1/mean age at diagnosis (GI : 31,3y Vs GII: 30,9y) ;2/gender : (SR : F/M : GI : 1,1 Vs GII: 1,1); 3/ Duration of disease before diagnosis (GI : 11,6 months Vs GII: 13,4 months); 4/ Occurrence of familial disease (GI : 8,4%Vs GII: 8,2); 5/Smoking habits (GI : 33,9%Vs GII: 33,6%) ; 6/ extra intestinal disease (GI : 17%Vs GII: 17,3%). In GI patients : 1/ colonic location of lesions was more frequent (GI : 33,3%Vs GII: 19,2 : p = 0,0698) ; 2/ Intestinal fistulazing disease was more frequent as well at diagnosis (GI : n=5/18 27,8%Vs GII: n=28/151 : 18,6% ;p 0,5382) as at the end of follow up (GI : n=20/59 : 33,9% Vs GII: n=20/110: 18,2% ; p = 0.0358) ; 3/intestinal flares were more frequent (GI : 0,8 Vs GII : 0,7); 4/ Some intestinal complications were more frequent : abcess (GI : 20,2%Vs GII: 4,5%) ; p = 0,0029) , fistulas (enteroenteral (GI : 11,7%Vs GII: 5,4% ; p = 0,2425) ; enterovesical (GI : 3,4%Vs GII: 0,9%; p = 0,5737) , enterocutaneous : (GI : 6,8%Vs GII: 3,6% ;p = 0,5790) 5/Need for intestinal resection (GI : 38,9%Vs GII: 32,7%; p = 0,5242); and number of a second surgical procedure (GI : 20,3%Vs GII: 12,7%; p = 0,2790); and a third one (GI : 8,5%Vs GII: 2,7%;p = 0,1889).

Conclusions: The Results of that prospective study support the view that perianal fistulization in CD is strongly associated with severe penetrating and complicated intestinal disease.

P210
Calprotectin predicts relapse of IBD even in the presence of a 'normal' colonoscopy

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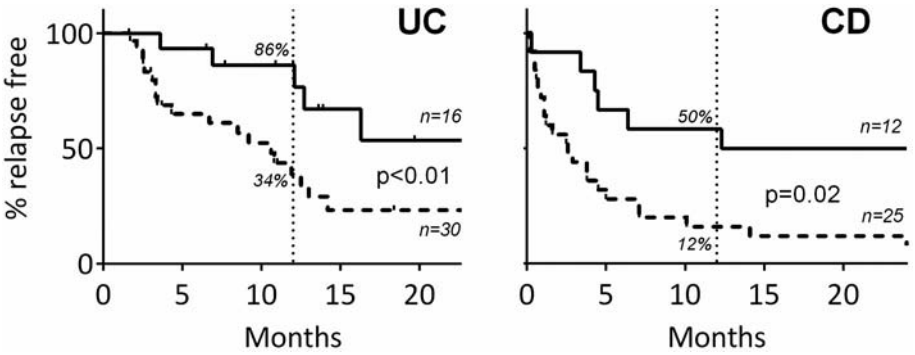
Background: Faecal calprotectin is a sensitive and reliable marker of mucosal inflammation and mucosal healing in IBD. It has always been compared against endoscopic appearance as the presumed gold standard for assessment of disease activity. Several strands of evidence - using magnifying or image-enhanced endoscopy as well as confocal laser endomicroscopy - highlight abnormalities in colonic mucosa reported as 'normal' by standard white light colonoscopy (WLC). This may be compounded by the difficulties in bowel preparation in IBD and the non-widespread use of high definition technology (although the latter has not been specifically studied in relation to IBD). We wished to determine whether an elevated FCALP could predict relapse even in the presence of an ostensibly normal WLC.

Methods: As part of a larger prospective study correlating FCALP to histologic assessment of disease activity, data was collected for consecutive patients with IBD on stable therapy undergoing colonoscopy for disease assessment. FCALP (Bühlmann ELISA) was collected as close as possible (prior) to the colonoscopy. When the colonoscopic appearances were reported as normal (Mayo endoscopic subscore 0 for ulcerative colitis, UC, and SES-CD=0 for Crohn's disease, CD), patients were followed to determine if they relapsed, with time to relapse (or last recorded follow-up) taken from the date of colonoscopy. For the purposes of this study, relapse was defined generally as "continuous or worsening intestinal symptoms requiring an escalation in therapy". Switching between 5ASA classes was not included in this definition unless the specifically stated to be in response to uncontrolled symptoms.



"Relapse from date of 'normal' colonoscopy in patients when FCALP was either normal (solid line) or elevated (hashed line). Dotted vertical line = 12 months. % labels indicate survival proportions."

Results: 46 patients with UC and 37 with CD were identified with the above criteria. Median time between FCALP measurement and colonoscopy was 0.70 (max 2.89) and 0.90 (max 1.5) months respectively. Normal FCALP was detected in 16 patients with UC and 12 with CD.

The figure shows relapse-free survival in those patients with normal FCALP (<60mcg/g faeces) compared to those with elevated levels. Median calprotectin in the 'high' group was 377 (229-794) in UC and 192 (118-247) in CD. At 12 months, survival proportions were 86% with UC and normal FCALP compared to 34% in those with high FCALP. In CD, these proportions were 50% and 12% respectively.

Conclusions: Elevated levels of FCALP predict relapse even in the presence of a macroscopically normal colonoscopy.

P211
Gender-related differences in work productivity impairment and quality of life in Inflammatory Bowel Disease (IBD): A cross-sectional survey from Southern Italy

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Background: IBD are chronic conditions affecting young people with a negative impact on their major life activities, such as school, work, self-care, and quality of life. Published literature has reported higher rate of unemployment, sick leave and working disability. Data on gender influence are scanty, especially in mediterranean countries. Aim of our study was to compare working impairment and quality of life between female and male patients with IBD followed-up in a referral center from southern Italy.

Methods: 102 patients with IBD (53 females, 49 males) consecutively observed in the IBD clinic were recruited. Data on clinical and demographic characteristics (age, type of IBD, disease behavior (Montreal) and activity (HBI, Mayo score), smoking habits, familial predisposition, current treatment, educational and marital status, current employment) were registered on a dedicated database. All patients agreed to fill in the WPAI (Work Productivity and Activity Impairment) questionnaire and the EQol-5D (European Quality of Life - 5 Dimension) VAS scale. Data of the National Institute of Statistics (ISTAT) on employment rates in Italy were used for comparison.

Results: There were no significant differences between males and females regarding age, educational and marital status and disease characteristics except disease activity rate, which was higher in males. There was a significant difference in the employment status since 58.5 % of women were unemployed versus 34.7% of men (p=0,02). Overall, there were no differences in WPAI scores (absenteeism, presenteism, overall work and regular activities impairment) and EQoL between males and females. In male patients with active disease absenteeism (p=0,04), presenteism (p=0,02) and work productivity impairment (p=0,04) rates were significantly higher as compared to patients in remission, quality of life was not affected, in females with active disease we observed a higher rate of absenteism (p=0,04) and daily regular activities impairment (p=0,04) as well as quality of life (p=0,015).

Conclusions: Gender significantly influences occupational status in IBD, since women are more often unemployed. Work productivity is impaired in both men and women with active disease, but women are more prone to the negative impact of the disease on daily regular activities and quality of life than men. These preliminary Results should be kept in mind in clinical management of IBD female patients.

P212
Serum biomarkers predict disease severity in Ulcerative Colitis

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Background: Clinicians rely on the clinical symptoms and measurements of acute phase proteins like CRP as surrogate markers of inflammation for assessment of the level of disease activity in ulcerative colitis (UC). This is, however, challenging as CRP is often only increased in patients with severe flares of UC, and novel biomarkers are thus needed for the identification of mild and moderate UC. With the use of a commercially available ELISA platform we aimed at identifying a limited panel of potential biomarkers for grading disease severity in UC.

Methods: 40 healthy controls along with 65 patients with varying disease activity of UC (Mayo-score 0-12) were enrolled. Using multiplex ELISA the concentration of 78 proteins was measured in the serum. Multivariate statistics using the SIMCA-P+ software were performed to select a limited number of proteins as potential biomarkers for assessment of the disease severity.

Results: For differentiating between patients with mild and moderate disease (i.e. Mayo score of 3-5 or 6-10, respectively), we identified alpha-1 antitrypsin (AAT) (AUC=0.79) with a sensitivity and specificity of 0.90 and 0.70, respectively, thereby outperforming the predictability of CRP (AUC=0.52). The combination of granulocyte colony stimulating factor (G-CSF) and AAT produced predictive models for differentiating mild and moderate disease (AUC=0.72) as well as moderate and severe disease (AUC=0.96) with the latter showing the same predictability as CRP.
Conclusions: Based on the measurements of AAT and G-CSF we were able to differentiate between patient having mild, moderate and severe disease activity. Identification of these potential serum biomarkers measured by a commercially available platform enables clinicians to optimize and individualize the treatment at an early stage while awaiting endoscopic examinations.

P213
A systematic review and meta-analysis of non-invasive biomarkers for assessing disease activity in Inflammatory Bowel Disease

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Background: Endoscopic disease activity in inflammatory bowel disease (IBD) is associated with poor outcomes. Endoscopic evaluation is the gold standard for the assessment of disease activity, but is invasive, expensive and potentially time consuming. Identification of non-invasive biomarkers of disease activity in IBD is a research priority.
Methods: The primary objective was to evaluate the diagnostic accuracy of 3 non-invasive biomarkers (fecal calprotectin [FC], stool lactoferrin [SL] and C-reactive protein [CRP]) used for the evaluation of disease activity in IBD. MEDLINE, EMBASE, the Cochrane Library, the ISI Web of Knowledge and conference abstracts were searched from inception to November 2014 for relevant studies. Grey literature databases (e.g. SIGLE) were also searched to identify studies not indexed in traditional databases. All cohort and case-control studies that evaluated the diagnostic accuracy of FC, SL or CRP for assessment of disease activity in symptomatic patients with previously diagnosed IBD (ulcerative colitis and Crohn's disease) were included. True positive, true negative, false positive and false negative rates were extracted for each biomarker and used to construct 2X2 tables for each cutoff. Sensitivity, specificity and area under the curve (AUC) estimates for FC, SL and CRP were calculated for each study based on different cut-offs and pooled together into single estimates for each test. Receiver operator characteristics (ROC) curves were then used to identify the cut-off values for each biomarker that best predicted endoscopic disease activity.
Results: Nineteen studies (2456 participants) met our inclusion criteria. Sensitivity, specificity, and AUC values for the 3 biomarkers are summarized in Table 1.

The best cut-off values to detect endoscopically active disease in IBD determined by ROC analysis were 50 µg/g, 7.25 µg/mL and 10 mg/dL for FC, SL and CRP, respectively.
Conclusions: FC and SL are highly accurate biomarkers that can be used to screen symptomatic IBD patients for endoscopic disease activity prior to colonoscopy.

"Table 1. Diagnostic accuracy of fecal calprotectin, stool lactoferrin, and C-reactive protein"

	Sensitivity	Specificity	AUC
Fecal calprotectin			
All IBD	0.88 (0.84, 0.90)	0.73 (0.66, 0.79)	0.89 (0.86, 0.91)
UC	0.88 (0.84, 0.90)	0.79 (0.68, 0.87)	0.91 (0.89, 0.94)
CD	0.87 (0.82, 0.91)	0.67 (0.58, 0.75)	0.85 (0.82, 0.88)
Stool lactoferrin	0.82 (0.73, 0.88)	0.79 (0.62, 0.89)	0.87 (0.84, 0.90)
CRP	0.49 (0.34, 0.64)	0.92 (0.72, 0.96)	0.72 (0.68, 0.76)

P214
Ulcerative Proctitis: Predictors and outcomes of disease extension in UC

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Background: Ulcerative proctitis is a variant of ulcerative colitis anatomically limited to the rectum.Extension of disease beyond the rectum in this subset of patients is associated with a poor prognosis and higher rates of chronic disease activity. We analysed outcomes of patients diagnosed with ulcerative proctitis who demonstrate extension of their disease, seeking to identify associated risk factors for extension and prognosis in these patients.
Methods: A retrospective study of a prospectively maintained electronic database of 3,200 patients with IBD attending a single centre. Those with disease extension were compared to patients with stable limited proctitis. A retrospective review of all clinical, endoscopic and histological records was performed to determine disease course and define any identifiable predictors of proximal disease extension.
Results: 481 patients with an initial diagnosis of ulcerative proctitis were identified. Records of 110 patients with stable limited proctitis, 42 patients with proctitis and disease extension, and 60 patients with pancolitis at diagnosis were analysed. Disease extension occurred in 33.3% at 1 year, in 45.2% at 1-5 years and in 21.4% at 6-20 years. When compared with patients with limited proctitis, factors significantly associated with extension included non-smoking ($p = 0.02$, Fishers exact test), and a more severe disease course characterised by greater use of immunosuppression ($p < 0.001$, Fishers exact test), use of systemic corticosteroids at diagnosis (n = 18,43.9% extenders, n = 12, 10.9% limited proctitis, $p < 0.001$, Fishers exact test) and history of >2 hospital admissions from diagnosis ($p = 0.006$, Fishers exact test). Features not predictive of disease extension included family history of IBD, age at diagnosis, and extra-intestinal manifestations. Patients with disease extension are more likely to require surgery (n = 19, 45.23%) than patients with extensive disease at index presentation (n = 14, 23.3%),($p <0.03$, Fisher exact test), with follow up from 6 months to 18 years. Extension at 1 year may be more likely to lead to colectomy ($p = 0.08$).
Conclusions: Proximal disease extension in patients with proctitis is more common in non-smokers and is associated with a more refractory disease course with greater requirement for immunosuppressant use as well as a history of oral or parenteral corticosteroids at diagnosis.

These patients are more vulnerable to failure of medical therapy and more likely to require colectomy than patients with extensive disease at diagnosis. Hence, proctitis with proximal disease extension is a poor prognostic indicator and greater understanding of the biology of this phenomenon might facilitate disease modifying treatments strategies.

P215
Correlation of histological activity and basal plasmacytosis with mucosal healing in ulcerative colitis patients

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Background: Microscopic activity in ulcerative colitis (UC) patients with endoscopic remission is becoming more and more important in the prediction of relapse. The presence of basal plasmacytosis and the increased number of eosinophils and neutrophils in the lamina propria have been supposed to predict clinical relapse in UC patients with complete mucosal healing. The aim of this study was to examine the correlation between the microscopic activity and the disease outcome in patients with endoscopically inactive UC.

Methods: Sixty-nine UC patients (mean age at diagnosis was 31.4 years, male/female ratio: 27/42) with endoscopic remission (eMayo 0 and 1) and at least 12-month follow-up between 2008 and 2013 were enrolled in this prospective observational study. An expert pathologist evaluated all colonic biopsies for histologic activity (Geboes score) and the presence of basal plasmacytosis. C-reactive protein (CRP), partial Mayo scores and the used medications were documented at the time of the endoscopy, and the follow-up appointments: at months 6, 12 and 24 and at the last visit. Disease relapse was defined as a partial Mayo score equal or more than 3.

Results: Histology revealed focal or diffuse basal plasmacytosis and microscopic inflammatory activity with a Geboes score equal or more than 3.1 in 81.2% and 37.7% of patients with mucosal healing. At 6, 12 and 24 months and at the follow up visit, clinical relapsed occurred in 19%, in 14.5%, in 13%, and in 16% of the patients. The mean time of follow-up was 3 years. Neither of the presence of basal plasmacytosis, nor Geboes score equal or more than 3.1 was predictive of disease relapse at 6, 12, 24 months and at follow-up. No difference was observed if the data were analyzed separately in subgroups of eMayo score of 0 or 1.

Conclusions: Our Results did not confirm the previous hypothesis that the presence of basal plasmacytosis and microscopic inflammation predicts UC clinical relapse in patients with mucosal healing.

P216
Defensins alpha 5 and 6 are up-regulated in the colonic mucosa from patients with Ulcerative Colitis and are associated with clinical outcomes

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Background: Ulcerative colitis (UC) is a chronic condition of unknown etiology that affects the colonic mucosa. Defensins are a family of cysteine-rich cytotoxic peptides that are found on the mucosal surface of the intestine and work as antimicrobial agents against the bacterial invasion of the intestinal epithelium. Most of the alpha defensing genes are clustered on chromosome 8, the proteins encoded by these genes (DEFA5 and 6) are highly expressed in the secretory granules of Paneth cells in the ileum. Their role has not been evaluated in patients with UC. The aim of the present study is to evaluate the expression of DEFA5 and DEFA6 genes in patients with UC.

Methods: A total of 118 individuals were included and divided into 3 groups: 1) UC active (n=43); 2) UC in remission (n=34); and 3) Control group (N=41). Total RNA was extracted from colonic mucosa biopsies, the relative expression of the DEFA5 and DEFA6 genes was determined using real time PCR. The following oligos were used, DEFA5 Left: AGGACCATCGCCATCCTT, Right:TCAGCTCT TTCCTGGAGTGAC;DEFA6 Left: CTGAGCCACTCCAAGCTGA, Right:GGGCATCAGCCTCATAAGC and GADPH Left: GCCCAATACGACCAAATCC, Right: AGCCACATCGCTCAGAC AC. The statistical package SPSS v.19 was used to perform the analysis.

Results: Fifty-seven percent of the patient with UC were female. The expression of the DEFA5 gene was significantly increased in the colonic mucosa of patients with UC active compared to the control group (P=0.002) and UC in remission group (P=0.04). Furthermore a significant difference was found in the expression between the UC remission group and the control group (P=0.009). On the other hand, an up-regulation of the DEFA6 gene was also observed in the UC active group compared with the control group (P=0.0001) as well as in the remission UC group as compared to the control group (P=0.001). Finally, a significant association was found between the high expression of DEFA6 and a favorable response to medical treatment (P=0.05, RM=0.20) and the presence of histological activity (P=0.01, RM: 11.4). The DEFA5 gene was also associated with the histological activity (P=0.01, RM=11.08).

Conclusions: The expression of the DEFA5 and DEFA6 genes were increased in patients with UC, this might indicate that an underlying defense mechanism that increases the production of the antimicrobial peptides (defensins) in order to decrease the bacterial invasion in the colonic mucosa.

P217
The use of imaging techniques in the diagnosis and management of Crohn's Disease: Results of a national survey (Raymond study) aimed at Spanish gastroenterologists and radiologists

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Background: Radiological imaging plays a major role in diagnosis of both luminal disease and extra-enteric complications in CD.
1. To describe the perception of the utility and real use of imaging techniques in the diagnosis and management of patients with CD among a sample of Spanish gastroenterologists(G) and radiologists(R). 2. To establish the degree of theoretical and practical agreement regarding the use of imaging techniques in both groups of professionals.
Methods: Descriptive study based on information obtained from a survey('RAYMOND' study) aimed at Spanish G and R. It included questions on the imaging and endoscopy techniques, their real use and their limitations in CD.
Results: Between May and July 2013, 324 professionals (69.3% G and 30.7% R) answered the survey. Of these, 9.5% of the R were specialised particularly in chronic IBD and 47.4% in abdominal imaging. Sixty eight percent of the G were specialized in CD. For the vast majority of G (99%), endoscopy is the most appropriate examination for the diagnosis of luminal CD while barium follow-through(BFT) is used by only 8%. With respect to imaging techniques, among all groups of professionals, MRI is considered the most appropriate technique, followed by CT, ultrasonography(US) and lastly barium follow-through in all clinical scenarios. Routine use of the Patency capsule is 15% higher among G working in centres with a larger volume of patients (> 300 beds). Among the limiting factors for the use of the different techniques are, in first , waiting lists for MRI (28%), unavailability for capsule endoscopy (21%), or lack of experience for US (37%). With respect to the degree of theoretical and practical agreement between G and R, 77 pairs of specialists from the same centre were matched up. The % of ponderated agreement in the use of imaging techniques for location and extent of active CD between G and R in the diagnosis of luminal CD was 64% for MRI, 73.6% for CT, 87.5% for US and 85% for BFT, and 54.6%, 61.6%, 70.8% and 95.7%, respectively, for detection of intra-abdominal fistulas and/or abscesses.
Conclusions: Among the imaging techniques for the diagnosis and management of CD, endoscopy and MRI are the most highly considered and widely used by G and R, while BFT is used only by a minority. The percentage of agreement between G and R is high in all scenarios for the different imaging techniques, both theoretically and in real use.

P218
Vitamin D status in IBD patients: a comparison of three different assays

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Background: Vitamin D (VD) is a fat soluble secosterol that is produced in the skin after the sun exposure. Epidemiological studies show significant associations of VD deficiency and immune mediated diseases. The plasma 25-OH vitamin D3 concentration is a reliable biomarker for VD status but assay's variability makes adequate monitoring of VD difficult.
Methods: The aim of this study was to determine the correlation between three different assays for measuring plasma concentration of 25(OH)-vitamin D3.
Blood samples from 50 IBD patients were evaluated in a blinded way in three different laboratories using diverse assays of 25 (OH) vitamin D monitoring such as high-performance liquid chromatography (A), IDS automated immunoassay (B) and competitive binding assay (C). We correlated the VD levels of different assays using Pearson correlation coefficient. In addition, we evaluated the clinical accuracy of each assay by examining the agreement of assays in sorting patients into distinct categories according to difference of VD levels using the cutoffs (< 5ng/ml) for acceptable agreement, (5-10ng/ml) significantly different and (>10ng/ml) insufficient.
Results: 25(OH) vitamin D concentrations assessed by competitive binding assay were in the range of 3.0 ng/ml to 39.3 ng/ml, by high-performance liquid chromatography of 4.6 ng/ml to 53.2 ng/ml and by automated immunoassay of 9.0 ng/ml to 48.0 ng/ml. All vitamin D assays showed a linear quantitative correlation (Pearson r=0.69 for A vs. B, 0.69 for A vs. C and 0.63 for B vs.C). Comparing VD assays according to difference of VD we observed agreement in 20 samples, significant difference in 18 samples and disagreement in 10 samples between A and C; agreement in 29 samples, significant difference in 10 samples and disagreement in 9 samples between A and B; agreement in 18 samples, significant difference in 20 samples and disagreement in 12 samples between B and C.
Conclusions: There is a clinically important bias between different VD assays.. Our Results indicate the need towards further standardizing assays for 25(OH)D measurement.

P219
The relevance of ileitis as diagnosed by capsule endoscopy: A comparison with double balloon enteroscopy

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Background: Capsule endoscopy (SBCE) is non-invasive and allows a complete view of the small bowel in the majority of cases. A drawback to SBCE remains the inability to obtain biopsies and the relevance of small bowel inflammation as detected by SBCE has been questioned. Current guidelines would suggest enteroscopy (DBE) with histological assessment should be performed when ileitis is detected on SBCE. This study aimed to determine the clinical accuracy of SBCE in diagnosing small bowel CD as compared to DBE.
Methods: Patients with evidence of ileitis on SBCE between June 2010 and July 2013 were identified from our database. Importantly, record was made of whether the capsule reader considered the ileitis to be consistent with CD in each case. All patients with evidence of ileitis were cross-referenced using our endoscopy database to identify patients who had undergone DBE at our institution. A retrospective chart review was undertaken to ascertain final diagnosis. Exclusion criteria included any documentation of NSAID use in the 3 months prior to SBCE and any patient with less than 6 months follow up post procedure.
Results: A total of 820 SBCE procedures were performed during the three-year time-period. Approximately 140 (17%) had documentation of ileitis on SBCE. Of these, data was available on 22 (16%) patients had undergone DBE; mean age 45 years (range 18-73), 12 (55%) male with a mean follow up of 7 months (range 6-18). Table 1 demonstrates the findings of both SBCE and DBE. There was a statistically significant, albeit weak, correlation between SBCE and DBE findings (R=0.516, p<0.013). In terms of final diagnosis, 8 (36%) patients were subsequently diagnosed with definitive small bowel CD. Final diagnosis was based on numerous factors including the SBCE, DBE and histological findings coupled with radiological investigations and clinical symptoms. Of the remaining 14 patients,

8 (36%) were diagnosed with functional bowel disease and 6 (27%) with NSAID enteritis. All patients who were eventually diagnosed with CD had abnormalities consistent with small bowel CD on SBCE. SBCE had a moderate degree of correlation with final diagnosis (R=0.638, p<0.001). The positive and negative predictive value for SBCE was 70% and 92%, respectively based on final diagnosis.

Conclusions: SBCE is effective at detecting ileitis. It has a high positive and negative predicitve value although there will always be a tendancy towards a poorer positive predictive value until capsules are developed which are capable of interacting with their environment. A high index of suspicion is required for alternated diagnoses and DBE should be performed if there are doubts about the likely diagnosis.

P220
Diagnostic challenges in inflammatory bowel disease: fully automated immunoassay profiling of fecal biomarkers

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Background: There is no "gold standard" laboratory test to diagnose inflammatory bowel diseases (IBD). Fecal calprotectin (FC) is an established biomarker for detection and follow-up of IBD. [2], [4] Fecal lactoferrin (FL), an iron-storing protein from neutrophil granulocytes is a sensitive marker for intestinal inflammation. [3] Secretory IgA (sIgA) reflects the immunological status of the gastrointestinal tract. Increases in sIgA may be associated with impaired mucosal permeability. [1]

Methods: Samples from 40 consecutive patients presenting at the Kaiser-Franz-Josef-Hospital, Vienna, either with symptoms suggestive for or with confirmed diagnosis of IBD were analyzed with 5 different test systems including two established FC ELISAs (ORGENTEC Diagnostika, Germany; Bühlmann, Switzerland), a rapid fully automated FC test, and two assays in development, FL and a novel sIgA test for the automated Alegria® system (ORGENTEC Diagnostika, Germany). FC, FL and sIgA were extracted and measured according to the manufacturer's instructions.

Results: The coefficients of determination (R^2) among the FC tests ranged from 0.84 to 0.98. The correlation of FC Alegria® and FC ORGENTEC ELISA with the Bühlmann FC test was 0.84 and 0.86. FC Alegria® and the FC ORGENTEC ELISA showed excellent correlation (R^2= 0.89), especially in the normal and the lower range of FC levels up to 200 µg/g (R^2=0.98). The number of samples with FC and FL concentrations below or above the respective cut-off are summarized in Table 1.

Number of samples with concentrations of fecal biomarker below or above the cut-off

	FC Bühlmann ELISA > 50 µg/g	FC Bühlmann ELISA < 50 µg/g
FC ORGENTEC ELISA > 50 µg/g	23	3
FC ORGENTEC ELISA < 50 µg/g	O	14
FC for Alegria® > 50 µg/g	23	3
FC for Alegria® < 50 µg/g	O	14
FL for Alegria® > 7.2 µg/g	22	1
FL for Alegria® < 7.2 µg/g	1	16

Only three samples tested positive with the ORGENTEC FC kits and negative with the Bühlmann test. The recently developed automated FL assay significantly correlated with the established FC test (R^2= 0.88). Seven samples showed elevated sIgA as well as elevated FC concentrations.

Conclusions: The novel easy going rapid ORGENTEC FC test for the fully automated Alegria® system showed excellent correlation with established FC tests. This was also the case for the novel FL assay. These new automated fecal immunoassays are possibly helpful candidates for diagnostic work-up of patients with IBD. sIgA concentrations varied, suggesting further studies to elucidate the value of sIgA testing among IBD patients.

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P221
Evolution of serological markers and their predictive value before and after right hemicolectomy with ileocolonic anastomosis in patients with Crohn's disease

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Background: Preventing postoperative endoscopic (ER) and clinical recurrence (CR) remains challenging in patients with Crohn's disease (CD) undergoing an intestinal resection. We previously identified a pre-operative risk panel (including smoking behaviour, Fla2, and pANCA) which may guide postoperative prophylactic therapy. We aimed to evaluate the post-operative evolution of serological markers and its association with both ER and CR.

Methods: The study population consisted of 71 consecutive patients (33 males, 20 active smokers, median age 42.7 years) undergoing an ileal resection with ileocolonic anastomosis for refractory CD, in whom a serum sample was available both within 1 week prior to surgery and 6 months thereafter. ER was defined as an endoscopic recurrence score of i3 or i4 at month 6. Sera were analysed blindly at Prometheus laboratories Inc. for the expression of anti-Saccharomyces cerevisiae IgA and IgG antibodies, three different anti-flagellin antibodies (CBir1, Fla2 and FlaX), antibodies to the outer-membrane porin C of Escherichia coli (OmpC), and atypical perinuclear antineutrophilic cytoplasmic antibodies (pANCA). The Q3 value of each individual marker was defined as the cut-off point.

Post-operative evolution of serological markers

	Pre-operative, median (IQR)	Post-operative, median (IQR)	Wilcoxon signed rank p-value
ASCA IgA	34.05 (9.56–89.34)	21.39 (11.59–73.18)	p<0.001
ASCA IgG	29.07 (11.10–63.86)	25.22 (12.00–35.91)	p<0.001
CBir1	30.31 (16.78–89.28)	24.91 (16.37–49.60)	p<0.001
Fla2	31.01 (16.04–66.79)	42.54 (19.61–55.95)	p=0.363
FlaX	52.49 (25.63–95.80)	51.47 (23.49–73.87)	p=0.001
OmpC	6.58 (2.63–13.17)	12.66 (9.29–22.38)	p<0.001

Results: At month 6, ER and CR were observed in 20 (28%) and 12 (17%) patients, respectively. During a median (IQR) follow-up of 26.8 (18.1-39.2) months, 24 (34%) of patients developed CR. As shown in Table 1, a significant decrease of ASCA IgA and IgG, CBir1 and FlaX was demonstrated post-operatively, while a significant increase was noted for OmpC. The absolute and relative post-operative changes of these markers were not associated with ER or CR. However, active smoking, ASCA IgA > 72 EU, OmpC > 23 EU and positive pANCA (n=15) at month 6, were associated with ER. In multivariate analysis, OmpC > 23 EU was associated with ER [Odds ratio 4.398 (1.379-14.028), p=0.012]. In 59 patients without CR at month 6, Cox regression multivariate analysis, revealed that both ER [7.926 (2.256-27.848), p=0.001] and pANCA [4.741 (1.378-16.313), p=0.014] were independent predictors of long-term CR.
Conclusions: In contrast to most previous findings, we observed a clear evolution of serological markers in the postoperative phase. This observation is probably reflecting a changing microbial environment. At 6 months, OmpC antibodies were independently associated with postoperative ER. Interestingly, not only ER but also presence of pANCA at month 6 was an independent predictor of long-term CR. Validation of these Results in an independent cohort is warranted.

P222
Delay in Meeting Diagnostic Criteria in Crohn's Disease.

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Background: Defined diagnostic criteria for Crohn's disease (CD) use histological, clinical, radiological, surgical and endoscopic criteria. (1,2) These criteria may not be met until some time after initial presentation.
Aim: To study the delay between presentation and formal meeting of diagnostic criteria for CD using the Lennard Jones (LJ) and European Crohn's and Colitis Organisation (ECCO) consensus histological criteria.
Methods: Patients and Methods: All patients managed as longstanding CD at a tertiary referral centre (Brisbane, Australia) diagnosed between Jan 1st 1994 and March 1st 2008 were analyzed. All clinical, radiological, endoscopic, surgical, histological and laboratory data were recorded longitudinally. LJ criteria were considered met when 3 of the following criteria were present (2 if one was granuloma): typical location, discontinuous macroscopic disease, transmural ulceration, fibrosis, lymphocytic aggregation, and presence of granulomas. ECCO histological criteria were considered met when 3 of the following criteria (2 if one was granuloma) were present on mucosal biopsies or surgical specimens: lymphocytic infiltrate, crypt architectural distortion, irregular villous architecture (ileum), crypt abscesses, submucosal fibrosis, fissuring ulceration, and granulomas. Two further diagnostic models were analyzed; an extended LJ criteria requiring 3 of either the LJ criteria described above and three additional criteria (CRP>25mg/L, ASCA>25 units/mL and a family history of Crohn's disease), and a reduced LJ criteria requiring only two parameters. These were compared to the original LJ and ECCO criteria.
Results: Results: 289 patients were analyzed, of whom 61.2% met LJ criteria within 1 year, and 76.7% within 5 years. Delay to meeting diagnostic criteria using LJ, ECCO, reduced LJ and extended LJ criteria is displayed in figures 1 and 2. The ECCO histological criteria were less sensitive than the LJ criteria in early identification of patients who eventually meet the LJ criteria. The extended LJ and reduced LJ criteria increased early identification of patients who eventually meet the original LJ criteria, however they also identify patients who never progress to meet LJ criteria.
Conclusions: Conclusion: There was a delay between presentation and diagnosis of greater than one year for 26% of CD patients who eventually met LJ diagnostic criteria. This highlights a need for new diagnostic criteria to identify these patients earlier in their disease course. This may be achieved by adding additional criteria to a diagnostic algorithm, or by reducing the number of existing criteria. However, these strategies would increase the number of patients with mild disease meeting diagnostic criteria, and need further study.

P223
Idelalisib-induced acute proctocolitis: Clinical and histological findings

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Background: Idelalisib (Zydelig®) is a highly specific small-molecule phosphatidylinositol-3-kinase (PI3K-delta) inhibitor with recent United States' FDA and pending EU approval as an oral treatment for relapsed B cell haematological cancers[1]. Phase 2 and 3 registration studies have demonstrated fatal and/or serious and severe diarrhoea or colitis in up to 14%, however the histological findings have not been well documented[2,3]. Here we report the clinical and histological features associated with Idelalisib gastrointestinal toxicity.
Methods: Two cases of Idelalisib associated colitis were identified from a single centre, information on their clinical management and outcomes were reported by the treating gastroenterologist and haematologist. Histology was reviewed by two expert gastrointestinal pathologists.

Results: Both patients presented with non-bloody, severe (grade III) diarrhoea and weight loss following 3 months of Idelalisib therapy. Both patients had negative stool culture, faecal multiplex PCR, and C. difficile PCR with elevated faecal calprotectin >1000ug/g. Both patients failed to improve despite Idelalisib withdrawal and empiric loperamide. Colonoscopy demonstrated patchy left-sided colitis in one patient and confluent pancolitis in the second patient. Upper gastrointestinal tract, proximal small bowel and terminal ileum were endoscopically normal in both patients. Colonic biopsies showed acute colitis with oedematous lamina propria, mixed inflammatory infiltrate comprising numerous eosinophils, crypt abscesses and crypt dropout, lymphocyte exocytosis in the crypts with apoptotic bodies. CMV was not found. Both patients responded rapidly to intravenous hydrocortisone with resolution in diarrhoea and normalisation of CRP. Follow-up biopsies on one patient demonstrated features of resolving colitis five months later.

Conclusions: Idelalisib may cause an acute toxic inflammatory reaction in the colon resembling infective proctocolitis with a marked eosinophilic infiltrate. Given the likely incorporation of this medication into the therapeutic approach for relapsed B-cell haematologic malignancies, clinicians may encounter an increasing number of such cases and should be aware of this potentially fatal and severe complication.

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P224
The Ulcerative Colitis Endoscopic Index of Severity (UCEIS) is useful to evaluate endoscopic improvement and to predict medium-term prognosis in ulcerative colitis patients treated with tacrolimus.

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Background: Various scoring systems have been used to assess endoscopic severity in ulcerative colitis (UC). The Ulcerative Colitis Endoscopic Index of Severity (UCIES) is a newly developed scoring system, consisting of vascular pattern, bleeding, and erosions and ulcers. The final score is the sum of these 3 items and ranges from 0 (remission) to 8 (severe). While the UCEIS is a validated scoring system, there has been no study that utilizes the UCEIS in clinical settings. This study aimed to evaluate usefulness of the UCEIS in UC patients treated with tacrolimus.

Methods: This was a retrospective cohort study. We enrolled a total of 90 patients treated with tacrolimus at Tokyo Medical and Dental University between September 2009 and August 2014. We used the UCEIS to evaluate endoscopic severity. The Lichtiger score was used to assess clinical response and a Lichtiger score <= 4 was defined as clinical remission.

Results: The mean UCEIS score before treatment was 5.4, with a score of 3-4 in 21 patients (23.3%), 5-6 in 56 patients (62.2%), and 7-8 in 13 patients (14.4%). Fifty-five patients underwent colonoscopy at 3-6 months after initiating tacrolimus. The mean post-therapeutic UCEIS score was 1.5 (range: 0-5), which was significantly lower in patients with clinical remission compared to those who did not achieve clinical remission (0.9 vs. 2.6, p< 0.01). Furthermore, although the pre-treatment UCEIS scores were not correlated with clinical response, patients with a post-therapeutic UCEIS score of 0-1 had a significantly higher rate of medium-term event-free survival, defined as no requirement of either colectomy or other induction therapy, compared with those with UCEIS scores >= 2.

Conclusions: The UCEIS is useful to evaluate endoscopic improvement in UC patients treated with tacrolimus. The UCEIS score of 0 or 1 after treatment is associated with a favorable medium-term outcome, suggesting a possibility that mucosal healing is defined as a UCEIS score of 0 or 1. Thus, the UCEIS is a useful instrument to evaluate UC patients on tacrolimus.

P225
Anticipate to defer: predicting surgical outcome at the moment of diagnosis of Crohn's disease

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Background: Several risk factors for surgery in Crohn's disease (CD) have been identified. However, little is known about predictors of surgery at the precise moment of the diagnosis, which could be determinative when considering the use of more aggressive medical therapies. The aim of this study was to identify risk factors for abdominal surgery at the time of diagnosis of CD.

Methods: Retrospective case-control study of patients followed in our department for CD. Cases were patients who had undergone an operation for CD as defined by standard clinical criteria. Controls were patients without any prior surgical treatment for CD. Data related to age, gender, family history, smoking, symptoms, extraintestinal manifestations (EIM), laboratory values, Montreal classification and medical treatment used at presentation were collected. Statistical analysis was performed using SPSSv20.

Results: A total of 279 patients were included in the final analysis: 76 patients in the case group and 203 in the control group. There were no differences in the mean age, gender or family history between groups but smoking were significantly more common in operated patients(p=0,014). Abdominal pain(p=0,013) and diarrhea(p<0,001) were more commonly found at the moment of diagnosis of CD in patients requiring surgery, while fever, weight loss and blood loss were not different between groups. No differences were found in cutaneous, ocular, articular or thromboembolic EIM. Cases were more prone to have lower hemoglobin values(p<0,001), thrombocytosis(p<0,001) and higher C-reactive protein(CRP)(p<0,001) and erythrocyte sedimentation rate(ESR) values(p=0,009). Leukocyte count and ferritin did not differ significantly. As for Montreal classification, ileocolonic location(p<0,001), penetrating or stricturing disease(p<0,001) and perianal disease(p=0,036) were more common in cases, but there were no differences in upper gastrointestinal involvement or in age of diagnosis. Cases had antibiotics prescribed at presentation more commonly(p=0,021), but the use of topic steroids(p=0,001)

or aminosalicylates(p=0,004) was rarer. No differences were found in the use of systemic steroids.

Conclusions: At the moment of diagnosis of CD, smoking, abdominal pain, diarrhea, lower hemoglobin values and higher CPR, ESR or platelet values, as well as ileocolonic location of the disease, penetrating or stricturing disease, and perianal involvement are associated with a subsequent surgical outcome. The early recognition of these features in newly diagnosed patients should be seriously taken into account when deciding for more aggressive medical treatments, such as immunosuppressors or biological agents, in order to defer the more invasive surgical procedures.

P226
Consistently high C reactive protein is associated with subsequent development of perianal fistulae in patients with Crohn's disease.

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Background: Laboratory tests are used longitudinally in the management of patients with Crohn's disease. Whether there is a correlation between longitudinal laboratory Results and the subsequent development of perianal disease is unknown.

AIM: To study the correlation between longitudinal laboratory testing and subsequent development of perianal fistula in patients with Crohn's disease.

Methods: Patients diagnosed at a tertiary referral centre with Crohn's disease between 1994 and 2014, with more than five years of clinical follow-up, had objective clinical, laboratory and genetic data recorded. Patients with a perianal fistula occurring within 6 months of diagnosis were excluded. Laboratory data were represented by the area under the curve of values measured in the complication free period leading up to development of a perianal fistula. Cox regression was used to analyse the association between development of a perianal fistula and laboratory values for: C reactive protein (CRP), platelet count, albumin level, faecal calprotectin, serum ferritin, serum haemoglobin and erythrocyte sedimentation rate (ESR). Laboratory values were converted to categorical variables with optimized cut-offs. Recognized predictors of development of perianal disease were added to the model to assess independence of identified associations.

Results: 382 patients were reviewed, of whom 57 had less than five years of clinical follow-up and 43 had perianal disease within 6 months of diagnosis. 257 had a complete clinical, biochemical and genetic record without perianal disease at diagnosis and were observed for a median of 10.25 (interquartile range (IQR) 7.39-13.78) years. 46 patients developed a perianal fistula a median of 2.06 (IQR 1.10 - 5.82) years after diagnosis. Blood testing was performed a median of 3.61 (IQR 2.24 - 5.79) times per year for each patient. Results of univariate analysis are tabulated. After multivariate analysis with inclusion of recognised predictor variables, CRP >31 (HR 7.12, p<0.001) and age at diagnosis <32 (HR 3.93, p=0.004) were independently associated with development of perianal fistula.

Conclusions: A longitudinally measured CRP consistently greater than 31 is independently associated with subsequent development of a perianal fistula in patients with Crohn's disease. Serial monitoring and a longitudinal analytic tool for serial CRPs may aid in identifying patients at risk of developing perianal disease.

P227
Lower serum albumin level on admission is a predictive factor of colectomy in patients with moderate to severe ulcerative colitis

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Background: Little is known about the predictive factor of later colectomy in patients with moderate to severe ulcerative colitis (UC). We aimed to identify the factors which predict colectomy in patients with mild to severe ulcerative colitis on admission.

Methods: This retrospective study used the data from the clinical database, including a cohort of 51 patients with moderate to severe UC who received induction therapy at a single center, Kyoto Prefectural University of Medicine between 2008 and 2014. Clinical parameters (age, sex, disease extent, and disease activity (CAI: Lichtiger index) on admission) and laboratory data (hemoglobin, albumin, C-reactive protein, and cytomegalovirus reactivation on admission) were evaluated in 51 patients. The clinical difference between cases to achieve remission and the colectomy were evaluated.

Results: 31 of 51 cases were achieved in the remission by induction therapy. The colectomy was performed in 20 of 51cases. Clinical parameters such as age, sex, disease extent, and disease activity on admission showed no difference between two groups (remission group and colectomy group). In laboratory data, only the lower levels of albumin on admission were the most significant predictors of the later colectomy [OR=0.213 95%CI=0.075-0.603)]. The patients with under 2.5g/dl of serum albumin on admission, 62.5% (15/24) cases were performed colectomy, in contrast, 15% (3/20) cases with over 2.5g/dl.

Table of laboratory tests.

Variable	Cut-off	Hazard ratio	p-value
CRP	>31 mg/L	6.96	<0.001**
ESR	>14 mm/hr	2.92	<0.001**
Albumin	<39 g/L	3.12	<0.001**
Platelets	>270 x 10^9/L	4.64	<0.001**
Haemaglobin	<137 g/L (m) <122 g/L (f)	2.07	0.019
Ferritin	<64 mcg/L	3.27	0.030
Faecal calprotectin	>192mcg/L	Not able to calculate	0.028

Conclusions: In this study, the serum albumin level on admission was the most important predictive factor for colectomy in patients with moderate to severe ulcerative colitis

P228
Vaginal delivery is not associated with fecal incontinence in IBD women

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Background: The best mode of delivery for pregnant women with inflammatory bowel disease (IBD)remains a continuing debate amongst physicians. Because patient reported outcomes (PRO) are increasingly included in the management of IBD patients the aim of this study was to investigate PRO on the influence of vaginal delivery (VD) on fecal incontinence (FI) in IBD women.

Methods: We conducted a PRO study on FI and distributed an online survey amongst all members of the Dutch Crohn's and colitis organization (CCUVN). FI was defined as sometimes, weekly or daily involuntary loss of liquid or solid stool. To assess FI complaints we used a validated score (Vaizey incontinence score). This scale has a minimum score of 0 (perfect continence) and a maximum score of 24 (totally incontinent).

Results: In total 343 women (211 CD(61.5%), 123UC(35.9%), 9IBDU(2.6%)) responded (278 responders from a research panel consisting of 443 IBD women, 65 through social media). In total 174(51.2%) females were childless, 136(40.0%)had a VD, 14(4.1%) had both a VD and caesarian section (CS), 16(4.7%)only CS (3 unknown). Mean age was 41,8 years(SD 13). Median follow up after last delivery was 16 years(IQR 5.5-25.4).

In total 73 females(24,0%)never had FI complaints, 89(29,2%) seldom, 91(29,8%) sometimes, 27(8,9%) weekly and 24(8,1%) daily (35 had a stoma, 5 unknown). There were 213(70.0%) premenopausal and 91(30.0%) postmenopausal women (39 did not answer this question). Sixty- one women had perianal fistulizing disease of which 24(39.3%)had one or more VD.

The overall median Vaizey score was 7(IQR 5-10). There was no difference in Vaizey score between CD and UC/ IBDU. Vaizey score was higher in women with VD (median 8,IQR: 5-11) compared to women that never had a VD (median7,IQR: 4-9)(p=0.02). The Vaizey score was also higher in postmenopausal women (median 8, IQR:6-11) compared to premenopausal women (median 6, IQR4-9) (p=0.001).

VD was associated with FI (cOR 1.91, 95%CI: 1,21-3.026), correction for menopause and perianal fistulizing disease showed no independent association with VD (aOR 1.58, 95%CI: 0.92-2.73). Menopause had an association with FI (cOR 2.38, 95%CI: 1.40-4.10), also after correction for VD and perianal fistulizing disease (aOR 2,03, 95%CI 1.12-3.69). Perianal fistulizing disease was not associated with FI.

Women with children experience FI more often after menopause (66.1%) compared to before (45.9%)(p=0.03). Childless women also experienced FI more often after menopause (46.2%) compared to premenopausal women (33.3%) but this was not statistically significant (p=0.26).

Conclusions: This study shows that FI complaints in IBD women are not significantly associated with a vaginal delivery.

P229
AlphaE (αE) integrin protein and gene expression are augmented in the ileum relative to the colon in Crohn's disease

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Background: Etrolizumab, a monoclonal antibody against β7 integrin, targets both α4β7 and αEβ7 expressing cells. αE integrin-expressing cells, the majority of which are T cells, are found throughout the gastrointestinal tract mucosa and can localize to the epithelium and lamina propria (LP). αE showed promise as a predictive biomarker for response to etrolizumab in a phase II trial with ulcerative colitis patients. To better understand αE expression in Crohn's disease (CD), we examined the prevalence and localization of αE+ cells and total αE gene expression in the ileum and colon of non-IBD (inflammatory bowel disease) controls and CD patients.

Methods: Ileal and colonic tissue were collected from controls and CD patients. αE+ cells, detected by immunohistochemistry, were counted by an automated algorithm that determines cellular localization relative to intestinal crypts and normalized to total cell counts in respective tissue compartments (mucosa, epithelium and LP). Lymphoid aggregates and Peyer's patches were excluded from analysis. Gene expression was assayed by qRT-PCR in control biopsies and in paired mucosal biopsies from inflamed and uninflamed regions of the colon and ileum from CD patients. Statistical test Kruskal-Wallis was used in analyses.

Results: In control and CD resections, significantly more αE+ cells were present in ileal than in colonic mucosa (Table 1), with significantly more αE+ cells present in ileal than in colonic LP (Table 1); in contrast, the numbers of crypt epithelium-associated αE+ cells were equivalent in both anatomical regions (Table 1). Consistently, αE gene expression levels were significantly higher in ileal than in colonic biopsies in both controls and CD (Table 1). Analysis of paired biopsies from CD patients showed no increase in αE gene expression in inflamed biopsies compared with uninflamed biopsies taken from either the ileum or colon.

Conclusions: These Results demonstrate that in both controls and CD, the number of αE+ cells and αE gene expression levels are increased in the ileum compared to the colon, and this anatomical observation is unaffected by inflammatory status. Furthermore, the greater number of αE+ cells and higher gene expression levels are entirely attributable to increased cell counts in the ileal LP, as both anatomical locations had equivalent crypt epithelial-associated αE+ cell counts. Further studies will be required to examine the role of αE+ cells in CD and whether αE may offer value as a predictive biomarker for response to etrolizumab.

P230
ECCO endoscopy consensus for Inflammatory Bowel Disease and daily clinical practice: A need for dedicated training

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Background: Ileocolonoscopy (IC) is indispensable for the diagnosis and disease activity evaluation in Inflammatory Bowel Disease (IBD). Of note there are only two guidelines establishing minimal standards for IC in IBD [1], [2] . The primary aim was to assess the adherence of endoscopists to the ECCO's Endoscopy Consensus for IBD (ECC). The secondary endpoint was to evaluate the impact of a standard report for IBD in the endoscopy report software.

Methods: Cross-sectional study in an Endoscopy Unit of a Central Hospital. Based on the ECC we constructed a checklist of parameters considered relevant in endoscopy reports of IBD patients, namely clinical and endoscopic data and biopsy sampling. Using the checklist a template report was produced and incorporated in the endoscopy report software; the template was also presented to

"Table 1" Increased αE+ Cell Numbers and Gene Expression Levels in the Ileum vs the Colon of Patients with Crohn's Disease and Non-IBD Controls

Median (min-max) N	Non-IBD			Crohn's disease			
	Ileum	Colon	*P* value	Ileum		Colon		*P* value
Mucosal αE+ cells per 100 cells[a]	17 (14-22) 8	9 (4-17) 20	< 0.05	18 (5-29) 19		8 (1-8) 19		< 0.01
LP αE+ cells per 100 cells	30.5 (23-41) 8	14 (5-28) 20	< 0.05	29 (6-50) 19		11 (2-21) 17		< 0.01
Epithelial αE+ cells per 100 cells	10 (5-22) 8	7 (2-11) 20	ns	7 (2-16) 19		4 (2-22) 17		ns
αE+ gene expression relative abundance	0.51 (0.11-1.79) 9	0.17 (0.06-0.36) 14	< 0.01	0.47 (0.09-2.05) 87		0.19 (0.02-1.01) 75		< 0.0001
				Uninflamed	Inflamed	Uninflamed	Inflamed	
				0.59 (0.09-1.56) 25	0.35 (0.10-2.05) 25	0.19 (0.08-0.72) 11	0.24 (0.11-0.52) 11	ns[b]

[a]Mucosa comprises both epithelium and LP.

[b]No significant difference between inflamed and uninflamed biopsies in both anatomical locations.

ns, not significant.

Quality parameter	Phase 1 (%)	Phase 2 (%)	p value
Disease extension (continuous/segmental)	92	100	ns
Ulcer size/depth	55	71	ns
Stenosis (passable/unpassable)	100	100	ns
Endoscopic Scoring Indexes	29	75	0,0001
Biopsies			
Suspected IBD (≥ 2 in six segments)	85	50	ns
Stenosis	56	80	ns
Dysplasia surveillance (≥ 4 every 10 cm)	50	33	ns
Polyp surrounding mucosa	50	11	ns

the endoscopy medical team composed by 8 gastroenterologists, 3 of them specialized in IBD (Implementation Phase: May and June 2014). We reviewed the endoscopy reports produced before (Phase 1: September 2013 to April 2014) and after (Phase 2: July to October 2014) the Implementation phase and sought in each report all the checklist parameters. Phases 1 and 2 were compared using the Qui-Square or Fisher's exact tests.

Results: 74 reports were evaluated: 50 in phase 1 and 24 in phase 2. The table depicts the percentage of reports that complied with the defined quality parameters for endoscopic findings description and biopsies. On phase 1 all endoscopists stated the type of IBD, however less than 10% described the disease duration and therapy; most reports described disease extension and type of segmental involvement but size and depth of ulcers was described in <55%. Also chromoendoscopy was not used for dysplasia surveillance. In phase 2 there was a considerable increase in the use of Endoscopic Scoring Indexes (Qui-Square, p <0,05).

Conclusions: In most reports endoscopists state the type of IBD, adequately describe the disease extension and stenoses and correctly sample the mucosa when IBD is suspected. On the contrary, ulcers description and biopsies taken in the setting of dysplasia and polyps needs improvement. The simple measure of implementing a report template has a positive impact on the use of Endoscopic Scoring Indexes an increasingly important tool to monitor disease activity. Finally, the overall adherence to ECCO's endoscopy standards is not ideal and specific training on Endoscopy in IBD seems the next step to further improve the quality of endoscopy in IBD.

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P231
Diagnostic delay is associated with higher rate of major surgery in a French prospective cohort of patients with Crohn's Disease

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Background: The aim of the study was to determine whether a diagnostic delay is associated with poor evolution of Crohn's disease (CD) as recently observed in the Swiss IBD cohort [1].

Methods: Medical and socioeconomic characteristics of consecutive Crohn's Disease (CD) patients followed in 3 referral centers were prospectively recorded using an electronic database (Focus_MICI®). Medical treatments and surgery procedures were recorded. Diagnostic delay was defined as the time period (months) from the first symptom onset to CD diagnosis. A long diagnostic delay was defined by the upper quartile of this time period. Univariate and multivariate analyses were performed to compare patients with long diagnostic delay to those with earlier diagnosis regarding the rates of: 1) the first major intestinal surgery (excluding anal surgery), 2) immunosuppressive therapies (IMS) and 3) anti TNF therapies. Analysis of the cumulative durations (months) from diagnosis to: 1) the first surgery, 2) the first anti-TNF therapy, and 3) the first IMS, were conducted using the Kaplan-Meier; distributions of these groups were compared with the log-rank method.

Results: A total of 497 patients with CD (53.6% women) were analyzed. Median age at diagnosis was 25.6 years (IQR 25-75: 19.4-35.2). Median diagnostic delay was 5 months. Early diagnosis corresponded to a period < 2 months from first symptoms to CD diagnosis (n=122). Late diagnosis was > 13 months. Median follow up was 9 years (IQR 25-75: 4-16.2). 138 (28.3%) patients were active smokers and 109 (22.4%) former smokers. CD location and phenotype according to Montreal classification were: 196 (41.1%) L1, 121 (25.4%) L2 and 154 (32.3%) L3; 272 (58.1%) B1, 143 (30.6%) B2 and 53 (11.3%) B3. 148 (29.8%) patients had major surgery. Regarding treatment history: 161 (37.1%) patients had ongoing thiopurines, whereas 132 (30.4%) had it in the past; 28 (65%) had ongoing methotrexate, whereas 50 (11.7%) had it previously; 87 (20.2%) had ongoing infliximab, whereas 69 (16%) had it previously; 118 (27.3%) had ongoing adalimumab, whereas 48 (11.1%) had it in the past. There were no significant differences between patients with late and earlier diagnosis regarding: age at diagnosis, location and phenotype, overall rates of IMS (p=0.6) and anti-TNF (p=0.7) and duration from diagnosis to the first IMS or the first anti-TNF. In contrast, the time period from diagnosis to the first major surgery was shorter in patients with late diagnosis (p=0.05).

Conclusions: In this large prospective cohort of CD patients, those with longer diagnostic delay have earlier surgery. In contrast, overall rates of IMS and anti-TNF therapies and time of their introduction are not affected by a diagnostic delay.

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P232
Real-time Shear Wave Ultrasound Elastography in distinguishing inflammatory from fibrotic stenosis in Crohn's disease

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Background: Differentiation between inflammatory and fibrotic strictures in Crohn's disease (CD) is difficult but crucial for therapeutic decisions. Prior work has demonstrated that ultrasound elastography imaging (UEI) can identify intestinal fibrosis in animal models of CD. The purpose of our study was to determine if real-time shear wave elastography (SWE), a new technique of UEI can be used to distinguish inflammatory from fibrotic strictures in CD patients.
Methods: A total of one hundred and twenty established CD patients underwent transcutaneous UEI by the technique of real-time SWE using the ultrasound system, Aixplorer (SuperSonic Imagine S.A., Aix-en-Provence, France). Thickened bowel wall and proximal normal bowel were analyzed by measuring Young's Modulus (YM) of the tissue. According to a formalized score combining endoscopy, CT/MR enterography and histology, strictures were classified as inflammatory and fibrotic stenosis. One-way ANOVA and Bonferroni were used for statistical analysis, and receiver operating characteristic (ROC) curves were created to assess diagnostic performance.
Results: YM was measured successfully in one hundred and ten CD patients(male n=40, female n=70; mean age 40y, range 13y-65y,). These 110 patients were divided into three groups: acute inflammatory non-stenotic (n=46), inflammatory stenosis (n=44) and fibrotic stenosis group (n=20), with the value of YM as 15.5 ± 6.7 KPa, 16.7 ± 5.7 KPa, and 25.8 ± 8.0 KPa respectively. Transcutaneous UEI demonstrated YM was higher in fibrotic stenosis than inflammatory stenosis (P=0.016) and acute inflammed non-stenotic group (P=0.015). No significant difference existed between acute inflammatory stenosis and acute inflamnatory non-stenotic bowel (P>0.05). The most accurate cut-off value for distinguishing inflammatory from fibrotic stenosis was 17.5 KPa, achieving 98% of sensitivity and 71.4% of specificity. The area under the receiver operating characteristic curve (AUC) was 0.883 (95% CI: 0.84-0.93) .
Conclusions: UEI provides a noninvasive new method in distinguishing inflammatory from fibrotic strictures in CD patients, and may thereby be helpful in guiding therapeutic decisions.

P233
Risk factors and clinical signicance of endoscopic entent progression in patients with Ulcerative Colitis

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Background: Ulcerative colitis (UC) may extend in a proximal and continuous fashion to involve varying bowel segments. However, the risk factors predictive of proximal extension and clinical outcome of extent progression have yet to be determined. The aim of this study was to identify risk factors predictive of subsequent extent progression in UC patients and to evaluate the clinical outcome of these patients.
Methods: We retrospectively analyzed 518 UC patients including proctitis , left-sided colitis and entensive colitis without ascending colond involvement at the time of diagnosis who were regularly followed and underwent colonoscopy between 2003 and 2013.
Results: A total of 87 (16.8%) patients experienced proximal disease extension. The median time of extent extension was 40.3 months (IQR: 8.3-42.2). Independent factors associated with proximal disease extension was steroid dependency during the course (p=0.032). In addition, proximal disease extension was associated with disease relapse and use of immunosuppresive agents (p=0.025 and p=0.000).
Conclusions: Steroid dependency in the disease course was associated with a higher probability of proximal disease extension during the follow-up period. Moreover, those with disease extension were more likely to experience relapse and use of immunosuppresive agents, indicating poor prognosis.

P234
Development of a patient reported disease activity score to screen for mucosal inflammation in inflammatory bowel disease.

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Background: Integrated care and patient empowerment improve the outcome of chronic diseases. Telemedicine programmes are of interest for Inflammatory Bowel Diseases (IBD), but should include adequate monitoring of mucosal inflammation to prevent longterm complications. Different clinical activity questionnaires have been developed for systematic follow-up of disease activity in Crohn's disease (CD) and ulcerative colitis (UC). However, none has been validated against endoscopy, which is the golden standard for assessing mucosal inflammation. Recently published validated clinical activity scores include laboratory parameters and are therefore not suitable for telemedicine programmes. The objective of this study was to develop the first patient reported disease activity score for IBD patients to predict endoscopic disease activity, which can be used in telemedicine programmes.
Methods: Twenty-three questions regarding disease activity in IBD were selected based on literature review and expert opinion. Consecutive patients undergoing a colonoscopy for clinical evaluation between March 2013 and April 2014 were invited to fill out this 23 item questionnaire 24 hours before endoscopy (i.e. prior to bowel cleansing). Mucosal inflammation was assessed during endoscopy with the simplified endoscopic activity score for CD (SES - CD) and the Mayo endoscopic subscore (MES) for UC. Questions were reduced to a total of 6, based on individual correlation coefficients with endoscopic inflammation and expert opinion. Then, logistic

regression was used to find the best fitting model. ROC curves were used to find the most sensitive cut-off value.

Results: Ninety-eight CD patients (41.8% male, mean±SD age 44.7±14.2 years, 55.1% active disease) and 80 UC patients (58.8% male, mean±SD age 52.2±15.3 years, 63.8% active disease) were included.The multivariable logistic regression model for CD with a sensitivity of 90.4% (specificity 40.9%) included questions on blood loss, number of stools, urgency, fatigue and IBD symptoms in general. The multivariable logistic regression model for UC with a sensitivity of 88.3% (specificity 65.5%) contained items on blood loss, number of stools, urgency, abdominal pain and IBD symptoms in general.

Conclusions: We developed a patient reported disease activity score with a high sensitivity for detecting endoscopic disease activity in IBD patients. Such a tool is warranted in telemedicine programmes for screening patients who need further assessment of disease activity with biochemical markers and/or endoscopy. At present we are validating the score in an independent patient cohort.

P235
Clinical utility of the Lémann index and Rutgeerts score to predict postoperative course of Crohn's disease: a retrospective single-center cohort study.

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Background: The Rutgeerts' score (RS) predicts the risk for clinical postoperative Crohn's disease (CD) recurrence. Recently, the Lémann Index (LI) has been developed to quantify bowel damage (abscess, fistula, stricture).

Methods: We evaluated CD subjects undergoing intestinal resection from 2007 to 2013 and having both endoscopy within 6 and 12 months after surgery and magnetic resonance enterography (MRE) at the same time point (±60 days) and then followed every 12-18 months with the same examinations. Subjects with active perianal disease were excluded because of the relevant impact on the LI. Data on preventive medications, clinical relapse, further surgery or complications were analyzed. The correlation between RS and the LI was assessed by the Spearman's correlation test, and the predictive value of LI increase was assessed by logistic regression and Kaplan-Meyer curves.

Results: Thirty-nine subjects were included in the analysis. Median follow-up (FU) was 29.0 months. Nineteen subjects (48.7%) had a RS of 3-4 within 12 months after surgery and 21 subjects (53.8%) had an increase in the LI during the same period as assessed by MRE. No subjects underwent further surgery, 7 subjects (18%) had clinical relapse, and 5 (12.8%) developed bowel damage (all strictures) during follow-up. The vast majority of subjects (84%) with early endoscopic recurrence (RS of 3-4) also had a an increase in the LI (p=0.0007). No significant correlation was found between RS and LI (ρ=0.26, CI 95% -0.05-53.8, p=0.09) MRE was able to see pre-anastomotic ulcers in 40% of subjects with RS>2, while pre-anastomotic bowel wall thickening was seen in 89% of subjects with endoscopic recurrence compared to 25% with no endoscopic recurrence (p=0.0002) . Subjects with bowel wall thickening were more likely to have endoscopic recurrence (OR 25.5, CI 95% 4.3-151, p=0.0004). Subjects with an increase in the LI alone within 12 months were more likely to have a clinical relapse in the FU period (HR 0.0, CI 95% 0.04-0.87, p=0.03). Combined endoscopic recurrence (RS of 3-4) and LI increase within 12 months after surgery were also associated to a higher risk of clinical relapse during FU (HR 0.03, CI 95% 0.0000 to 0.0051, p<0.0001), while it was not predictive of further disease complications (OR 1.87, p=0.61).

Conclusions: Although in a small cohort, the assessment of endoscopic recurrence by RS and bowel damage by LI within 12 months since surgery may predict clinical recurrence. Bowel thickening after surgery is associated with endoscopic recurrence. Bowel damage as assessed by LI seems to be independent from endoscopic disease activity assessed by RS.

P236
Placebo response and remission rates in Ulcerative Colitis clinical trials: Systematic review and meta-analysis

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Background: Defining the magnitude and modifiers of placebo (PBO) rates in randomized controlled trials (RCTs) of ulcerative colitis (UC) is essential for the design and conduct of efficient trials and to optimize the detection of true drug-PBO differences. We conducted a contemporary meta-analysis of PBO response and remission rates in induction and maintenance phases of RCTs for active UC and assessed factors influencing these rates. We report the Results of our analysis of induction trials here.

Methods: MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials and the Cochrane IBG group specialized trials register were searched from inception to April 2014. Conference proceedings were searched between 2002-2014. Eligible studies were PBO-controlled trials of UC in adult patients which: (1) contained an induction and/or maintenance phase; (2) used the UCDAI (Mayo/Sutherland/partial equivalent) as criterion for enrolment and assessment of response/remission; and (3) evaluated the efficacy of 4 drug

classes (steroids, aminosalicylates, immunosuppressives, biologics). Data were extracted independently in pairs and disagreements resolved with a third reviewer. PBO rates for each outcome were pooled using a binomial-normal model for meta-analysis of proportions.

Results: We identified 7,587 citations and 55 studies eligible for inclusion (46 induction, 9 maintenance). Pooled PBO remission (n=40) and response (n=43) rates were 10% (95% CI 7%-13%; range 1%-49%) and 33% (95% CI 28%-38%; range 6%-92%) respectively, both with significant heterogeneity (P < 0.001). Features associated with a lower PBO response were longer disease duration prior to enrolment (33% for >5 yrs vs 47% for ≤ 5 yrs), endoscopy subscore ≥ 2 at study entry (34% for score ≥ 2 vs 46% for score ≥ 1) and requirement for improvements in endoscopy and bleeding subscores as outcome measures. Features associated with lower PBO remission rates were longer disease duration prior to enrolment (10% for >5 yrs vs 19% for ≤ 5 yrs), endoscopy subscore ≥ 2 at study entry (11% for score ≥ 2 vs 24% for score ≥ 1), the requirement for improvement in the endoscopy subscore from baseline as an outcome measure and publication date after 2005 (12% for ≤ 2005 vs 9% > 2005). No difference in PBO rates was observed when disease was classified as mild-moderate vs moderate-severe at study entry, for a UCDAI cut-point ≥ 6 vs <6, or follow-up duration.

Conclusions: Lower PBO response and remission rates were observed in UC induction trials enrolling patients with more active disease defined by endoscopic subscore, rather than a higher composite UCDAI. This reinforces the importance of enrolling patients and assessing outcomes using objective markers of active disease.

P237
Accuracy of a rapid fecal calprotectin test as a predictor of mucosal healing in patients with Ulcerative Colitis (UC)

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Background: Predicting mucosal healing in UC patients by measuring non-invasive biomarkers could be useful to avoid unnecessary colonoscopies. Aims of this study were 1) to evaluate the predictive value of a quantitative rapid fecal calprotectin (FC) test for mucosal healing in UC patients as defined by the Mayo score, and 2) to evaluate the difference in FC between endoscopic Mayo -0 and Mayo-1 score.

Methods: A prospective observational cohort study was carried out. Every adult UC patient referred to our Endoscopy Unit for a colonoscopy were consecutively included. Patients were asked to collect a small sample of feces within the 48 hours prior to bowel cleansing for colonoscopy. Fecal calprotectin was measured using a rapid test (Quantum blue®), which allows obtaining the result in less than 30 minutes. Mucosal healing was defined as an endoscopic Mayo sub-score of 0 or 1. Mayo-0 was defined as normal or inactive disease and Mayo-1 as presence of erythema, decreased vascular pattern or mild friability. A ROC curve analysis was applied to define the optimal FC cut-off value for mucosal healing. The correlation analysis between FC, endoscopic score and clinical activity was based on Spearman's correlation coefficient rank (r).

Results: 59 consecutive UC patients were prospectively included (mean age 47 years, range 21 to 74 years, 28 female). Thirty one patients (52.5%) were classified as Mayo 0, 12 (20.3%) as Mayo 1, 6 (10.2%) as Mayo 2 and 10 (16.9%) as Mayo 3. FC levels correlated with the Mayo endoscopic score (r = 0.677; p < 0.001). Median FC levels were 50µg/g for Mayo 0, 111µg/g for Mayo 1, 413µg/g for Mayo 2 and 1406µg/g for Mayo 3. FC as predictor of mucosal healing (Mayo 0 or 1) presented an area under the ROC curve (AUC) of 0.973 (95% IC = 0.893-0.998), and of 0.861 (95% IC=0.765-0.937) to predict endoscopic Mayo score 0. FC showed an ROC AUC of 0.782 (95% CI 0.634-0.930) to differentiate Mayo 0 from Mayo 1. A FC >35µg/g has a sensitivity of 72.2%, specificity of 84%, positive predictive value of 64.8% and negative predictive value of 88.1% to predict endoscopic activity.

Conclusions: FC is a good predictor of endoscopic activity in UC patients. Although patients with a Mayo sub-score of 1 present higher FC levels than those with Mayo sub-score of 0, FC is especially accurate to predict mucosal healing as defined by a Mayo score of 0 or 1.

P238
Accuracy of fecal calprotectin predicting endoscopic activity in Inflammatory Bowel Disease patients

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Background: Fecal calprotectin (FC) is a noninvasive marker of inflammation used in inflammatory bowel disease (IBD).

Aim: To evaluate the accuracy of FC to predict the presence of endoscopic activity in patients with IBD. To establish the best cut-off concentrations to predict endoscopic activity.

Methods: We prospectively included 88 patients with IBD who underwent an endoscopy for clinical indication. The Quantum Blue® Bühlmann kit was used to determine FC concentration. Two different kits, of low and high range, were used for each sample. Endoscopic activity was calculated by the Mayo endoscopic subscore for ulcerative colitis (UC), and the SES-CD for Crohn's disease (CD). CD patients with ileal disease whose ileum had not been examined during the endoscopy were excluded. Clinical activity was calculated by the partial Mayo score for UC and the Harvey-Bradshaw index for CD, and the values of various serum markers of inflammation (platelets, leukocytes, CRP and albumin) were recorded

Results: 88 patients have been included up to now. The concentration of FC was higher in UC patients with endoscopic lesions compared with those without endoscopic activity, with the low-range kit (216 ± 110 vs. 53 ± 61 mg/g, p<0.05) as well as with the high-range kit (635 ± 401 vs. 146 ± 149 mg/g, p<0.05). We also found statistically significant differences in the concentration of FC in CD patients with and without endoscopic activity, with the low (158 ± 113 vs. 77 ± 92 mg/g, p<0.05) and with the high-range kit (507 ± 474 vs. 223 ± 294 mg/g, p <0.05). The concentration of the different serological markers (platelets, leukocytes, CRP and albumin) was not different in patients with and without endoscopic activity. The area under the ROC curves of FC concentration for the prediction of endoscopic activity in UC were 0.88 and 0.86 with low and high-range kits, respectively, and 0.75 with both kits in CD. The best cut-off points for the detection of endoscopic activity in UC patients were 50 mg/g for the low-range kit (sensitivity 88%, specificity 86%, positive predictive value [PPV] 75% and negative predictive value [NPV] 91%) and 102 mg/g for the high-range kit (sensitivity 78%, specificity of 77%, PPV 74% and NPV 88%). In CD patients, the best cut-off points were 54 mg/g for de low-range kit (sensitivity 75%, specificity 72%, PPV 75% and NPV 71%) and 115 mg/g for the high-range kit (sensitivity 75%, specificity 71%, PPV 74% and NPV 78%).

Conclusions: The determination of FC concentration has good diagnostic accuracy for the detection of endoscopic activity in IBD (better for UC than for CD patients).

P240
Correlation between the Ulcerative Colitis Endoscopic Index of severity (UCEIS) and intestinal mucosal calprotectin (IMC) in acute severe ulcerative colitis.

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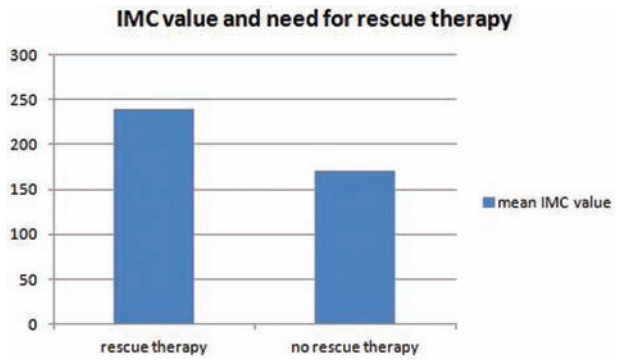
Background: Predicting the outcome of acute severe colitis (ASC) with endoscopic information has been examined using the Ulcerative Colitis Endoscopic index of Severity (UCEIS). Higher scores predict the need for rescue therapy, but this index has yet to be correlated with calprotectin, a marker of intestinal inflammation. Intestinal mucosal calprotectin (IMC) itself has yet to be examined as a predictor of outcome in ASC.

Methods: We retrospectively examined a cohort of 52 cases of ASC admitted between July 2010 and November 2012, using a database that included clinical parameters and UCEIS score on admission, inpatient management, response to therapy, and outcome defined as need for colectomy or rescue therapy with either infliximab or ciclosporin. Sections of archived biopsies taken during admission were stained for calprotectin using immunohistochemistry for the S100A8/A9 heterodimer. The IMC count was defined as the average number of calprotectin positive cells per 20x high power field (hpf) determined by counting 5 hpfs per specimen. IMC counts and other data were analysed using multivariate logistic regression. Relationships between UCEIS (range 0-8) and IMC count were analysed using Student's t-tests and rank sum Mann-Whitney tests as appropriate.

Results: 24/52 (46 %) patients had rescue therapy and 11/52 (21 %) underwent colectomy. In the entire cohort, the mean IMC count was 202 (SD ± 112, median 204, range 1 to 540). The UCEIS score was grouped into three: <4, 5-6 and 7-8. No significant differences in mean IMC numbers were found between the three UCEIS groups (171, 237, 183 positive cells/hpf with p-values 0.07, 0.71 and 0.24 respectively). IMC did not predict the need for colectomy (p= 0.10) (mean IMC count for colectomy and non-colectomy patients was 145 and 216 respectively). However, higher IMC counts were associated with rescue therapy (95 % CI 1.00-1.002; p=0.03) (mean IMC count for rescue therapy and non-rescue therapy patients 239 and 171 respectively). The odds ratio of having rescue therapy increased with the IMC; an increase by 50 calprotectin positive cells/hpf increased the odds by 1.54. On multivariate logistic regression analysis, a model that significantly predicted the need for rescue therapy included the IMC count, the UCEIS score, and age as predictors (p= 0.0008).

Conclusions: Intestinal mucosal calprotectin did not correlate with UCEIS in this small cohort, although it did predict the need for rescue therapy in ASC. IMC may therefore provide a valuable correlate in evaluating the severity of mucosal inflammation.



"Figure 1: Mean IMC count and the need for rescue therapy with ciclosporin or infliximab"

P241
Limitations in using fecal Calprotectin as a biomarker of IBD disease activity during Pregnancy

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Background: Inflammatory bowel diseases (IBD), mainly Crohn's disease (CD) and ulcerative colitis (UC), may affect young female patients, including their childbearing years. Managing patients with IBD during pregnancy can be challenging. An objective biomarker for disease activity could serve as an important decision making tool, and may render unnecessary invasive diagnostic procedures. Fecal calprotectin level is being used as a non-invasive bio-marker in IBD patients. However, its use in pregnant IBD patients, is not well validated. We aimed to evaluate the use of fecal calprotectin levels as a biomarker for disease activity in pregnant IBD patients.
Methods: A prospective study was conducted among pregnant women in our IBD MOM clinic. All clinical data including Partial Mayo score and Harvey Bradshaw index were calculated as well as fecal calprotectin, ESR, CRP and albumin values. Statistical analysis was done to assess the correlation between the fecal calprotectin levels, clinical scores and laboratories indexes.
Results: Study population included 33 pregnant women with IBD, twenty patients with CD and 13 with UC. Mean age was 29 ± 5 years. Mean calprotectin in UC and CD were 376 ± 218 and 241 ± 860 mg/kg, respectively. No differences were noted in calprotectin levels during the pregnant trimesters. Interestingly, no correlation was noted between calprotectin and clinical scores, albumin levels, ESR or CRP (p=0.285, p=0.986, p=0.327 and p=0.491, respectively).
Conclusions: This prospective study in pregnant IBD patients, demonstrated the limitations of using fecal calprotectin as a non-invasive biomarker for disease activity during pregnancy. Clinicians should be aware of this limitation, and further studies to validate such markers should be considered.

P242
Length of small bowel resection, SeHCAT retention value and frequency of diarrhoea: is there a link?

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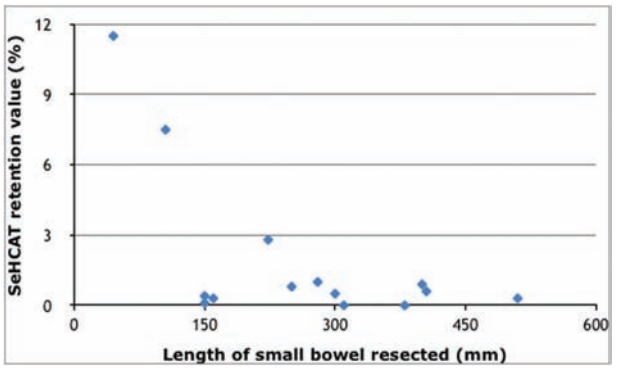
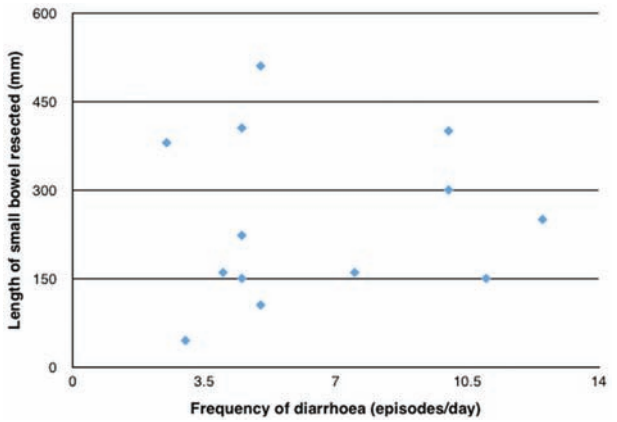
Background: Bile Acid Malabsorption (BAM) is a well-recognised cause of chronic diarrhoea, commonly secondary to ileal resection, Crohn's Disease or cholecystectomy. [1]
Selenium-75 labelled homotaurocholic acid test (SeHCAT) is used to measure bile acid absorption at Frimley Health Hospital.
We hypothesise that there is a correlation between the length of small bowel removed, SeHCAT retention value and frequency of diarrhoea. Anecdotal evidence suggests that had patients known about their risk of BAM and associated diarrhoea they may have opted for further medical treatment before undergoing surgery.



"Graph 1. Length of small bowel resected compared to SeHCAT retention value" "Graph 2. Frequency of diarrhoea compared to length of small bowel resected"



"Graph 2. Frequency of diarrhoea compared to length of small bowel resected"

Methods: A list was generated of all SeHCAT tests completed at Frimley Health Hospital between 2011-2014. The SeHCAT retention values were matched to out-patient clinic letters detailing the frequency of diarrhoea and previous surgical macro-histology reports.
Results: 341 SeHCAT tests were completed between 2011 and 2014, of which 23 had undergone a previous small bowel resection. 21 had a SeHCAT test of <15%, indicating an abnormal result. 6 patient's histology was unavailable and were therefore excluded.
80% of patients had a small bowel resection due to Crohn's Disease.

Conclusions: There is a statistically significant negative correlation between the length of small bowel resected and the SeHCAT retention value (correlation coefficient -0.56, P value 0.03),Graph 1. 21 (91.3%) of patients who had undergone small bowel resection had an abnormal SeHCAT result. We suggest that in patients with ongoing diarrhoea post small bowel resection due to Crohn's Disease,an empirical trial of bile acid sequestering agents should be tried as first-line, rather than a SeHCAT test which is highly likely to be positive. There is no relationship between the length of small bowel removed and frequency of diarrhoea in this study group. Symptom burden in this study population is an unreliable marker of BAM with no corrleation between frequency of diarrhoea and SeHCAT value. Recall bias and poor clinic documentation may have impacted on this and a prospective study with a larger patient sample would need to be undertaken.

A positive correlation between length of bowel resected and risk of BAM would improve the consenting process for surgery. Patients would be better informed about the risks of BAM diarrhoea post-surgery and guide treatment options.

References:

[1] Westergard H, (2007), Bile Acid Malabsorption, Treatment Options in Gastroenterology, 28-33, 10

P243
Prevalence of extraintestinal manifestations in paediatric patients with Inflammatory Bowel Disease: Results from the Swiss IBD Cohort Study

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Background: There is a paucity of data from large cohort studies on the prevalence and type of extraintestinal manifestations in pediatric patients with Crohn's disease (CD) and ulcerative colitis (UC). We aimed to assess the prevalence and type of EIM in pediatric patients with inflammatory bowel disease (IBD).

Methods: Data from patients enrolled in the Pediatric Swiss IBD Cohort Study (P-SIBDCS) were analyzed. Since 2008 the P-SIBDCS collects data on patients aged 2-17 from hospitals and private practices across Switzerland. Results of continuous data are reported as median and interquartile range.

Results: A total of 266 pediatric IBD patients were recruited (146 [54.9%] with CD, 63% boys, median [interquartile] age at diagnosis 12 [9.9-13.6] years, median age at enrollment 13.6 [11.7-15.3] years, median disease duration 3.3 [1.6-4.9] years, and 120 [45.1%] with UC, 47.5% boys, median age at diagnosis 11.5 [8.2-13.6] years, median age at enrollment 13.5 [10.9-15.3] years, median disease duration 3.2 [1.6-5.7] years. A total of 90 patients (33.8%) suffered from one to a maximum of three EIM during their disease course (74/90 patients [82.2%] had one EIM, 14/90 patients [15.6%] had two EIM, and 2/90 patients [2.2%] suffered from three EIM. EIM were more frequently observed in CD patients (61/146, 41.8%) when compared to UC patients (29/120, 242%, $p < 0.001$). The following types of EIM were observed: 37/266 (13.9%) peripheral arthritis / arthralgia (17.8% in CD vs. 9.2% in UC); 5/266 (1.9%) uveitis / iritis (2.7% in CD vs. 0.8% in UC; 26/266 (9.8%) oral aphthous ulcers (12.3% in CD vs. 6.7% in UC); 2/266 (0.8%) ankylosing spondylitis (0.7% in CD vs. 0.9% in UC); 5/266 (1.9%) erythema nodosum (2.7% in CD vs. 0.8% in UC); 2/266 (0.8%) pyoderma gangrenosum (0.7% in CD vs. 0.8% in UC).

Conclusions: EIM appear in pediatric IBD patients in similar prevalence when compared to the adult population. As a general rule, EIM are more frequently observed in pediatric CD patients when compared to pediatric UC patients. The most frequent EIM are peripheral arthritis / arthralgia, followed by oral aphthous ulcers.

P244
Performance of Tuberculin skin test in routine screening for latent tuberculosis infection in patients with inflammatory bowel diseases

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Background: Screening for latent tuberculosis infection (LTBI) before starting therapy with anti tumor necrosis factor (anti-TNF) antibodies has decreased the risk of active tuberculosis. Corticosteroids (CS) or immunosuppressive (IS) therapy may affect the performance of the Tuberculin skin test (TST). The aim of this study was to determine the likelihood of detecting LTBI using a 2-step TST in two cohorts of patients with inflammatory bowel diseases: candidates and non-candidates for anti-TNF therapy. We also analyzed factors associated with the performance of the TST.

Methods: This prospective multicenter case-control study included 240 consecutive patients selected for anti-TNF therapy and 326 controls. LTBI risk factors were recorded and patients underwent chest X-ray and 2-step TST. TST was considered positive if induration was ≥ 5 mm in the first or the second (booster) test. Factors associated with TST Results were analyzed by logistic regression.

Results: Ninety-three of 566 patients (16.4%) had a positive TST (21/93 [22.6%] in the second test). Twenty-three of 240 (9.6%) patients in the anti-TNF group and 70 of 326 (21.5%) in the control group had a positive TST (odds ratio [OR] 0.39; 95% confidence interval [CI] 0.23-0.64; $p<0.001$). The proportion of Crohn´s disease patients was higher in the anti-TNF group (169/240 [70.7%] vs. 180/326 [56.3%]; $p=0.002$). More anti-TNF group patients were receiving CS therapy (37.6% vs.

28.5%; p=0.023), IS therapy (64.6% vs. 34.6%; p<0.001), or CS+IS therapy (21.5% vs. 12.5%; p<0.001). The proportion of patients who had normal C-reactive protein (CRP) was lower in the anti-TNF group (38.3%) compared to the control group (64.5%; p<0.001). In the univariate analysis, positive TST was associated with age, Bacille Calmette-Guerin vaccination and mesalazine therapy. Negative TST was associated with CS therapy, IS therapy, CS+IS therapy, Crohn´s disease vs. ulcerative colitis, anti-TNF group vs. control group and elevated CRP. In the multivariate analysis, positive TST was associated with age while negative TST was associated with CS therapy (OR 0.32; 95% CI 0.15-0.70; p=0.004), IS therapy (OR 0.34; 95% CI 0.18-0.61; p<0.001) or CS+IS therapy (OR 0.16; 95% CI 0.06-0.40; p<0.001).

Conclusions: CS and IM therapy strongly negatively affected TST performance. As a result the likelihood of having a positive TST was lower in patients candidates for anti-TNF therapy than in controls. Therefore, current guidelines for TB screening prior to anti-TNF therapy appear inaccurate in patients under CS or IS. Patients should be screened for LTBI prior to initiation of CS or IS therapy. The second TST is useful because it increases detection sensitivity by 22%.

P245
Accuracy of fecal M2-Pyruvate Kinase compared with fecal calprotectin to assess endoscopic severity in patients with inflammatory bowel diseases

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Background: M2-Pyruvate Kinase (M2-PK) is a key dimeric enzyme involved in the glycolytic pathway and expressed in undifferentiated and proliferating tissues. Fecal M2-PK levels are increased in case of gut inflammation and therefore might represent a promising marker in inflammatory bowel diseases (IBD). We performed a head-to-head comparison of diagnostic accuracy of fecal M2-PK (fM2-PK) and fecal calprotectin (fCal) in predicting endoscopic disease severity in ulcerative colitis (UC) and Crohn's disease (CD).

Methods: A total of 78 consecutive patients with IBD (26 UC and 52 CD) undergoing an ileo-colonoscopy were prospectively enrolled. All patients provided fecal samples for fCal (Bühlmann) and fM2-PK (Schebo Biotech) measurements. Endoscopic disease activities were scored independently according to the SES-CD score and the Rachmilewitz index, respectively for CD and UC (active disease defined as both scores >2 points). Accuracies of both fecal markers were determined using AUROC curves and sensitivities (Sen), specificities (Spe), predictive values (PV) and overall accuracies (OA) were also assessed at adjusted cutoffs determined by the ROC curves. Spearman rank correlations were also calculated.

	Sen (%)	Spe (%)	PPV (%)	NPV (%)	OA (%)
fM2-PK					
CD (cutoff = 1.35 UI/mL)	48	62	65	45	53
UC (cutoff = 13.6 UI/mL)	89	85	94	75	88
fCal					
CD (cutoff = 250 µg/g)	51	95	93	61	71
UC (cutoff = 250 µg/g)	89	71	89	71	85

Results: Whereas fM2-PK concentrations did not differ between endoscopically active and inactive CD patients, levels of fM2-PK were significantly higher in active UC when compared with those measured in inactive UC patients. In contrast, fCal concentrations differed significantly both in patients with active CD and UC when compared with those in patients with inactive disease. Accuracies of fM2-PK and fCal to predict endoscopic activity were higher in UC (AUROC 0.95 and 0.93, respectively) compared with those in CD (AUROC 0.60 and 0.80, respectively). fM2-PK concentrations were significantly correlated with endoscopic severity scores in UC and at a lesser degree in CD (correlation coeff r=0.75 (p<0.001) and r=0.37 (p=0.006); respectively). In addition, fM2-PK and fCal concentrations were also significantly correlated for UC (r=0.83, p<0.001) and for CD (r=0.43, p=0.001). Sen, Spe, PV and OA of both fecal markers are summarized in Table1.

Conclusions: fM2-PK is a reliable, surrogate and promising marker, as or even more accurate as fCal, to identify UC patients with endoscopic active disease.

P246
Intracavitary contrast-enhanced ultrasound in evaluating fistula of Crohn's Disease: a preliminary study

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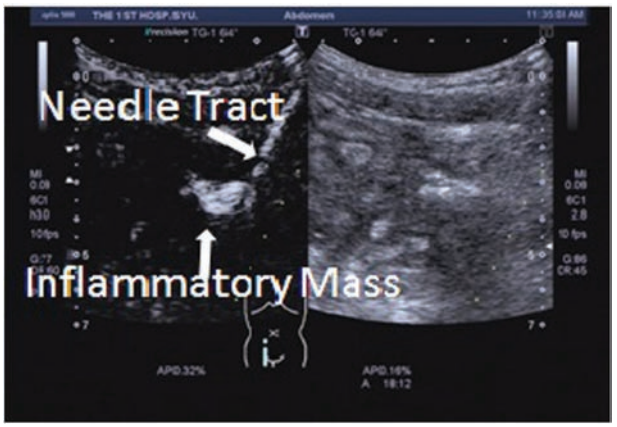
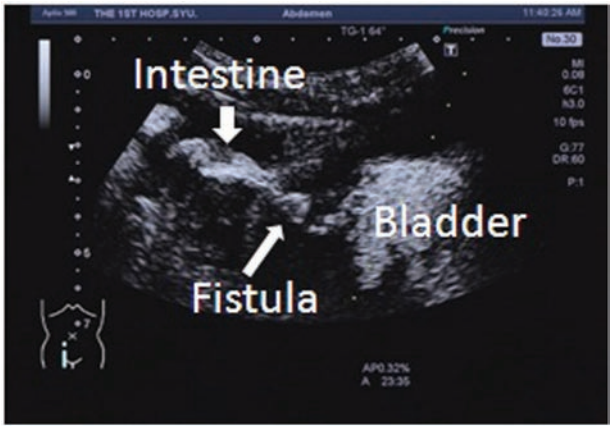
Background: Fistula is a common complication of Crohn's disease (CD), and accurate detection of fistula is of great clinical significance for guiding treatment. The aim of our study was to evaluate intracavitary contrast-enhanced ultrasound in detecting fistula of Crohn's disease using surgery as reference standard.

Methods: Six CD patients who were suspected to have fistula were enrolled in the preliminary study. The patients underwent intracavitary contrast-enhanced ultrasound by injecting the contrast agent into the cavity through percutaneous needle. The result were compared with CT enterography and gastrointestinal barium . The reference standard was surgical fingding.



"The Early Stage"



"The Late Stage"

Results: Among these six patients which were confirmed to have fistula intraoperatively, five fistulas were detected by intracavitary contrast-enhanced ultrasound including 3 cases with intestinal fistula and 2 cases with intestinal-bladder fistula (Figure.intestinal-bladder fistula was delineated by intracavitary contrast-enhanced ultrasound,the contrast agent perfused into the bladder after injection, the remaining one intestinal fistula was missed. All these six fistulas were not detected neither by CT enterography or gastrointestinal barium.

Conclusions: Our preliminary study showed that intracavitary contrast-enhanced ultrasound is feasible and accurate in detection of fistula. Because of non-ionizing radiation , it could be used as a novel method in evaluating disease behavior of CD.

P247
C-reactive protein is elevated with clinical disease activity during pregnancy in women with Inflammatory Bowel Disease

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Background: Inflammatory bowel disease (IBD), Crohn's disease (CD) or ulcerative colitis (UC), is a chronic inflammatory condition of the gastrointestinal tract that affects women in their reproductive years. Women with IBD have a risk of flaring their IBD during pregnancy, which is associated with worse maternal and fetal outcomes. C-reactive protein (CRP) is often used as a marker of IBD disease activity, but CRP can also be elevated during healthy pregnancies. In other words, it is unclear whether CRP can be used as a non-invasive biomarker of clinical disease activity in pregnant women with IBD.

The objective of this study was to determine if an elevated CRP is associated with clinical disease activity during pregnancy among women with IBD.

Methods: Female IBD patients (18 to 45yrs) were enrolled preconception (PC) or at each trimester of pregnancy (T[n]). At each clinic visit, women were grouped by clinical disease activity, using the Modified Harvey Bradshaw Index (mHBI) for Crohn's disease, and the partial Mayo score (pMayo) for ulcerative colitis. Women with a mHBI>5 or a partial Mayo score >2 were identified as having clinically active disease. CRP was also measured at each clinic visit; only patients who had previously documented CRP elevations (levels greater than 8.00 mg/L) with flares of their IBD were included for analysis. To examine the association of CRP with clinical disease activity, we compared CRP in women with clinically active and non-active disease, at each visit.

Results: Twenty-three women (13 UC and 10 CD) with median age 29.0 yrs who were seen over 52 clinic visits were included for analysis. There were 14 PC visits, 12 T1 visits (median gestational age 9.22 weeks), 13 T2 visits (median gestational age 20.57 weeks), and 13 T3 visits (median gestational age 31.86 weeks). The median CRP was numerically higher in women with clinically active disease compared to those with clinically inactive disease at PC (6.95 vs 2.80 mg/L; p=0.559) and T1 (24.75 vs 6.00 mg/L; p=1.000), respectively. However, the median CRP was lower in women with clinically active disease compared to those with clinically inactive disease at T2 (8.85 vs 12.40 mg/L; p=0.5923), and T3 (5.45 v. 11.90 mg/L; p=0.592), respectively.

Conclusions: Women with IBD who had clinically active disease during preconception and the first trimester of pregnancy had numerically higher CRP levels than women who had clinically inactive disease. This suggests that CRP remains a potential tool for assessing IBD disease activity in the early trimesters of pregnancy.

P248
Non-invasive Methods for monitoring mucosal healing in paediatric ulcerative colitis with usage of faecal calprotectin.

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Background: Faecal calprotectin (FC) is a good marker in monitoring mucosal healing in adults with ulcerative colitis. Its concentrations in faeces is closely related to state of mucosa observed in endoscopy. There are a few studies concerning FC in mucosa status assessment in paediatrics population with UC. The aim of the study was to assess the usefulness of FC as a biomarker of endoscopy proven mucosal healing in monitoring of children with UC.

Methods: 66 patients with UC (F 36, M 30, ±14,16 years) were involved to the study and had elective colonoscopy performed, FC level and erythrocyte sedimentation rate (ESR) within a week before endoscopy measured. Each patient had also body mass index (BMI) and paediatric ulcerative colitis activity index (PUCAI) calculated. Mucosa status during endoscopy was assessed with Baron score. Full mucosal healing was defined as Baron score=0. We have identified two subgroups: those with full mucosal healing, and patients with inflamed gut mucosa. The receiver operating characteristic curve (ROC) was used as a statistical method to establish cut-off points. The cut-off points are calprotectin threshold for simple model and posterior probability threshold for the linear discriminant analysis (LDA). The area under the curve (AUC) assesses the differentiation quality of the study group based on the model score. To increase sensitivity at high specificity the LDA with FC, ESR, BMI and PUCAI was taken.

Results: AUC for the simple model was 0,90. The selected cut-off level of discrimination between subgroup with full mucosal healing vs. subgroup with mucosal inflammation present was 189 µg/g with sensitivity 0,96 and specificity 0,75. When specificity was outweighed over sensitivity the cut-off point was 62 µg/g with sensitivity 0,50 and specificity 0,95. Due to the low sensitivity accompanying high specificity we used LDA with other parameters to increase sensitivity

rate. With LDA used on FC, ESR, BMI and PUCAI the AUC was 0,90, and we could discriminate our patient with sensitivity 0,61 and specificity 0,97.

Conclusions: FC is a good marker of mucosal healing in monitoring of children with UC. FC above 189 µg/g enable to select 75% of patients with active inflammation in gut mucosa. LDA with FC, ESR, BMI and PUCAI let us select 61% of patients with full mucosal healing. Using these two Methods, step by step, we could discriminate patients with unknown mucosa status, that requires endoscopy.

P249
Worries in IBD patient relatives. Why and how much do they worry?

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Background: The Rating Form of IBD Patient Concerns (RFIPC) is a self-administered questionnarie covering 25 important worries graded from 0 to 100 with a horizontal visual analogue scale. These ítems can be resumed in factors. IBDQ32 expresses HRQoL in IBD patients. We want to establish the worries and concerns in IBD relatives, to compare relatives and patients worries and to analyze predictor for a high relative RFIPC sum score.

Methods: From June to September 2014 70 IBD patients with one relative or friend were asked to participate in our study. Finally 61 patients (22 UC and 39 CD) and 51 relatives accepted. The colaboration consisted in some basic questions, IBDQ32 and RFIPC answered by the patient and RFIPC answered by the relative. Five factors were identified with RFIPC factor analysis: "consequences", "social aspects", "intimacy/couple relationship", "surgery/assistance" and "physical appearance". Patient clinical data were obtained from medical charts. Spearman correlation and Wilcoxon test were used to compare patients and relatives factor and mean RFIPC sum scores. We analyzed predictors for a high relative RFIPC sum score with univariant and multivariant lineal regression analysis.

Results: Patients and relatives RFIPC sum scores were similar (47,1 DS19,8 vs 49,1 DS19,6, pNS). The factor with a highest score was "surgery/asistance" for patients and "consequences" for relatives. Relatives had a higher score than patients in the factor "consequences" (65,8 DS22,4 vs 56,7 DS23,5 p 0,019). "Medicine adverse event" was the most worrying item for patients (70,3 DS29,3) and "cancer risk" was the most worrying ítem for relatives (79,4 DS28,3). Spearman test showed correlation betwen patients and relatives in factors: "consequences" (r 0,299 p 0,039), "social aspects" (r 0,459 p 0,001), "intimacy/couple relationship" (r 0,327 p 0,021) and "surgery/assistance" (r 0,286 p 0,044). There was also Spearman correlation in 11 of the 25 items. Type of relationship, relative sex, time from the last corticosteroid treatment, time from surgery, patient RFIPC sum score and 11 of 32 IBDQ32 items predicted of a higher relative RFIPC sum score in the univariant analysis. Time from surgery and three (emotional) items in IBDQ32 were independent predictors of a higher relative RFIPC sum score.

Conclusions: Relatives and patients worries are not strictly the same. Relatives seem to worry about consequences of the disease more than patients. Some aspects of medical history and emotional aspects of patient QoL predict a higher relative RFIPC score.

P250
Validation of the Portuguese version of a questionnaire for the assessment of healthcare quality from the point of view of a patient with inflammatory bowel disease (QUOTE-IBD)

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Background: The perspective of patients on the healthcare they receive has become increasingly important in the assessment of quality of healthcare, especially in chronic diseases such as inflammatory bowel disease (IBD). A questionnaire to measure quality of care through the eyes of patients with inflammatory bowel disease (QUOTE-IBD) has been designed and validated specifically for the English language and culture. The objective was to translate the QUOTE-IBD into Portuguese and to determine its validity, reproducibility and acceptability.

Methods: Observational longitudinal unicentric study with 3 sequential phases: 1) translation and cultural adaptation of QUOTE-IBD and assessment of its comprehensiveness; 2) assessment of validity through determination of Spearman's correlation coefficient between scores of the QUOTE-IBD (composed by 23 items that together represent Overall Care and are grouped in 8 dimensions - Accessibility, Accommodation, Autonomy, Continuity of Care, Competence, Costs, Courtesy and Information - which are assessed according to performance, importance and quality impact) and visual analog scales (VAS); 3) assessment of reproducibility through a second administration of the questionnaire to stable patients, at a minimum 4-week span.

Results: One hundred and fourteen patients with IBD (77 with Crohn's disease and 37 with ulcerative colitis) participated in the study. The Spearman's correlation coefficient between the Overall Care score and the VAS was positive and significant both for Performance and Quality Impact (table 1). The same was observed for the dimensions Accessibility and Information (table 1). Thirty-four (30%) patients completed the questionnaire in the second round. The Spearman's correlation coefficient for Overall Care score between the first and second rounds was positive and significant, both for Performance and Quality Impact (table 2). The same was observed for the dimensions Accessibility, Continuity of Care, Courtesy and Information (table 2). Only 3 items regarding Performance had response rate below, but very close to, 90%.

Conclusions: The Portuguese version of the QUOTE-IBD is a valid, reproducible and acceptable instrument for the assessment of quality

"Validity of QUOTE-IBD: Spearman's correlation coefficient for Performance and Quality Impact between dimensions of QUOTE-IBD and VAS."

	Quality Impact	n	Performance	n
Overall Care	.33***	114	.35***	114
Accessibility	.45***	112	.42***	112
Accommodation	.10	113	.09	113
Autonomy	n/a		n/a	
Continuity of Care	.17	113	.15	113
Competence	-.05	112	-.05	112
Costs	n/a		n/a	
Courtesy	.08	111	.16	111
Information	.22*	112	.20*	113

*p < .05; **p < .01; ***p < .001; n/a - not applicable because these dimensions are composed by only 1 item

"Reproducibility of QUOTE-IBD: Spearman's correlation coefficient for Performance and Quality Impact of dimensions of QUOTE-IBD between round 1 and 2 (34 patients)."

	Quality Impact	Performance
Overall Care	.55**	.62***
Accessibility	.56**	.54**
Accomodation	n/a	n/a
Autonomy	n/a	n/a
Continuity of Care	.41*	.39*
Competence	.22	.27
Costs	.27	.53**
Courtesy	.53**	.49**
Information	.49**	.49**

*p < .05; **p < .01; ***p < .001; n/a – not applicable because there was no variance in these dimensions.

of Overall Care from the point of view of Portuguese patients with IBD.

P251
Diagnostic delay in IBD: a comparison in the last thirty years, an Italian multicentric study

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Background: IBD patients are still under-diagnosed or diagnosed with serious delay. The aim of our study was to examine whether diagnostic delay in IBD has changed over the last thirty-three years and to investigate its correlation with Crohn's disease (CD) phenotype and Ulcerative Colitis (UC) location at diagnosis.
Methods: Cases included all IBD patients recorded in the registry of four IBD referral Centres in Italy. Diagnostic delay was calculated from the onset of the symptoms indicative of CD or UC to the definitive diagnosis. Data reported included date of birth, gender, IBD location and CD behavior at diagnosis, according to the Montreal classification.
Results: Of 3393 IBD patients, 2499 (74%) had a diagnostic delay ≥ 1 month, 1046 (31%) ≥ 12 month. Median diagnostic delay was 3 months (7 months in CD e 2 months in UC). Mean diagnostic delay was 19 month, standard deviation (SD) 45, (significantly higher in CD than UC, 29 vs 11 months,SD 54 vs 34, p<0.0005). In CD, mean diagnostic delay was higher in patients with penetrating/stricturing behavior at diagnosis (n=870) compared to patients with inflammatory behavior at diagnosis (n=667), (32 vs 23 month,SD 49 vs 57, p<0.0005).
242 patients were diagnosed between 1952-1979 (historical cohort), while 3151 were diagnosed between 1980 and 2013 (modern cohort). Mean diagnostic delay was significantly higher in the historical cohort in comparison to the modern cohort (31 vs 18 month,SD 58 vs 44, p<0.0005).
IBD patients belonging to the modern cohort were stratified according to the time of diagnosis into three subgroups (1980-89, 1990-99, 2000-13). There was no significant difference in the mean diagnostic delay between the three periods (18, 17 and 19 months, SD 41,37 and 50 respectively).
No significant difference was found in the mean diagnostic delay according to gender or disease location at diagnosis.
Conclusions: Diagnostic delay in IBD was significantly decreased in recent years (1980-2013) in comparison to the past (1952-1979), however it did not change over the last thirty-three years, despite increasing the diagnostic tools.
Compared with UC, diagnostic delay is higher in CD, especially in patients with penetrating/stricturing behavior at diagnosis.

P252
Fulminant hepatic failure requiring transplantation after initiation of infliximab therapy in Ulcerative Colitis

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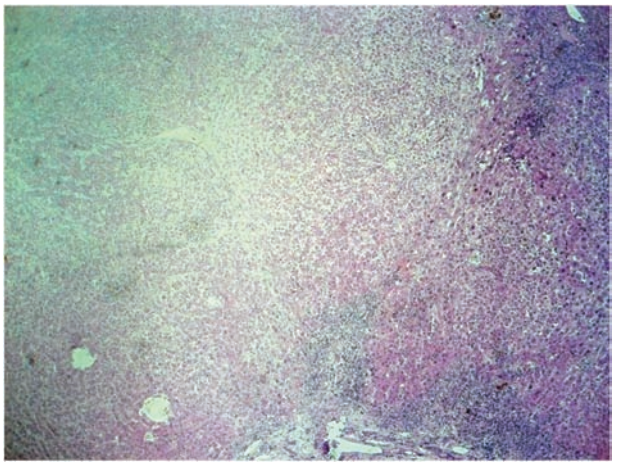
Background: Antibodies against tumor necrosis factor alpha, such as Infliximab (IFX) have a well-established efficacy in the treatment of inflammatory bowel diseases. However, they have been associated with drug-induced liver injurt (DILI)
Methods: We report a 38-year-old female with refractory UC that developed fulminant hepatic failure temporally linked to initiation of IFX, which required urgent liver transplantation
Results: Baseline liver function were entirely normal. Routine laboratorial exams after last IFX infusion showed increase in transaminases levels. There was no history of alcohol abuse or infection or other drugs. Serology for hepatitis B and C viruses, HIV, CMV and EBV were negative. Abdominal ultrasound was normal. No serum smooth-muscle, anti-nucleic, or antimitochondrial antibodies could be detected. Following, the patient developed fatigue and jaundice. At this time the exams showed severe cholestasis. Nuclear magnetic resonance demonstrated liver damage. The patient was transferred to the liver transplant unit, where the clinical condition further deteriorated. Grade III hepatic encephalopathy was observed 5 days after admission to the transplant unit. Liver transplant (LT) was performed 2 days later. The liver biopsy revealed extensive necrosis compatible with fulminant hepatic failure. The patient got well and was discharged 12 days after LT. Her hepatic function tests slowly normalized.



"Hepatic necrosis. H&E staining, original magnification 10x"

Conclusions: IFX has been reported to induce acute liver failure by at least three mechanisms: induction of autoimmune hepatitis, cholestatic liver injury and direct toxicity. Considering the exclusion of main liver diseases, the temporal correlation between infliximab exposure and laboratorial changes, an IFX-induced hepatitis diagnosis was admitted. Current consensus guidelines recommend baseline liver function tests with a hepatic risk factor screen (hepatitis serology, auto-antibodies) prior to onset of therapy. It is suggested screening for liver dysfunction at 4-month intervals and discontinuation of IFX therapy if transaminase levels reach three times the upper limit of normal. This study highlights an important and potentially lethal complication of IFX therapy and reinforces need for caution and increased vigilance in prescreening and ongoing surveillance for patients on IFX

P253
De novo Inflammatory Bowel Disease following paediatric liver transplantation: A case series of three patients and world literature review

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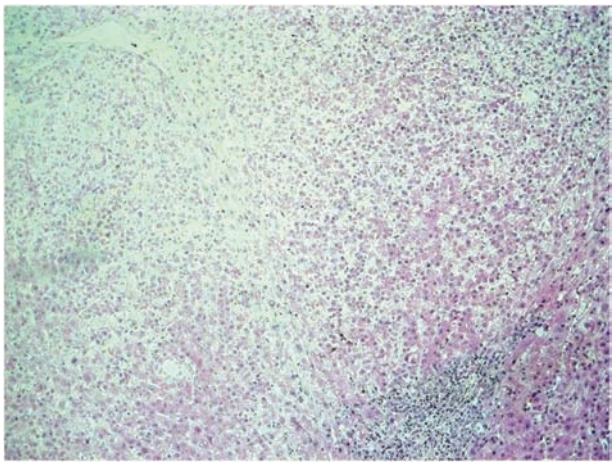

"Hepatic necrosis. H&E staining, original magnification 20x"

Background: Inflammatory Bowel Disease (IBD) is a T-cell driven inflammatory process due to inappropriate and enduring activation of the enteric immune system, generally treated with immunosuppressant therapy. Following solid organ transplantation (SOT), recurrent and de novo IBD have been described despite immunosuppressive therapy. The majority of cases in adult patients occurred post liver transplantation (LT) (136/175) with 96/136 cases reported having been originally transplanted for sclerosing cholangitis (SC) or autoimmune hepatitis (AIH). In paediatrics, 14 cases have been described post liver, heart and renal transplant. 9 cases have been described post LT (3/9 cases transplanted for SC/AIH). Various risk factors have been implicated in the development of post-transplant IBD. Herein, we describe 3 cases of de novo IBD post LT for causes other than SC/AIH.

Methods: Case 1 was the index case and the other 2 patients were identified through an electronic search of the Birmingham Liver Unit Paediatric Transplant database that holds the data of 782 patients who have undergone a liver transplant between 1983 and 2014. Medline and Embase were searched for "de novo inflammatory bowel disease" and "transplantation". The search was extending by scanning reference lists of related articles and free text web search. A total of 46 articles were included in the systematic review.

Results: 3 patients (2 females) were identified with de novo IBD following LT. 2 patients were originally transplanted for a1 antitrypsin deficiency and 1 for extra-hepatic biliary atresia. Risk factors for the development of post LT IBD are shown in table 1.

Mean age at the time of de novo IBD diagnosis was 7.3 years (range 3-11 years) with a mean of 4.6 years post LT. Diarrhoea was the presenting symptom in 2 patients and intermittent rectal bleeding in 1. All patients were investigated for possible IBD according to Porto criteria. The patients underwent on average 2.6 upper and/or lower GI endoscopies prior to diagnosis, while the time of presentation to diagnosis varied from 3 months to 1 year. Crohn's Disease was diagnosed in 2 patients and Indeterminate Colitis in 1. Infliximab was used in 1 patient while the other 2 were treated with 5-aminosalicylic acids. All patients are in clinical remission.

Conclusions: De novo IBD does occur following liver transplantation in children but is rare. De novo IBD should be considered in the differential diagnosis of chronic diarrhoea post-transplant.

Risk Factors for De Novo IBD and Immunosuppressive Rx before and after De Novo IBD Diagnosis

	Case 1: Crohn's disease	Case 2: Indeterminate Colitis	Case 3: Crohn's disease
CMV mismatch (donor / recipient)	-ve/-ve	+ve / -ve	-ve/-ve
CMV infection post LTx	No	No	No
Acute / Chronic Rejection	No / Yes	No / No	No / No
Biliary stasis	No	No	No
PMHx of Autoimmunity	No	No	No
FHx of Autoimmunity	No	No	No
Immunosuppression at presentation with de novo IBD	Tacrolimus, Prednisolone, MMF	Cyclosporine	Cyclosporine
Immunosuppression after diagnosis with de novo IBD	Tacrolimus, Prednisolone, AZA	MMF, Prednisolone	MMF, Prednisolone
Other IBD Tx following diagnosis	Infliximab	Mesalazine	Mesalazine

P254
Use of immunomodulators reduces early readmission in patients admitted to hospital with an acute flare of inflammatory bowel disease.

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Background: Acute exacerbations of inflammatory bowel disease carry a negative prognosis for the patient and their disease trajectory, and significantly increase costs to the healthcare system. Immunomodulators have been shown previously to be the initial treatment of choice for maintenance of remission in Crohn's disease and ulcerative colitis [1], but are only sporadically prescribed in the initial hospitalization of a patient with IBD exacerbation or new diagnosis of IBD.

Methods: We analysed the case notes of all patients admitted to Southmead Hospital, Bristol during 2014 with a flare or new diagnosis of IBD (identified via coding data as codes K50 or K51). We identified a number of factors associated with the patients' admission and sought to identify those which predicted admission, length of stay and 30 day readmission rates.

Results: 54 patients were identified that matched the selection criteria. The mean age was 43.7 years (range 17 to 85). 24 males and 30 females were identified. The median length of stay was 10 days (range 2-69). 36 had Crohn's disease and 18 ulcerative colitis.

Younger patients were more likely to be admitted with terminal ileal Crohn's disease (p=0.001) and indeed this diagnosis represented 30% of all admissions with an IBD flare.

Immunomodulator prescription in hospital was the most significant predictor of no readmission at 30 days (p=0.002). This was particularly significant in Crohn's disease with only 3/22 patients who were taking an immunomodulator being readmitted. There was no significant association of biologic use (p=0.361), steroid use (p=0.358) or surgery (p=0.621) with 30 day readmission.

Length of stay was shorter in patients admitted to a specialist gastroenterology ward (p=0.005), and significantly more patients on a gastroenterology ward received steroid therapy (p=0.048).

Conclusions: We present a real-world snapshot of admissions with acute inflammatory bowel disease to a large district general hospital. Of particular interest is the observation that immunomodulator therapy is strongly associated with no readmission at 30 days. This is plausible given the role of these drugs in maintenance of disease remission. The resultant message to clinicians is clear; the use of an immunomodulator as early as possible during the index admission of a patient admitted with a flare of IBD has the potential to reduce the burden of morbidity and associated healthcare costs from IBD flares.

[1] Dignass. A. et al. Second European evidence-based consensus on the diagnosis and management of ulcerative colitis Part 2: Current management. Journal of Crohn's and Colitis (2012) 6, 991-1030

P255
Proximal extension rate of distal disease in Ulcerative Colitis

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Background: Long term proximal extension (PE) of distal disease in Ulcerative Colitis (UC) has been variously assessed

Methods: To determine the incidence, characteristics and predictive factors of PE of distal lesions of UC, we have reviewed the outcome of 324 UC patients hospitalized from 1/1/1989 to 31/12/1998 and followed-up at least during 10 years after diagnosis or until colectomy. All patients underwent complete investigation at diagnosis and clinical controls every 6 or 12 months and on demand. The cohort included 168 females (51,8%) and 156 males (48,2%); mean age at diagnosis : 32,6 years; 22,4% were active smokers and 8,6% previous smokers. At diagnosis 54 patients (16,6%) had Proctitis (PR), 207 (63,8%). Left Sided Colitis (LSC) and 63 (19,6%) Extensive Colitis (EC). 192 patients (59,3%) received only Aminosalicylates, 132 (40,7%) Corticosteroids and 46 (14,1%) Immunosupresive drugs (ISD). Statistical Analysis X2 and Fisher's exact tests.

Results: - PE was evaluated from 0 to 1, 1 to 5, 5 to 10 years (y)

- PR remained stable from 0 to 1 y; extension of disease to LSC was noted in 7 cases (13%) at 5 y and in 5 patients (9,2%) at 10 y; extension to EC was observed in 5 cases (9,2%) at 10 y. Total PE of PR : 31,5% at 10y
- Progression of LSC to EC was noted in 13 patients (6,3%) from 0 to 1 y, in 27 cases (13%) from 1 to 5 y and 23 cases (11,1%) at 10y. Total PE of LSC: 30,4% at 10y Regarding to predictive factors of PE : 1/there was no influence of age (p=0,9994), gender (p=0,9208) smoking habits (p=0,7609), need for corticosteroids (p=0,6088) or severity of the initial flare (p=0,3755). 2/on the contrary severity the disease on the long term (p<0,0001) and need for ISD (p<0,0001) were predictive factors for PE.

Conclusions: In that 10 year follow up study PE of PR and LSC in UC has been noted in 24,7% of cases and was strongly associated to severity of disease and need for IS drugs.

P256
Characterization of de novo colonic stricture due to Crohn's Disease

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Background: The development of colonic stenosis is a rare complication of Crohn's disease (CD) without a surgical anastomosis history. So, the management and long-term follow-up Results of colonic stricture due to CD have not been clearly defined. In this study, we aimed to characterize de novo colonic stricture due to CD.

Methods: We evaluated 702 patients with CD to investigate colonic stricture. Colonic stricture was considered to exist when passage of a standard colonoscope was not possible and was diagnosed radiologically and endoscopically in this study.

Results: Of the 702 patients, 14 had colonic stricture according to the definition above. Of the 14, 8 were male. The interval between diagnosis of disease and recognition of the stricture varied from 0 to 13 years. Localization of the strictures differed from the rectum to cecum. Of the 14, 3 patients had more than 1 stricture. Pathological examination of the stricture(s) did not show dysplasia or malignancy initially or during the follow-up.

Conclusions: De novo colonic stricture due to CD is a rare condition according to the presented study's Results. Distribution of the stricture(s) varied from the rectum to cecum without increased colonic cancer risk. We observed the antifibrotic role of thiopurines and biologic agents in this study.

P257
Data on Surgery in Paediatric IBD (pIBD) over a 4 year period using the ImproveCareNow (ICN) Collaboration data base

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Background: Paediatric Inflammatory bowel disease (pIBD) is commonly severe. The natural history pIBD is varied and can result in surgery to control unremitting disease. Colectomy rates(CR) of up to 20% have been reported by other centres. Previous data on Ulcerative Colitis (UC) patients at our center was 3.6%. Our centre joined Improve Care Now (ICN) in 2010 where we could benchmark our clinical outcomes against 66 other pIBD centres.

Methods: All surgical procedures performed were captured from our ICN database over a 4 year period in 283 paediatric patients (167 male, range 0.4y -16y, median 9.7y). 54% had Crohn's disease, 23% ulcerative colitis and 23% indeterminate colitis/IBDU.

Results: All patients received standard pIBD treatment, escalating to biologic treatment on relapse. This aggressive approach lead to 5 (1.7%) of 283 IBD patients requiring surgery.

P1 (15y) had intractable fistulating Crohn's disease (CD) requiring a laparoscopic total colectomy/terminal ileum resection, developing peristomal fistulae, requiring further revision.

P2 (13y) with Crohn's-like IBD had spontaneous perforation, needing defunctioning ileostomy.

P3 (11y) had intractable ulcerative colitis (UC, 1/66, 1.64%) requiring subtotal colectomy

P4 (14y) had IBD unclassified (IBDU) with CD-like features with transfusion dependence, requiring subtotal colectomy/ileostomy formation.

P5 (8y) had intractable right-sided/TI CD requiring right hemicolectomy/loop ileostomy formation. Due to on-going small bowel inflammation, stoma ulcerations and rectal prolapse, stem cell transplant treatment was given and reconstructive surgery at our centre was performed one year later achieving continuity and being off all immunosuppressive medication.

Conclusions: In our institution surgical interventions rates are only 1.85 % of patients identified within the ICN database having received early and aggressive immunomodulatory and immunosuppressive treatment.

P258
Prevalence of anemia at presentation in pediatric Crohn's Disease patients: single center experience

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Background: Anemia is a frequent extra-digestive manifestation of inflammatory bowel disease (IBD), in both pediatric and adult patients with IBD and especially in Cronh's disease (CD). Iron deficiency (IDA) and anemia of chronic disease (ACD) play a major role in these patients. Although prevalence of anemia in IBD in adult patients has been reported in different settings (active disease vs disease in remission, hospitalized vs ambulatory patients), its true prevalence in pediatric patients is not yet well known and recent studies suggest it may be higher than in adult patients.

This study aimed to evaluate the prevalence of anemia (global prevalence, IDA and ACD prevalence) in newly diagnosed CD pediatric patients in a single pediatric center.

Methods: Retrospective and descriptive study of newly diagnosed pediatric CD patients referred to a Gastroenterology Pediatric Unit during January 2001-November 2014. Anemia was defined according to OMS criteria. Distinction between IDA and ACD was established according to hematological parameters, serum ferritin, transferrin saturation and ESR. Symptoms previous to diagnosis, Paris classification and disease activity (PCDAI) were determined in all patients and data collected from clinical registries.

Results: During the study period, CD diagnosis was established in 56 pediatric patients (33 male), median age: 17 years (25-7), median age at diagnosis: 12 years (18-0,2); median follow-up time is currently 54.5 months (166-1,2). Concerning anemia diagnosis, 42 patients were included (14 excluded - missing data). At presentation, anemia was documented in 32 patients (76,2%). Ten patients (all with mild disease) had no anemia at diagnosis (median hemoglobin (Hb) 13,8g/dL [16,1-12,7], ferritin 69mg/dL [125,8- 26,1] and ESR 31mm/h [62-8]). Of the 32 patients with anemia, 16 (50%) had IDA (median Hb 10.7g/dL [11,9-7,2], median ferritin 34,7mg/dL [75,2-4,1] and median ESR 46mm/h [93-2]); considering disease activity (11/16)-moderate:8, mild:3; and 6 of them (6/16, 37,5%) had ileal involvement. Sixteen patients had ACD (median Hb 10,9g/dL [12-7,7], median ferritin 220mg/dL [850-108,4], median ESR 71mm/h [120-11]); regarding disease activity (14/16)-severe:2, moderate:9, mild:3; and 9 of them had ileal involvement (9/16, 56,3%).

Considering duration of symptoms before diagnosis, patients with anemia had a median duration of 3 months (87-0) and patients without anemia a median of 2 months (41-0).

Conclusions: The Results of this single center study are consistent with the current scientific evidence. As expected, both IDA and ACD anemia were frequent at pediatric CD presentation, although ACD was more prevalent in patients with more active disease. A similar disease location was observed in both IDA or ACD patients.

P259
Improvement of Patient's Disease Activity in Paediatric Inflammatory Disease (pIBD) after adoption of ImproveCareNow (ICN) Quality Improvement (QI) Tool

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Background: ImproveCareNow (ICN) a QI program benchmarking patient visit outcomes against currently 66 pIBD centres, monitoring 18 000 pIBD patients in a live database. Agreed outcomes include Clinical Remission, Steroid-free remission, Nutrition and Growth, Disease Classification and Treatment. We joined ICN in 2010, allowing us to look at our patient's outcomes. Our aim is to report improvements from adoption of ICN quality improvement tool benchmarking ourselves against agreed international standards.
Methods: 270 IBD patients (P) (154 male, 0.4m-16years, median age at diagnosis 9.7y) were registered over a 4 year period. Data was collected prospectively with each clinic visit and entered into the database. This included diagnosis, nutrition, anthropometrics, Results, medication and physicians global assessment (PGA). The QI tool required pre-clinic planning meetings and Results were stratified allowing implementation of approved treatment plans. Monthly QI meetings set/review 90 day goals enabling service development. Results were stratified and discussed within weekly meetings, where individual treatment plans were initiated. Monthly QI meetings set and reviewed outcome goals.
Results: Over a 4year period the following outcome measures were achieved: Overall remission rates increased from 46% to 78%, Steroid-free remission increased from 60% to 92%, Satisfactory nutritional status increased from 82% to 97%, Satisfactory growth from 92% to 96%, Nutritional failure decreased form 9% to zero, Mild disease activity decreased from 23% to 16%, Occurence of moderate to severe disease activity decreased from 31% to 6% and has been consistently below 10% over the last year.
Conclusions: By adopting the ICN standards and utilizing the QI tool, we achieved measurable improvement of pIBD outcomes, using accurate collection and monitoring of data (24-hourly updated reports) and benchmarking against set standards, allowing us timely intervention. Patient care was standardized. Overall ICN has dramatically improved patient outcomes.

P260
Virtual chromoendoscopy with FICE is superior to standard colonoscopic surveillaillance for flat visibile dysplasic lesions and raised lesions (polyps and pseudopolyps) evaluation in long-standing ulcerative colitis: a prospective, randomized, trial.

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Background: Conventional surveillance colonoscopy in long-standing ulcerative colitis (UC) is based on multiple random biopsies and targeted biopsies of suspicious lesions, but its diagnostic yield has been criticized in favor of dye-based, targeted chromoendoscopy. No studies have analyzed the performance of the Fuji Intelligent Colour Enhancement (FICE) in this setting. We compared FICE with standard white light endoscopy (WLE) for the surveillance of long-standing UC in a prospective, randomized, single-operator, parallel study.
Methods: Consecutive patients with long-standing (≥ 8 years) UC, scheduled for surveillance colonoscopy, were randomized to withdrawal with FICE or WLE. All procedures were performed by a single operator. At least one raised lesion for each patient was required for inclusion, as a sample size of at least 100 raised lesion in each arm. In both arms, four types of histological samples were obtained for dysplasia detection: 1) quadrantic every 10 cm, random, biopsies from otherwise normal flat mucosa, 2) targeted biopsies of flat visible lesions, 3) targeted biopsies or removal of suspicious raised lesions, and 4) targeted biopsies of unsuspicious raised lesions. True and false positive lesions, false negatives as well as sensitivity, specificity, positive- and negative-predictive value and accuracy were compared between FICE and WLE, overall and for each type of histological sample collection.
Results: 91 patients were randomized to FICE (n=41) or WLE (n=50). No dysplasia was found in each arm from random biopsies of "normal" flat mucosa (0/879 FICE, 0/888 WLE), while flat visible lesions were found only by FICE (6 suspicious lesions, of whom 5 true dysplasic lesions). 132 raised lesions were analyzed in each arm: 19 and 12 were judged suspicious by FICE and WLE, respectively, but true positives were higher using FICE than WLE (15/19 vs 5/12; p=0.0346). Among unsuspicious raised lesions, a not significant higher rate of false negatives for dysplasia were found using WLE (3/120; 2.5%) than FICE (1/123; 1%).
Sensitivity of FICE was higher than WLE, both overall and after exclusion of random biopsies (95% vs 63% in both cases; p=0.0000). Specificity was significantly higher using targeted biopsies of flat visible and raised suspicious lesions than when including also random biopsies, both with FICE (96% vs 11%) than with WLE (94% vs 12%), as was accuracy (96% vs 13% and 92% vs 12%, respectively; p=0.0000).
Conclusions: Virtual chromoendoscopy with FICE can support the detection of dysplasia in flat mucosa and the characterization of polyps and pseudopolyps in long-standing UC, thus making less important the role of random quadrantic biopsies.

P261
Diagnostic performance of the Simple Clinical Colitis Activity Index (SCCAI) in Ulcerative Colitis (UC) self-administered by the patient at home through an on-line platform compared with the onsite evaluation by a gastroenterologist. CRONICA-UC study

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Background: New e-health technologies can improve patient-physician communication and contribute to patient's optimal care. In patients with UC and at least one flare within the previous year, we aim to assess the diagnostic performance of the SCCAI self-administered by patients at home (through a website) compared with the SCCAI assessed by gastroenterologists at the clinic (considered as reference).

Methods: Patients were followed-up for 6 months. In 2 consecutive visits, at months 3 (V1) and 6 (V2), they completed the SCCAI at home through a website, and thereafter (< 48 hours later) it was completed onsite by gastroenterologists, who were blinded to patient's score. SCCAI scores were dichotomized to remission (≤ 2 points) or activity (>2), and changes in SCCAI from V1 to V2 as: exacerbation (increase >2 points), stability (variation ≤ 2 points) or improvement (decrease >2 points).

Results: 199 patients (mean age: 39 years [SD 11]; min: 18.5; max:67.4, 55.8% women), contributed with 340 pairs of questionnaires. Correlation of SCCAI scores by physicians and patients was good (Spearman's Rho: 0.79). For the status of remission or activity, the agreement was 85.0% (95% CI: 80.8-88.4, kappa: 0.657, table 1). The negative predictive value (NPV) for activity was 94.5% (91.4-96.6) and the positive predictive value (PPV) 68.0% (58.8-69.2). Results were similar irrespective of gender or age. The agreement between patients and physicians scores of SCCAI was higher in the 168 V2 pairs of questionnaires (89.3% [83.6-93.1] vs 80.8% [74.2-86.0], p= 0.027) The percentage of agreement in the change from V1 to V2 was 82.6% (95% CI: 75.9-88.1, kappa: 0.51, Spearman's: 0.60), with PPV for relapse: 91.9% (85.9-95.9) and NPV: 88.3% (81.9-93.0). (table 2).

Conclusions: In patients with UC, self-administration of the SCCAI through an on-line tool resulted in high percentage of agreement with the onsite evaluation by gastroenterologists, with high NPV for disease activity. Remote monitoring of UC patients, especially of those with stable disease, is possible and might avoid unnecessary visits to the hospital.

Funded by Merck Sharp & Dohme, Spain [1] [2]

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P262
Protein biomarker measurement in non-invasively collected colonic mucus samples as a new approach to inflammatory bowel disease (IBD) detection.

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Patient self-administered SCCAI versus onsite evaluation by gastroenterologist.

		Patient SCCAI Remission (SCCAI ≤2)	Activity (SCCAI >2)	Total
Gastroenterologist SCCAI	Remission (SCCAI ≤2)	206 (60.6%)	39 (11.5%)	245 (72.1%)
	Activity (SCCAI >2)	12 (3.5%)	83 (24.4%)	95 (27.9%)
	Total	218 (64.1%)	122 (35.9%)	340 (100%)

Change from V1 to V2

		Patient SCCAI Improvement	Stability	Relapse	Total
Gastroenterologist SCCAI	Improvement	8 (5.0%)	3 (1.9%)	0 (0%)	11 (6.8%)
	Stability	8 (5.0%)	113 (70.2%)	14 (8.7%)	135 (83.9%)
	Relapse	0 (0%)	3 (1.9%)	12 (7.5%)	15 (9.3%)
	Total	16 (9.9%)	119 (73.9%)	26 (16.1%)	161 (100.0%)

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Background: The detection of biomarkers in non-invasively collected samples is an attractive approach to IBD diagnosis and monitoring. The only clinically accepted method of this type is calprotectin determination in stool, which requires inconvenient stool sample preparation. We have developed a new technique of non-invasive collection of material rich in colonic mucus from the surface of the anal area immediately following defaecation. Quantitative testing of a group of IBD-related protein biomarkers comprising Eosinophil-derived Neurotoxin (EDN), Calprotectin, Protein S100A12 (markers of inflammation) and Soluble Cytokeratin 18 (CK18, epithelial cell death marker) was undertaken in a pilot study addressing IBD detection and differentiation from irritable bowel syndrome (IBS). Preliminary Results of the study are presented.

Methods: Excreted colorectal mucocellular layer samples were obtained by the new technique from 58 patients with active IBD (27 CD cases and 31 UC cases), 49 patients with IBS and 33 healthy volunteers. Protein biomarkers were quantitatively analysed in the samples using ELISA assays for EDN, Calprotectin, Protein S100A12 and CK18. The Results were expressed as biomarker amount per ml of sample lysate. Result distributions and statistics by group as well as values of test sensitivity and specificity were determined for each biomarker.

Results: Patients with IBD had significantly higher mean values for all biomarkers analysed compared to both IBS and control groups. EDN appeared to be the best biomarker for IBD detection. Its average (M±SE) levels were 181.97 ± 19.18ng/ml, 15.92 ± 5.44ng/ml and 6.26 ± 2.15ng/ml for IBD, IBS and control groups respectively. For the same groups average Calprotectin levels were 14.10 ± 1.44µg/ml, 2.18 ± 0.33µg/ml and 2.15 ± 0.82µg/ml respectively. Intergroup differences detected for S100A12 and CK18 were less pronounced. ROC curve analysis for discriminating between IBD and IBS by EDN quantification produced sensitivity and specificity values of 82.8% and 91.8% respectively (AUC=0.896). Sensitivity and specificity values for Calprotectin were 75.9% and 91.8% respectively (AUC=0.893). When the Results of the EDN and Calprotectin tests were combined using a simple algorithm, the sensitivity and specificity levels for the combined test were 91.4% and 87.8% respectively (AUC=0.931).

Conclusions: The Results show that our new method of non-invasive collection of colonic mucocellular layer samples provides material suitable for quantitative analysis of biomarkers and allows efficient IBD detection and also discrimination between IBD and IBS. The best diagnostic Results were achieved by using a combined test based upon simultaneous measurement of EDN and Calprotectin.

P263
Agreement between on-line patient reported and onsite physician assessed activity on the Simple Clinical Colitis Activity Index (SCCAI) domains. CRONICA-UC study

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Background: In the CRONICA-UC study, the performance of the SCCAI self-administered by the patient through an online tool was evaluated compared to the SCCAI assessed by the gastroenterologist in the clinic (considered as reference). We here report the agreement on the different domains of the SCCAI between patient and gastroenterologist assessments.

Methods: Patients aged ≥18 years-old with UC and at least one flare within the previous year were included and followed-up during 6 months. After a screening baseline visit, patients completed the SCCAI at home through a private website at months 3 and 6, and thereafter (<48 hours later) it was completed onsite by the

Agreement in the different domains.

	Percentage of agreement (95% CI)	Kappa	Sperman's Rho
Bowel frequency during the day	89.9% (86.1–92.8)	0.661	0.716
Bowel frequency during the night	93.3% (90.1–95.7)	0.641	0.646
Urgency of defecation	75.4% (70.5–79.9)	0.57	0.675
Blood in stool	81.3% (76.7–85.3)	0.603	0.814
General well being	80.4% (75.8–84.5)	0.629	0.706
Arthritis	88.5% (84.7–91.5)	0.584	0.602

Concurrence between the patient self-assessed and the physician scores in the "Urgency of defecation" domain

		Patient SCCAI				
		None	Hurry	Immediately	Incontinence	Total
Gastroenterologist SCCAI	None	131 (38.3%)	52 (15.2%)	4 (1.2%)	0 (0%)	187 (54.7%)
	Hurry	9 (2.6%)	117 (34.2%)	9 (2.6%)	1 (0.3%)	136 (39.8%)
	Immediately	0 (0%)	4 (1.2%)	10 (2.9%)	2 (0.6%)	16 (4.7%)
	Incontinence	0 (0%)	0 (0%)	3 (0.9%)	0 (0%)	3 (0.9%)
	Total	140 (40.9%)	173 (50.6%)	26 (7.6%)	3 (0.9%)	342 (100%)

gastroenterologist who was blinded to patient score. The agreement between patient and physician SCCAI scores was assessed for each SCCAI domain with the percentage of agreement, the Cohen's kappa and the Spearman's Rho coefficients.

Results: We included 199 patients (mean age: 39.3 years [SD 11.4 (18.5-67.4)], 55.8% women). The highest agreement was seen for the domains "bowel frequency during the day" and "bowel frequency during the night" (table 1). The prevalence of extra-intestinal manifestations (EIMs), except arthritis, was very low, but agreement was high (88.5% for arthritis, and >90% for the remaining EIMs). The lowest agreement was seen for the "urgency of defecation" domain: patients scored the "urgency of defecation" higher than clinicians in 68 cases, whilst they scored lower in 16 cases (table 2).

Conclusions: In general, the agreement in the assessment of each domain of the SCCAI between patients and physicians was high. The lowest concurrence, seen in the "urgency of defecation" domain, was mainly due to underestimation by the physician, which could be due to suboptimal patient-physician communication or symptom misunderstanding.

Funded by Merck Sharp & Dohme, Spain [1] [2]

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P264
Revised Predictive Values for IBD Colitis-associated Neoplasia in the Modern Era

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Background: Due to historical reports of synchronous adenocarcinoma (CA) with low-grade dysplasia (LGD) (19%) and high-grade dysplasia (HGD) (42-60%), colectomy has been advocated when neoplasia of any grade was confirmed in an inflammatory bowel disease (IBD) patient with colitis. More recently, it is understood that most neoplasia in colitis is visible with improved technologies, and that the prognosis of such colitis-associated neoplasia may be different than previously described. This study is a modern assessment of the predictive value of IBD colitis-associated neoplasia found during colonoscopy.

Methods: We performed a retrospective review of all IBD patients at our Center who were found to have pathologist-confirmed neoplasia on surveillance colonoscopy ("index lesion") and underwent a subsequent colectomy between 2005-2014 (the dates of our high definition colonoscopes and monitors). Data included the location/grade of the index lesion at colonoscopy, and the location/grade of any macroscopic or microscopic lesion found on the subsequent standard protocol dissected colectomy specimen. The index lesion found on colonoscopy was compared to the lesion found in the same location at colectomy. Simple statistical analysis was performed.

Results: 35 IBD patients met criteria and underwent colectomies for confirmed neoplasia (20 UC (57%, n=13 extensive colitis), 14 CD (40%, n=8 pancolitis) and 1 indeterminate pancolitis). The 36 index lesions included 24 LGD, 4 HGD, 7 CA, and 1 indefinite dysplasia. Of the 24 LGD index lesions (19 white light, 5 chromo), 11 (46%) were confirmed at colectomy (0 were upstaged) and 7/24 (29%) pts had synchronous lesions found at colectomy (4/7 LGD, 3/7 HGD, 0/7 CA). Of the 4/36 HGD index lesions, 3 were found at colectomy (1 of the 3 was upstaged as CA) and the 4th lesion had been resected entirely in polypectomy. 0/4 HGD patients had synchronous lesions. Of the 7/36 index CAs, 5/7 of them were found at colectomy (2 were resected completely prior to colectomy); 1/5 (20%) was downstaged to HGD. 2/7 patients were found to have synchronous lesions: 1 HGD and 1 CA.

Conclusions: With modern visualization techniques and mostly white light exams, we have revised the predictive value of IBD colitis-associated neoplasia. We found no CAs when colectomy was performed for LGD, and only one additional cancer in the index HGD and Ca patients. These findings provide further evidence for active surveillance or subtotal colectomy rather than proctocolectomy in many IBD patients found to have dysplasia.

Comparison of Colonoscopy Findings and Colectomy Findings in 35 IBD Patients

Index Grade of Neoplasia	Primary Lesion at Colonoscopy	Index Lesion Found at Colectomy	Upstage or Downstage Index Lesion?	Synchronous Lesion at Colectomy	Grade of Synchronous Lesions at Colectomy
LGD	24/35	11/24	0/11	7/24	4 LGD, 3 HGD, 0 CA
HGD	4/35	3/4	1/3 upstage (CA)	1/4	0 LGD, 0 HGD, 1 CA
Cancer (CA)	7/35	5/7	1/5 downstage (HGD)	2/7	1 HGD, 1 CA

P265
Decreased plasma ADAMTS13 antigen and ADAMTS13 activity as a risk factor for hypercoagulability in patients with ulcerative colitis.

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Background: The etiopathogenesis of thrombosis in patients with inflammatory bowel disease (IBD) is multifactorial and not fully explained. Von Willebrand factor (vWF) occurs in plasma as different size multimeres. High molecular weight (HMW)

multimeres are broken down by metaloproteinase 13 (A Disintegrin And Metaloprotease with ThromboSpondin-type1 motif 13 - ADAMTS13) into smaller multimeres which are less active in hemostasis. A proper level and activity of ADAMTS13 protects platelets hyperagregation and in consequence clots creation.

Methods: 47 patients with ulcerative colitis (UC), 38 with Crohn's disease and 50 healthy controls were involved in the study. In all patients detailed medical history including duration of the disease, smoking habits, occurrence of thromboembolic complications, location and activity of the disease has been taken. vWF antigen concentration (vWF:Ag), vWF ristocetin cofactor activity (vWF:RCo), vWF collagen binding test (vWF:CB), ADAMTS13 antigen concentration (ADAMTS13:Ag) and ADAMTS13 activity were measured in all subjects.

Results: Plasma vWF:Ag was higher in CD and UC patients than in controls (166, 145, 111 IU/dL respectively, for both $p<0.0001$). vWF:CB was lower only in UC patients as compared to the controls ($p<0.000$). In UC patients both ADAMTS13:Ag and ADAMTS13 activity were lower in comparison to the controls (for both $p<0.0001$) as well were lower than in CD group (for both $p<0.0001$). In UC group the disease activity inversely correlated with ADAMTS13:Ag ($r=-0.76$, $p<0.0001$) and ADAMTS13 activity ($r=-0.81$, $p<0.0001$) but such a relation was not observed in the CD group. In UC patients we observed inverse correlations of ADAMTS13Ag and ADAMTS13 activity with white blood cells, C-reactive protein and fibrinogen. In the CD group only ADAMTS13 activity inversely correlated with C-reactive protein and fibrinogen.

Conclusions: This study is the first to show that ADAMTS13Ag and ADAMTS13 activity are decreased in UC with comparison to CD. Low plasma ADAMTS13Ag and ADAMTS13 activity may be a risk factor for hypercoagulability in patients with UC. In UC patients ADAMTS13Ag and ADAMTS13 activity correlate with disease activity and inflammatory markers. They might be also a marker of exacerbated UC, but not CD.

P266
Assessing fatigue in Inflammatory Bowel Disease comparison and validation of three fatigue scales: IBD-F, MFI and MAF scales

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Background: Patients with inflammatory bowel disease (IBD) report fatigue in both quiescent (41%) and active disease (86%). Fatigue is an unpleasant, multifactorial and multifaceted symptom that affects quality of life; however, due to its subjective nature it is difficult to assess. Many different fatigue scales have been developed to assess fatigue, although most have not been tested with IBD populations and only one scale has been developed specifically for people with IBD. We aimed to assess validity and reliability of three fatigue assessment scales in an IBD adult population and to determine factors correlated with fatigue.

Methods: A cross-sectional study with postal self-completed questionnaires with one reminder was undertaken. Participants (n=605) were randomly selected from Crohn's and Colitis UK members' database and completed questionnaires assessing fatigue, anxiety, depression, quality of life and IBD activity. A sub-group of responders (n=70) were sent the same mailing 6 weeks later for test-retest. Three fatigue assessment scales were used: the Inflammatory Bowel Disease Fatigue Self-Assessment Scale (IBD-F), the Multidimensional Fatigue Inventory (MFI) and the Multidimensional Assessment Fatigue (MAF). Internal consistency was measured by Cronbach's alpha and test-retest reliability by the intra-class correlation coefficient (ICC).

Results: 465 (77%) questionnaires were completed for the test and 69% for retest. Results suggest all three scales are highly correlated ($p<0.001$). Test-retest suggests good agreement for all scales' total scores with ICC values of 0.74 and 0.83 (IBD-F Section 1 and 2 respectively), 0.74 (MAF) and 0.65-0.84 (MFI all five sections). Age, gender, bowel condition, anxiety, depression and all parts of the IBDQ (IBD quality of life questionnaire) score were significantly associated with level of fatigue ($p<0.001$) for all three fatigue scales. Older patients had lower fatigue scores and females had higher scores than males. Colitis patients had significantly lower scores than Crohn's patients, and patients with a higher level of anxiety and depression had higher fatigue scores. Better IDBQ was associated with lower fatigue scores.

Conclusions: All three tested fatigue scales were found to be valid and reliable measures of IBD fatigue. Factors such as age, gender, bowel condition, quality of life, anxiety and depression are significantly associated with fatigue and should all be taken into account in the process of care delivery to people with IBD and fatigue.

P267
Long-term outcomes after restorative proctocolectomy and ileal pouch anal anastomosis in paediatric patients; more than 20 years of experience in a tertiary care facility

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Background: Inflammatory bowel disease (IBD) in children has a more aggressive disease course when compared to adults. Restorative proctocolectomy with ileal pouch anal anastomosis (IPAA) has become the treatment of choice in paediatric patients who have failed medical therapy or diagnosed with familial adenomatous polyposis (FAP). A higher incidence of postoperative complications is expected in IBD, since these patients are in a more disease-affected state with more medication use. However, data regarding the long-term outcomes in these patients compared to FAP patients are limited. The aim of our study is to compare the long term outcomes between paediatric patients with IBD and FAP who underwent restorative proctocolectomy with IPAA.

Methods: In a retrospective study, 53 (27 ulcerative colitis, 3 indeterminate colitis, 4 Crohn's disease, 19 FAP) consecutive children

under the age of 19 that underwent IPAA surgery between February 1991 and September 2014 were included. Pouch outcomes of paediatric IBD patients with a median age of 16 years (IQR, 14 - 17) were compared to paediatric FAP patients with a median age of 16.5 years (IQR, 15-17). The mean follow-up was 4.1 years (range, 1.2 - 22.3 years) and was comparable between both groups.

Results: IBD patients were in a more disease-affected state than FAP with an ASA score of more than 2 (73.2% vs 14.7%, p=0.001). In line with this, 48.3% of the IBD patients were treated with steroids and 3.3% with biologicals within 3 months before surgery compared to no treatment in FAP. The majority of IBD patients had a pouch procedure in multiple stages, that is an initial subtotal colectomy followed by completion proctectomy with IPAA at a later stage (76.5% vs 36.8%, p=0.007). Interestingly, the short-term anastomotic leak rate was comparable between IBD and FAP (15.8% vs 17.6%, p=0.863). Although not significant, fewer IBD patients had strictures compared to FAP (3.8% vs 16.7%, p=0.146). IBD patients had higher fistula (19.2% vs 0%, p=0.048) and pouchitis rates (57.7% vs 11.1%, p=0.002) compared to FAP patients. However, long-term Results showed comparable pouch failure rates between both groups (15.8% vs 11.8%, p=0.691).

Conclusions: Surgeons perform more multi-staged procedures in paediatric IBD patients in order to wean of medication and restore their nutritional state before restoring the continuity. However, postoperative complications rates are high which is possibly due to the inflammatory state of the resected colon in IBD patients. On the long term, pouch failure rates remain comparable between both groups. Although these complications do not alter the clinical course, attention should be paid on lowering the high fistula and pouchitis rates since it may negatively affect a child's life.

P268
Hospitalisation and surgery risk in Crohn's disease in the biological era - Results from the Dutch population-based IBD-SL cohort

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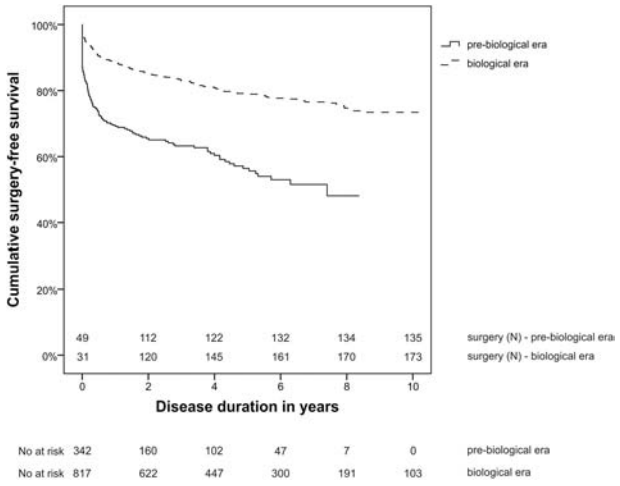
Background: Many patients with Crohn's disease (CD) require hospital admission or surgery for CD-related complications or refractory inflammatory disease. As from biological availability, more aggressive treatment strategies (e.g. early use of immunomodulators and biologicals, and combination therapy) are advised for patients with expected poor prognosis to improve long-term outcome. Its effect on disease outcome is yet unknown, mostly due to lack of data before and after biological availability from the same source population. Therefore, we aimed to compare disease outcome of CD patients diagnosed in the pre-biological era to CD patients diagnosed in the biological era in a population-based cohort.



"Risk of surgery in the pre-biological and biological era"

Methods: Since 1991, incident IBD cases in the South-Limburg (SL) area are included in our population-based IBD-SL cohort, with over 93% completeness. All CD patients were divided in two time cohorts. The pre-biological cohort comprised patients diagnosed between 1991 and 1998, followed until 1999 (registration of biological therapy for CD). The biological cohort comprised patients diagnosed between 1999 and July 2011, followed until 2014. Disease outcome, in terms of hospitalisation and surgery risk, was analysed with a Kaplan-Meier survival curve, and hazard ratios (HR) were calculated using a Cox regression model.

Results: In total, 342 patients in the pre-biological and 820 patients in the biological era were included, with a mean follow-up of 4.0 (SD 2.5) and 6.4 (SD 3.6) years, respectively. At diagnosis, patients in the biological era were less often hospitalised (21.1% vs. 36.8%, HR 0.45; 95%CI 0.34-0.60) and less often operated (3.8% vs. 14.4%, HR 0.23; 95%CI 0.15-0.38). During disease course, patients in the biological era had a 2.2-fold lower risk of surgery (HR 0.46; 95%CI 0.34-0.63) (Figure). In particular, less surgery for inflammatory disease (5.9% vs. 11.7% HR 0.41; 95%CI 0.25-0.68) was observed, but not for stricturing (9.4% vs. 12.3%, HR 0.73; 95%CI 0.48-1.11) or penetrating disease (5.0% vs. 8.3%, HR 0.58; 95%CI 0.33-1.02). We also observed a lower hospitalisation risk during follow-up in the biological era (51.4% vs. 34.4%, HR 0.65; 95%CI 0.49-0.87).

Conclusions: In this population-based CD cohort, the risk of hospitalisation decreased 1.5-fold and the risk of surgery for inflammatory disease was 2.2-fold lower in the biological era as compared to the pre-biological era. These findings indicate an improvement in disease outcome in more recently diagnosed CD patients.

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Serum neutrophil gelatinase B-associated lipocalin and matrix metalloproteinase-9 (NGAL-MMP-9) complex as a surrogate marker for mucosal healing in patients with Crohn's disease.

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Background: The current standard to assess mucosal healing in patients with Crohn's disease (CD) is endoscopy. However, frequent assessments are costly and contain a risk for complications. Earlier, we described that serum NGAL-MMP-9 is a surrogate marker for mucosal healing in patients with ulcerative colitis (UC). In this study, we wanted to investigate whether serum NGAL-MMP-9 can also be used in CD patients as a surrogate marker for mucosal healing.
Methods: Serum NGAL-MMP-9 levels were determined with sandwich ELISA before and up to 5 years after first infliximab infusion in 108 patients with active CD (median age at first infliximab 35.8 years, 57% female) and in 43 healthy controls (HC, median age 27.3 years, 60% female). Endoscopic healing was defined as complete absence of ulcerations, whereas partial healing was defined as significant endoscopic improvement, but still with ulcerations present. Histological healing was defined as an absence of epithelial damage (d'Haens score). Data were analyzed with SPSS 22 using non-parametric tests and p-values <0.05.
Results: Of the 108 patients with active CD, 72 patients showed endoscopic healing (n=38 complete, n=34 partial) whereas 36 patients showed no endoscopic healing. At baseline, median [interquartile range, IQR] NGAL-MMP-9 levels were significantly higher in active CD patients *versus* HC (77.6 [36.9-141.0] *vs* 25.5 [17.8-42.8] ng/ml; p<0.001). After treatment, NGAL-MMP-9 levels significantly decreased in healed CD patients (69.0 [32.6-135.5] to 35.2 [9.4-56.1] ng/ml; p<0.001). In non-healed CD patients, NGAL-MMP-9 serum levels also decreased after treatment (100.9 [43.4-152.6] to 43.8 [27.0-96.8] ng/ml; p=0.002), however, the decrease was significantly more profound in complete healers (p=0.020). NGAL-MMP-9 levels correlated with amount of neutrophils (Spearman's rho [r]=0.470, p<0.001), CRP levels (r=0.448, p<0.001), endoscopic activity (Kendall's tau [T]=0.296, p<0.001) and histological activity (T=0.312, p<0.001). Receiver operating characteristic (ROC) analysis defined a serum NGAL-MMP-9 cut-off level of 26.4 ng/ml corresponding to complete endoscopic healing (AUC=0.79, 58% sensitivity, 85% specificity, 56% PPV and 85% NPV) and histological healing (AUC=0.73, 63% sensitivity, 84% specificity, 50% PPV and 90% NPV). Of importance, CRP was not elevated (<5 mg/L) in 33% of active patients at start of treatment, whereas 81% of these patients did have elevated NGAL-MMP-9 levels.
Conclusions: In the search for surrogate markers to assess mucosal healing in IBD, measurement of serum NGAL-MMP-9 complex can supplement CRP in both UC and CD. We therefore propagate that the use of NGAL-MMP-9 serum levels can be implemented in clinical practice, thereby potentially overriding the need for endoscopy.

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Maintenance of remission after prolonged therapy with Infliximab: a "real-life" experience from a single Italian centre in patients affected by Crohn's Disease and Ulcerative Colitis

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Background: The efficacy of anti-TNF alpha Infliximab (IFX) in the treatment of Crohn's Disease (CD) and Ulcerative Colitis (UC) is widely recognized. Guidelines are present worldwide on when and on which patients IFX therapy could be initiated, however less evidences are available regarding the exit strategies and the clinical outcome once stopped the drug. To date it has been claimed that after IFX discontinuation, about 50% of patients with CD show a relapse (Gastroenterology 2012, 142:63-70), but still little has been reported on patients with UC. Aim of this study has been therefore to analyze, in the "real-life" setting of our centre, the remission rate of a group of CD and UC patients undergoing prolonged therapy with Infliximab, during the follow-up after the interruption of the drug.
Methods: a prospective study on 37 patients (13 CD, 24 UC) in stable steroid-free remission after receiving scheduled Infliximab for a median time of 49 months (range 21-88) was conducted at the end of anti-TNF treatment. The steroid-free remission and the relapse rate were analysed up to 24 months following discontinuation of the drug.
Results: after discontinuation of Infliximab, 11 out of 13 CD (84.7%) and 19 out of 24 UC (79.2%) were in complete steroid-free remission, identified as a CDAI <150 for CD and Mayo Score < 2 for UC. Two out of 13 CD patients (15.3%) and 5 out of 15 UC patients (20.8%) showed a clinical relapse. There was no statistical difference in the amount of relapse between CD and UC. No surgery was required in these patients. Re-treatment with IFX was scheduled and resulted effective in all the relapsers. Among the risk factors evaluated, history of disease at the beginning of IFX (>3 years) and the ileocolonic location of the disease seemed to play a major role in CD patients; female sex and left-side colitis seemed to represent predictive factors for relapse in UC.
Conclusions: : in our centre about 80% of patients with either UC and CD remained in remission up to 24 months after interruption of prolonged treatment with IFX, a percentage greater than reported in controlled studies. Although a longer follow-up and a larger population in this "real-life" setting is mandatory, in the meanwhile these Results not only confirm the efficacy and safety of Infliximab but also reinforce the hypothesis of a potential effect of the drug on the natural history of both CD and UC.

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Ulcerative colitis patients undergoing pouch surgery due to non-refractory disease have a better outcome compared to those operated due to refractory inflammation

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Background: Up to one-quarter of patients with ulcerative colitis (UC) may require total proctocolectomy with ileal pouch anal

anastomosis (IPAA, pouch surgery) for either refractory disease or for dysplastic/neoplastic lesion(s) - non-refractory disease. Up to 60% of pouch patients may develop inflammation of the previously normal ileum, and in ~ a third the inflammatory process is chronic, i.e. chronic pouchitis (CP) or Crohn's-like disease of the pouch (CLDP). Predictors for a normal pouch (NP) phenotype are vague. We hypothesized that patients operated for non-refractory rather than refractory disease have better prognosis.

Methods: Adult UC patients, after pouch surgery, followed at a tertiary pouch clinic were recruited. Characteristics of patients with NP outcome, including demographic, inflammatory, serologic, and genetic markers (NOD2 InsC mutation; R702W/rs2066844) were analyzed and compared to those of patients who developed CP and CLDP (together defined as "pouchitis"). Patients with dual indication for surgery were excluded. Stepwise logistic regression was used to assess possible predictors.

Results: Overall, 128 eligible pouch patients were identified: mean age 47.2 ± 15.6 years, females-45.3%, Ashkenazi Jewish- 45.3%, non smokers-71%, PSC- 3.9%. Fifty-three patients (41.1%) had a favorable outcome- a NP phenotype. Disease extent before pouch surgery was pancolitis in 58% and proctitis in 4.3%. Mean follow-up period was 136.1 ± 79.1 months. Family history of IBD was more prevalent in the pouchitis group compared with NP (41.9% vs. 21.2% respectively, p=0.021). BMI was decreased in pouchitis compared with NP (23.5 ± 4.6 vs. 25.5 ± 5.7 p<0.001, respectively). Patients who developed pouchitis were younger at the time of UC diagnosis, as well as at the time of operation, compared with patients who had a NP phenotype (mean age: 22.3 ± 11.1 vs. 27.9 ± 12.0 years, p=0.001, and 32.6 ± 14.6 vs. 41.3 ± 15.5 years, p= 0.007, respectively). Only 28 patients (18%) were operated for non-refractory disease, and most (69.6%) had a NP phenotype, in contrast to 35.5% NP phenotype in the refractory disease group (p=0.004). Inflammatory markers and serology were similarly distributed. NOD2 insC mutation was detected in 4 patients- all were operated for refractory disease and following surgery developed pouchitis (P=NS). Stepwise logistic regression revealed two significant predictors for a favorable outcome: surgery due to non-refractory disease, OR=3.73 (95%CI=1.339-10.393), and increased BMI OR=1.151 (95%CI=1.063-1.247).

Conclusions: UC patients undergoing pouch surgery due to non-refractory disease have better outcome compared with those operated due to refractory disease. This suggests different immunopathology and may affect therapeutic decisions.

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A pilot study assessing the viability of the Pillcam Colon 2 capsule as a "one-stop" pan-endoscopic test for patients with Crohn's Disease

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Background: Colon capsule endoscopy (CCE) was developed to provide a noninvasive, painless technique for colonic exploration without sedation and gas insufflation. CCE photographs the small bowel at a similar rate to current small bowel capsules. CCE should be capable of providing images of both small and large bowel in a single minimally invasive investigation. To date, no studies have assessed the potential of CCE to accurately examine both small and large bowel images. This study prospectively assesses whether CCE is a viable method of detecting both small and large bowel Crohn's disease (CD).

Methods: Following ethical approval, patients with established CD requiring colonoscopy were recruited. Exclusion criteria included known small bowel stricture and chronic NSAID use. The degree of severity of small bowel disease was graded using the CECDAI score; the degree of severity of large bowel disease was graded using the SES-CD score. CCE and colonoscopy were scheduled within 2 weeks of SBCE. CCE findings were compared with SBCE for small bowel disease and with colonoscopy findings for large bowel disease. Correlations were assessed between variables using Spearman's correlation co-efficient (p value of <0.05 was considered significant).

Results: In total, 10 patients were recruited; median age 31 years (range 19-47), 7 (70%) female, 5 (50%) smokers. All patients had ileo-colonic disease location, 4 (40%) had inflammatory and 6 (60%) had stricturing disease phenotype. In total, 6 (60%) study participants had a previous surgical resection. At SBCE, 2 (20%) participants had a normal small bowel examination (CECDAI = 0), 5 (50%) had mild/moderate disease activity (3.5< CECDAI >5.8) with the remaining 3 (30%) being diagnosed with severe small bowel CD (CECDAI>5.8). In comparison, CCE demonstrated 2 (20%) normal, 6 (60%) mild/moderate with the remaining 2 (20%) severe disease. There was good overall correlation between SBCE and CCE images (R=0.896, p<0.0004). In terms of colonoscopic assessment, 8 (80%) had inactive disease (SES-CD=0-3) with 2 (20%) having mild disease activity (SES-CD=4-10). The majority of participants (9, 90%) were also graded as having inactive disease on CCE with only one participant meeting the criteria for mild disease activity. There appeared to be good overall correlation between the two modalities (R=0.6667, p<0.035).

Conclusions: The future direction of capsule technology is likely to pursue a pan-endosopic approach and this pilot study would suggest that current generation colon capsules have the capability to accurately detect changes consistent with both small and large Crohn's disease.

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Validation of a smartphone-based patient monitoring system measuring Calprotectin as the therapy follow-up marker

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Background: Inflammatory Bowel Disease (IBD) is a chronic inflammation of the gut comprising active inflammation, remission and flares. The disease course can be followed by biomarkers such as calprotectin which is measured in patients' stool samples. Most studies have shown that a threshold around 250 µg/g correlates well with mucosal healing. Hence, one of the therapy goals is to achieve calprotectin values below 250 µg/g. We have developed a system, called IB*Doc*®, which allows the patient to perform calprotectin tests at home. The IB*Doc*® consists of a stool extraction device (CALEX® Valve) and an immunochromatographic rapid test, which is measured by a smartphone App (CalApp®) controlling the phone's camera. Results are automatically sent to a webserver (IB*Doc*® Portal).
The objective of this study was to validate the IB*Doc*® home testing system and to compare its performance with laboratory-based stool extraction and Calprotectin ELISA Methods.

Methods: A multitude of leftover stool samples, kindly provided by a local routine clinical laboratory, were extracted with the CALEX® Valve device and by conventional laboratory Methods. The stool extracts were then either loaded onto immunochromatograhic test cassettes or analyzed with a commercial ELISA test. The test cassettes were read via the CalApp® installed on different iPhones and Android phones, whereas the ELISA was performed in a spectrophotometer. All common technical performance characteristics of the IB*Doc*® system were determined, and the quantitative IB*Doc*® Results were compared to the Results obtained by the laboratory-based ELISA method.

Results: The IB*Doc*® test system produces a quantitative test result between 30 and 1000 µg of calprotectin/g of stool which covers the clinically relevant range of this biomarker. Smartphone model specific calibration parameters were established to correct the measured raw data for differences in camera optics and image processing resulting in correct and equal test Results among a broad range of smartphone models. Measuring the same test cassette 20-times resulted in CVs of 3-6%, while measuring the same stool extract on 20 different cassettes gave CVs of 10-20%. The total imprecision considering variations in stool extraction, test cassette runs and smartphone readouts is in the range of 25% CV. The IB*Doc*® home test correlates well with a state-of-the-art laboratory-based ELISA method showing a bias of < 20% and R^2 of >0.85.

Conclusions: IB*Doc*® is the first complete and validated test system which allows the IBD patient to monitor and follow his inflammatory status by measuring the IBD biomarker, fecal calprotectin, using his own smartphone. The performance of the IB*Doc*® home testing system is comparable to professional, laboratory-based Methods.

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Diagnostic accuracy of fecal calprotectin and M2-pyruvate kinase in the prediction of endoscopic activity Crohn's disease

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Background: Fecal calprotectin and M2-pyruvate kinase (M2-PK) are useful biomarkers to diagnose inflammatory bowel disease. Several studies have shown a high correlation between intestinal injury and the levels of fecal biomarkers but no consensus on the optimal cutoff for establishing endoscopic activity. The aim this of study is to analyze the diagnostic accuracy of fecal calprotectin and M2-PK to predict endoscopic activity in Crohn´s disease (CD).

Methods: An observational and prospective study was designed. 71 patients with CD underwent a colonoscopy calculated simple endoscopic score for Crohn´s disease (SES-CD) and Crohn disease activity index (CDAI). Fecal calprotectina, M2-PK, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were measured.

Results: Forty-nine (69%) patients had endoscopic activity (SES-CD > 2). The fecal calprotectin concentration was higher among the patients with endoscopic activity than in remission: 375 µg/g (95% CI 303-448) versus 80 µg/g (95% CI 53-107); p<0.01. For the fecal M2-PK concentration also differences were observed: 17.4 U/l (95% CI 14-21) versus 4.7 U/l (95% CI 1.8-7.6); p<0.01. The SES-CD correlated closest with calprotectin (Spearman´s rank correlation coefficient r=0.739), followed by M2-PK (r=0.576), CRP (r=0.534) and ESR (r=0.516). The overall accuracy for the detection of endoscopically active disease was 92% for calprotectin (cutoff 120 µg/g), 85% for M2-PK (cutoff 4.5 U/l), 81% for CDAI, 74% for CRP and 72% for ESR.

Conclusions: Fecal calprotectin was the biomarker to predict more accurately endoscopic activity, followed by M2-PK. Serological biomarkers and CDAI have less accuracy. Fecal biomarkers, especially calprotectina, are tools with high precision to predict endoscopic activity.

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Relevance of ultrasonographic parameters in predicting inflammatory bowel disease in a pediatric population.

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Background: Bowel ultrasound (B-US) has been widely recognized as a useful examination in patients with suspected IBD, particularly in children, owing to its lack of invasiveness. However, its accuracy relies essentially on one criteria: the detection of increased bowel wall thickening (BWT). The relevance of BWT and the additional value of other US parameters, such as lymph node enlargement and mesenteric hypertrophy (MH), in the diagnosis of IBD have not been investigated so far. This study aims at investigating the diagnostic accuracy of several US parameters in detecting IBDs in a pediatric population.

Methods: All patients aged 2-18 years referred to the Pediatric Gastroenterology Clinic of our Hospital from 2007 to 2013 for initial assessment for recurrent abdominal pain and/or altered bowel habits were retrospectively considered.Patients presenting with known organic diseases or already investigated with digestive endoscopy were excluded. Patients were considered eligible if they had a complete B-US report including: altered US bowel pattern (US-BP), BWT, MH, pathologic lymph nodes, free abdominal fluid, presence of stenosis, abscesses or fistulae. Ileocolonoscopy, performed in patients with a high index of suspicion of IBD, on the

Variables	Se, % (95% CI)	Sp, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
Altered US-BP	78.3 (69.3–85.2)	93.3 (86.6–96.9)	75.0 (65.8–82.5)	94.4 (87.9–97.6)
Mesenteric hypertrophy	65.2 (55.6–73.8)	92.2 (85.2–96.2)	68.2 (58.7–76.4)	91.2 (84.0–95.5)
BWT > 3 mm	69.6 (60.1–77.7)	96.7 (90.9–99.0)	84.2 (75.9–90.1)	92.6 (85.6–96.4)
BWT>3 mm + US-BP + MH	56.5 (46.9–65.7)	100 (95.9–100)	100 (95.9–100)	90.0 (82.6–94.6)
BWT>3 mm or US-BP or MH	82.6 (74.1–88.9)	86.7 (78.7–92.1)	61.3 (51.6–70.2)	95.1 (88.9–98.1)

basis of paediatrician's assessment and biochemical test Results (e.g. calprotectin, CRP)has been used as reference standard. Moreover, children who were not selected for endoscopy initially, were followed for at least one year for the appearance of possible additional symptoms.

Results: 113 patients (mean age 10.8 years [range 2.1-17.7], 65 male) were enrolled. 23 IBD (20.4%; 8 ulcerative colitis, 12 Crohn's disease and 3 indeterminate colitis) were diagnosed. Among the bowel US variables considered, only US-BP, MH and BWT>3 mm were found useful to identify IBD on univariate binary logistic analysis. On multivariate analysis, these factors were independent predictors of IBD, even after adjustment for age and sex: US-BP (OR 9.8;95%CI 1.6-59.0); MH (OR 5.2;95%CI 1.1-25.1) and BWT>3 mm (OR 5.4;95%CI 0.7-40.1). Diagnostic accuracy of single US parameters and their combination, in distinguish between IBD and non IBD patients, is reported in table.

Conclusions: Among several US parameters suggestive of IBD, only the increased BWT, MH and altered echopattern are independent predictors of IBD and useful in distinguishing IBD from non-IBD patients. Owing to their high specificity and NPV, these parameters can be useful in identifying patients who did not need diagnostic invasive procedures in the short time.

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Evaluation of histological parameters in patients with clinical remission of ulcerative colitis

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Background: Clinical remission and endoscopic mucosal healing are important endpoints in management of ulcerative colitis (UC). But even in asymptomatic patients with healed mucosa, a variety of histological patterns can be found in the large bowel mucosa. The goal of the study was to examine histological changes in the mucosa of patients with clinical remission of UC and compare them.

Methods: 25 patients with clinical remission of UC underwent fibrocolonoscopy with biopsy (ascendum, descendum and rectum) and histological assessment of disease activity on the Gebos scale. Due to limited number of observations, it was possible to identify comparable study and control groups only for two parameters: increased eosinophil count and increased density of the cellular infiltrate in the mucosa. In the study group studied parameter was present, and in the control group did not.

Results: Erosions, cryptitis, hyperplasia of lymphoid structures and infiltration of the intestinal mucosa with neutrophilic leukocyte often observed in the presence of increased eosinophil count in the mucosa and/or increased density of the cellular infiltrate. Our Results are shown in Table 1 and Table 2.

Conclusions: Increased eosinophil count and/or increased density of the cellular infiltrate in the mucosa often accompanied by other signs of lack of the mucosa healing. Confirmation of complete remission of UC requires histological control for exclusion of the inflammation signs.

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Table 1 The frequency of other histological changes in a group with an increased eosinophil count in the mucosa

Histological parameter	Study group 1 (with increased eosinophil count in the mucosa)			Control group 1 (without increased eosinophil count in the mucosa)		
	Ascendum N=10	Descendum N=9	Rectum N=8	Ascendum N=15	Descendum N=16	Rectum N=17
Cryptitis	40%*	33,3%	37,5%	0%*	0%	0%
Hyperplasia of lymphoid structures	40%*	44,4%	37,5%	0%*	12,5%	29,4%
Infiltration of the intestinal mucosa with neutrophilic leukocyte	30%	22,2%	37,5%	0%	6,3%	5,9%
Increased density of infiltrate	80%**	77,8%**	50%	6,6%**	6,3%**	29,4%
Erosions	20%	44,4%	37,5%	0%	6,3%	5,9%

* - p < 0,05
** - p < 0,001

Table 2 The frequency of other histological changes in a group with an increased density of the cellular infiltrate in the mucosa

Histological parameter	Study group 2 (with increased density of infiltrate in the mucosa)			Control group 2 (without increased density of infiltrate in the mucosa)		
	Ascendum N=9	Descendum N=8	Rectum N=9	Ascendum N=16	Descendum N=17	Rectum N=16
Cryptitis	44,4%*	37,5%	33,3%	0%*	0%	0%
Hyperplasia of lymphoid structures	44,4%*	62,5%*	66,6%*	0%*	5,8%*	12,5%*
Infiltration of the intestinal mucosa with neutrophilic leukocyte	33,3%	37,5%	44,4%*	0%	0%	0%*
Increased eosinophil count	50%	87,5%*	44,4%	22,2%	11,7%*	25%
Erosions	22,2%	62,5%*	44,4%*	0%	0%*	0%*

* - p < 0,05
** - p < 0,001

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Background: Diagnostic delay (DD) in Inflammatory Bowel Disease (IBD) has important clinical impact. There is increasing evidence showing a higher success rate when treatment is administered early in the disease

Objective: To evaluate DD in paediatric IBD in Spain.

Methods: Multicentric prospective observational study including paediatric IBD patients diagnosed in 2013 and 2014 in 20 paediatric centers. Data from 18 months were analyzed. Information was obtained from a questionnaire filled in by the treating paediatric gastroenterologist. Data were analyzed with the program SPSS 18.

Results: Data from 80 patients (51 males) were obtained. Mean age at diagnosis was 11.24 years (95% Confidence Interval 10.55-11.92). Disease distribution: Crohn's disease (CD) 50 patients (62.5%), ulcerative colitis (UC) 27(33.8%), IBD unclassified (IBDU) 3 (3.8%). Median DD was 19.64 weeks (interquartile range[IQR] 37.46), being significantly longer (p=0,005) in CD (27.85 w; IQR 39.71) than in UC (16.57 w; IQR 18.54). Family IBD history was not associated with shorter DD. Median time from appearance of symptoms to consultation with the first physician involved in the process was 2 weeks (IQR 4.07), from this first visit to being sent to the paediatric gastroenterologist(PG)7.3 weeks (IQR 20.71); from referral to the PG visit 0.93 weeks (IQR 4.14), and from this visit to the diagnosis 2 weeks (IQR 5.18). The time span from the first physician consultation (FPC) to the PG referral was significantly longer in CD (10.43w, IQR35.29) than in UC(3.78w, IQR 6.54). It was also significantly longer the time interval from the FPC to the final diagnosis in CD (18.57w, IQR 38.21) than in UC (9.18w, IQR18). There were no differences in the rest of the time intervals. The median of physicians visited before the PG was 2(IQR 2), but 25.6% of patients went to 3 or more physicians. A negative correlation between the DD and the z-score for height in CD patients was observed(r=-0.36, p=0.015)

Conclusions: DD in CD was significantly longer as compared to UC. The major component responsible for DD in IBD was the time spent between the FPC and the PG referral. A significantly negative correlation was found between the DD and the z-score for height in CD patients.

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THIOPURINES AND ANTI-TNFS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE AND A POSITIVE HISTORY OF CANCER

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Background: Whether patients with Inflammatory Bowel Disease (IBD) and a positive history of cancer may be treated with immunomodulators is undefined. In a retrospective cohort study, the outcome of IBD patients treated with immunosuppressors (IS: thiopurines, methotrexate and/or cyclosporine) and/or anti-TNFs after a diagnosis of cancer was evaluated.

Methods: Clinical characteristics of all IBD patients in follow up at our tertiary IBD center from 2000 to 2013, with a diagnosis of cancer were reviewed. Among IBD patients with a history of cancer, the subgroup treated with IS and/or anti-TNFs after the diagnosis of cancer were included. Parameters considered: 1.IBD type (Crohn's Disease,CD vs Ulcerative Colitis,UC); 2. Gender; 3. Age at diagnosis of IBD; 4. Age at diagnosis of cancer (yr); 5. IS or anti-TNFs (Infliximab, IFX, Adalimumab, ADA) use; 6. IBD duration at time of diagnosis of cancer; 7. Time interval between diagnosis of cancer and IS or anti-TNFs use; 8. Follow up duration after the diagnosis of cancer; 9. Characteristics of cancer. Data were expressed as median (range).

Results: In the 13 years follow up, 82 IBD patients had a history of cancer. Among these 82 patients, 15 (18.2%) were treated with IS after the diagnosis of cancer. These 15 patients included 12 CD and 3 UC (8M; age at diagnosis of cancer 41,range 21-69; age at diagnosis of IBD 27,range 12-66, IBD duration at diagnosis of cancer 10, range 1-38). After the diagnosis of cancer, 12 were treated with IS (AZA 8; 6MP 4), 3 with anti-TNFs (ADA 2;IFX 1). Cancer in these 15 patients involved: thyroid (n=4), skin (NMSC n=2; 1 basal cell carcinoma, 1 spinal cell carcinoma); breast (n=2), colon (n=2), prostate cancer (n=2) lymphoma (HL n=1), seminoma (n=1), appendiceal carcinoid (n=1). The time interval between the diagnosis of cancer and IS or anti-TNFs use was 6 years (range 1-26). After a median of 10 years (range 3-30) from the diagnosis of cancer, none of the 15 patients treated with IS or anti-TNFs after the diagnosis of cancer showed recurrence or new onset of cancer. No cancer-related deaths were observed, and only 1/15 patients had a cirrhosis-related death.

Conclusions: In a retrospective study, the use of thiopurines or anti-TNFs did not appear to worsen the outcome of IBD patients with a positive history of cancer. Larger prospective longitudinal studies are needed to further address this relevant issue in IBD.

P279
Fecal calprotectin is elevated with clinical disease activity during pregnancy in women with Inflammatory Bowel Disease

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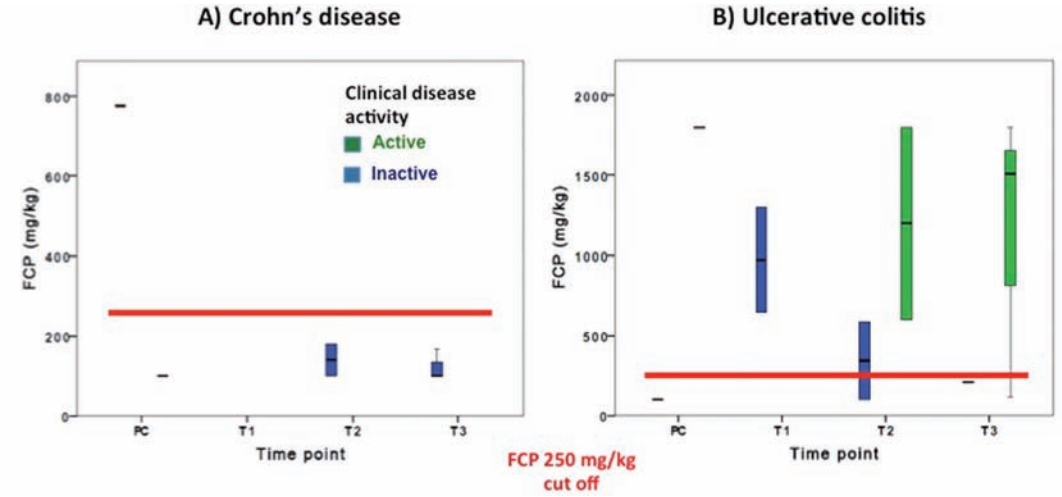
Background: Women with inflammatory bowel disease (IBD) often have gastrointestinal symptoms during pregnancy. Fecal calprotectin (FCP) is a non-invasive biomarker that detects intestinal inflammation and therefore can be used to determine if patients with IBD have symptoms due to active disease. However, the validation of FCP as a biomarker in pregnant women with IBD who have gastrointestinal symptoms has not been studied.

The objective of this study was to determine if an elevated FCP is associated with clinical disease activity during pregnancy among women with IBD.

Methods: Female IBD patients (18-45yrs) were enrolled pre-conception (PC) or at each trimester of pregnancy (T[n]). At each visit, women were grouped by clinical disease activity using the modified Harvey Bradshaw Index (mHBI) for Crohn's disease, and the partial Mayo score for ulcerative colitis. Women with a mHBI>5 or a partial Mayo score >2 were identified as having clinically active disease. FCP on a first morning stool was determined using the Quantum



"Figure 1. Fecal calprotectin and disease activity during preconception and pregnancy in women with IBD"

Blue High Range reader. To examine the association of FCP with clinical disease activity, we compared, at each visit, the median FCP of the women with clinically active disease to those with clinically inactive disease.

Results: Seventeen patients (median age 33.0 (IQR 28.0 - 37.0) years were seen over 19 visits. There were 7 women with Crohn's disease (7 data sets) and 10 with ulcerative colitis. There were 4 PC visits, 2 T1 visits (median gestational age 10.50 weeks), 6 T2 visits (median gestational age 23.36 weeks), and 7 T3 visits (median gestationla age 30.37 weeks). The median FCP of the women with clinically active disease was numerically higher than the median FCP of women with inactive disease at all time points: PC (950 vs 438 mg/kg; p=1.00), T1 (no active vs 973 mg/kg), T2 (1200 v. 140 mg/kg; p=0.40), T3 (1510 v. 134 mg/kg; p=0.486), respectively. Women with ulcerative colitis had higher FCP throughout pregnancy than women with Crohn's disease (Figure 1).

Conclusions: Women with IBD who had clinically active disease during preconception and pregnancy had higher fecal calprotectin levels than women who had clinically inactive disease. Fecal calprotectin has the potential to be used as a biomarker for assessing disease activity during pregnancy in women with IBD.

P280
Comparison of MR enteroclysis and MR enterography findings with endoscopic findings in paediatric patients with small bowel disease

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Background: The purpose of this study was to evaluate the efficacy of MR enterography and MR enteroclysis in paediatric patients with suspected small bowel disease compared to ileocolonoscopy and histology. The route of contrast administration, the image quality and bowel distention, the side effects, and performance estimates of MR enterography and MR enteroclysis were also evaluated.

Methods: A retrospective analysis of the pediatric gastroenterology clinic database (2010-2014) was performed. Thirty-four MR enterography studies and eleven MR enteroclysis studies in thirty-six patients were performed without sedation. The main indications were obscure gastrointestinal bleeding (n = 5), suspected Crohn's disease (n = 25), suspected eosinophilic gastroenteropathy (n = 3) and familial polyposis (n = 3). A water solution containing mannitol 5% was administered orally or through a nasojejunal tube. Patients were imaged on a 1.5-T MR scanner with T1-weighted and T2-weighted sequences. Retrospectively, image quality, mucosal lesions and inflammation were assessed. Correlation between radiographic findings and endoscopic findings was tested by the Fisher exact test.

Results: Thirty-four MR enterography studies and eleven MR enteroclysis studies in thirty-six patients were performed without sedation (mean age, 11.6 years; age range, 4-16 years) over 48 months. Patients who failed to cooperate or drink the contrast media were selected for MR enteroclysis. The Results of the MRE were compared to the colonoscopy and pathology reports to determine the presence or absence of disease in evaluable bowel segments. Individual imaging parameters (including wall thickening, enhancement, T2 signal) were also separately analyzed to determine their independent predictive value. The amount of oral contrast material ingested correlated with patient age (p = 0.005), with acceptable bowel distention occurring in 86%. Four patients had nausea or emesis following oral administration of the contrast agent. The overall sensitivity and specificity of MRE (using endoscopy as a gold standard) were 82% and 76% respectively (kappa=0.64).Sensitivity and specificity of MR enterography and MR enteroclysis for active disease of the terminal ileum, right colon, and left colon were 89% and 84.2%, 70,2% and 68,2%, and 91.2% and 68.6%, respectively.

Conclusions: MR enterography and MR enteroclysis is feasible in patients 5 years old and older without sedation. Small minority will have suboptimal bowel distention or minor adverse events. MRE compares favorably to ileocolonoscopy for evaluation of known or suspected Crohn's disease noninvasively.

P281
Diverticular disease-associated segmental colitis and inflammatory bowel disease: a new subgroup of patients?

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Background: Diverticular disease-associated segmental colitis (SCAD) is a rare form of chronic colitis surrounding diverticula with rectal sparing. It affects 0.3-1.3% of all patients (pts) with diverticulitis, mainly men older than 60 years old. Clinical and histological features are similar both in SCAD and in inflammatory bowel disease (IBD). Association between SCAD and IBD is well documented in literature, although etiology is still unknown.
Methods: We evaluated the prevalence of SCAD (defined by clinical, endoscopic and histological features) in all IBD-Unit pts at Negrar Hospital (Verona-Italy) from January 2008 to October 2014 (598 pts, 298 females and 300 males).
Results: Diverticulosis was present in 89 IBD pts (15%). Out of them, 9 pts (10%) presented SCAD (5 females and 4 males; 8 ulcerative colitis (UC): 4 pancolitis, 2 left-sided, 2 distal; 1 left-sided Crohn's disease; mean age at diagnosis (Dg) 48 years old). Prevalence of SCAD was 1.5%. Dg of IBD and SCAD was concomitant in 4/9 patients (mean age 60 years old). First dg of SCAD followed by IBD occurred in 3/9 pts (mean age 66 years old), viceversa in 2/9 pts (mean age 49 years old). Corticosteroid-resistance recurred in 5/9 pts. Surgery was necessary in 2 pts for diverticulitis complications (perforation and abscesses). Symptoms were overall diarrhea, rectal bleeding and abdominal pain. Extraintestinal manifestations occurred in 2/9 pts (arthritis).
Conclusions: In our cohort of study IBD pts with SCAD had a later onset of disease and a worse clinical course, with higher risk of surgery and reduced response to conventional treatments. SCAD was more frequent in pts affected by UC. Further evaluations are needed in order to identify the best treatment options and prevent surgery.

P282
Fecal calprotectin is correlated to Seo index in prediction of relapse in Iranian patients with Ulcerative Colitis

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Background: The natural clinical course of Ulcerative Colitis (UC) is characterized by episodes of relapse and remission. Fecal Calprotectin (FC) is a relatively new marker of intestinal inflammation and is an available, non expensive tool for predicting relapse of quiescent UC. Seo colitis activity index also is a clinical index for assessment of the severity of UC. The present study aimed to evaluate of the accuracy of FC and Seo colitis activity index as well as their correlation in prediction of UC exacerbation.
Methods: In this study, 157 patients with clinical and endoscopic diagnosis of UC who were selected randomly from 1273 registered patients in Fars province's IBD registry center were followed, since October 2012 to October 2013, for 12 months, or shorter, if they had a relapse. Two patients left the study before completion and one patient had relapse because of discontinuation of drugs. The participants' clinical and serum factors were evaluated every three months. Also Stool samples were collected at the beginning of the study and every three months and FC concentration (commercially available enzyme linked immunoassay) and Seo Index were assessed. Univariate analysis, multiple variable logistic regression, Receiver Operating Characteristics (ROC) curve analysis, and Pearson's correlation test (r), were used for statistical analysis of the data.
Results: According to the Results, 74 patients (48.1%) relapsed during the follow up (33 men and 41 women). Mean ± SD of FC was 862.82 ± 655.97micro. g/g and 163.19 ± 215.85micro.g/g in relapsing and non-relapsing patients, respectively (P<0.001). Multiple logistic regression analysis revealed that age, number of previous relapses, FC and Seo index were significant predictors of relapse. ROC curve analysis of FC level and Seo activity index for prediction of relapse demonstrated area under the curve of 0.882 (P<0.001) and 0.921(P<0.001) respectively. Besides FC level of 341 micro.g/g was identified as the cut-off point with 11.2% and 79.7% relapse rate below and above this point, respectively. Additionally Pearson correlation coefficient (r) between FC and Seo index was significant in prediction of relapse (r=0.63, P<0.001).
Conclusions: As a simple and noninvasive marker, FC is highly accurate and is significantly correlated to Seo activity index in prediction of relapse in the course of quiescent UC in Iranian patients.

P283
Effectiviness of fecal calprotectin measurement determining deep remission in Inflammatory Bowel Disease

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Background: Deep remission is the desired end point of the treatment of inflamatory bowel disease (IBD). Deep remission criteria involve invasive procedures (colonoscopy and biopsy) which are unpleasant for patients. For this reason, non-invasive markers which are correlated with endoscopic and histopathological remission are being identified. Fecal calprotectin (FC) is one of these markers [1] . We aimed to study FC levels and its correlation with other inflamatory markers and colonoscopic-histopathological findings among our IBD patients who are at clinical remission.
Methods: 43 patients with ulcerative colitis (UC), 38 patients with Crohn's disease (CD) who were at clinacal remission for at least 6 months and none of them was using steroids, and 41 healthy volunteers (who were admitted to screen for colon malignancy and whose colonoscopy were normal) were included in this study. CRP, sedimentation rate (SR), fibrinogen and FC levels were measured. Colonoscopy was performed to all IBD patients.
Results: Age and gender were similar between groups (UC: male 58%, female 42%, mean age 49; CD:male 50%,female 50%, mean age 46, Control:male 46%, female 53%,mean age 40). 70% of UC were distal and left-sided type, 25% of them was pancolitis. 85% of

CD were ileocolic, 15% were colitis; 82% were inflamatory type. Mean FC and fibrinogen levels were high at UC and CD groups, and this difference between control and UC and CD group were statistically significant. CRP levels and SR were similar between the groups. CRP and FC levels were low at UC who were at endoscopic remission (statistically significant); SR and fibrinogen levels didn't show statistical difference. At histological remission, only FC was different between who were at histological remission and not. There were no difference between the levels of CRP, fibrinogen, and SR. In CD group, only FC level was low at endoscopic remission. There were no any difference between CRP, fibrinogen levels, and SR. There were no statistical difference between all inflammatory biomarkers to show histopathological remission at CD.

Conclusions: Although patients were at clinical remission, they could not be at endoscopic and histopathological remission. These Results show that clinical activity indexes are inadequate to show endoscopical and mucosal improvement [2] . FC levels are helpful to distinguish active disease from inactive disease. FC levels in patients with IBD are correlated with clinical, endoscopic and histopathological activity . FC was found more valuable than routinely used tests such as CRP and sedimentation rates to determine the disease activation.

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P284
Surveillance for dysplasia in IBD: are we doing it right? Results from our daily practice

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Background: Dysplasia is a known complication of long-standing Inflammatory Bowel Disease (IBD). Guidelines for surveillance were recently updated, but their applicability in daily clinical practice is largely unknown. We planned to survey our regular clinical practice in the light of these new guidelines.

Methods: From an IBD clinic with 202 registered patients, we evaluated 59 patients under dysplasia surveillance, in a 3 year period. Demographic, clinical, endoscopic and histological data were collected from patient files.

Results: In 59 patients, 66 colonoscopies under sedation were performed during the studied period: 50% were females; 54 years-old mean-age at study entry; 88% had ulcerative colitis (79% pancolitis) and 12% had Crohn's colitis (CC). Mean duration of disease was 16 years (8-32). One patient had primary sclerosing cholangitis and 8 had family history of colorectal cancer; 74% of patients had one risk factor for dysplasia in IBD and 13% had 2 or more; 89% were using aminosalicilates, 32% thiopurines and 12% anti-TNF therapy. Nine UC patients had endoscopic activity (Mayo subscore ≥ 2) and 2 others had only histological active inflammation. One CC patient had active colonic disease, both by endoscopy and histology. Macroscopic lesions were found in 61% of patients by conventional colonoscopy. 44% patients had adenoma-like lesions (mean size 5 mm) - from these, only 45% had low-grade dysplasia at histology. Two patients had non-adenoma-like lesions (10 and 15 mm): one was a tubulovillous adenoma with low-grade dysplasia and the other was a hyperplasic polyp. The mean number of random biopsies was 29 (16-40). Low-grade dysplasia at random biopsies was found in 1 patient. No high-grade dysplasia or adenocarcinomas were found. Chromoendoscopy was only possible in 11 patients, due to inadequate bowel cleansing in all others. Lesions were found in 7 patients; in 2 of them, lesions with low-grade dysplasia had been missed by conventional colonoscopy.

Conclusions: The majority of patients had at least one risk factor justifying colonoscopic surveillance. Most of them were receiving aminosalicilates as recommended. However, the mean number of random biopsies was below standards. Moreover, chromoendoscopy was only performed in a minority of patients, but it identified 2 cases of dysplasia missed by conventional colonoscopy. In conclusion, IBD dysplasia surveillance in community practice has practical limitations, but chromoendoscopy must be endorsed, as well as patient education for optimized bowel preparation.

P285
A novel scoring system for differential diagnosis between Crohn's disease and intestinal tuberculosis: A prospective study

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Background: Although colonoscopy is useful for differentiating between Crohn's disease (CD) and intestinal tuberculosis (ITB), there have still been some limitations. Therefore, we tried to develop clinically useful predicting model in differentiating between CD and ITB using laboratory and radiologic features in addition to colonoscopic diagnosis.

Methods: We prospectively enrolled newly diagnosed CD (n = 40) and ITB (n = 40) patients from June 2011 to October 2014. On the basis of discriminant analysis using colonoscopy, laboratory and radiologic parameters, a scoring system for differentiating between two diseases was developed and was validated on additional 40 patients (CD 20, ITB 20)

Results: The colonoscopic evaluation was performed by blinded two experienced endoscopists. The accuracy of colonoscopic diagnosis was 81.2% and the positive predictive values for CD and ITB were 100% and 84.7%, respectively. On univariate analysis for laboratory and radiologic parameters, positive IgA or IgG ASCA (anti-saccharomyces cerevisiae antibody), anemia, hypoalbuminemia, elevation of ESR and abnormal lesions on small-bowel follow-through (SBFT) were significantly more common in CD, whereas QuantiFERON®-TB Gold In-Tube Test (QFT-G) and typical findings for pulmonary TB on chest X-ray (CXR) were more common in ITB. On multivariate analysis, positive IgA or IgG ASCA, positive QFT-G, abnormal SBFT and abnormal CXR were independent parameters differentiating two diseases. Final multivariate discriminant analysis was performed to construct a new predicting model: Discriminant function (DF) = 0.555 + (1.159 x CE) + (0.589 x ASCA) + (0.755

x SBFT) - (1.474 x QFT-G) - (0.633 x CXR)*. A score for CD was 1.784 and for ITB was -1.784 and the cutoff value was zero. The accuracy of discriminant function was 92.5% and the area under the curve for receiver-operating characteristic (AUROC) to assess the ability of these features to discriminate between two diseases was 0.991 (95% CI 0.978-1.000). In a validation model, the accuracy of discriminant function was 95.0% and AUROC was 0.981 (95% CI 0.950-1.000).

Conclusions: Simple laboratory and radiologic parameters including ASCA, QFT-G, SBFT and CXR are useful diagnostic aid in combination with colonoscopic evaluation for the differentiation between CD and ITB (ClinicalTtrials.gov registration number NCT01392365).

* CE: zero for indeterminate, -1 for ITB, and 1 for CD; Other parameters: 1 for positive, zero for negative

P286
Prevalence of Ulcerative Colitis and Crohn ileocolitis in patients with celiac disease

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Background: It was reported that involvement of lower gastrointestinal (GI) tract is rare in patients with celiac disease. Because of both diseases, inflammatory bowel disease (IBD) and celiac disease, have a similar autoimmune background, the occurence of IBD was questioned by lower GI endoscopy with biopsy in this study. Our aim was to evaluate IBD in patients with celiac disease.

Methods: We evaluated our celiac disease clinic records, retrospectively. Lower GI tract abnormalities were evaluated by colonoscopy, rectoscopy and/or double balloon enteroscopy (DBE).

Results: Of the 198 patients with celiac disease, 36 had documented lower GI tract endoscopic examination Results. Lower GI tract examination was performed by colonoscopy with ileum entubation (IE) and biopsy in 18 patients, rectoscopy in 17 patients and in one patient with DBE. Of the 36 patients with celiac disease, 5 patients had IBD (14%). Of the 4 patients with ulcerative colitis diagnosed, 2 had moderate or severe active pancolitis. The other two patient had left-side ulcerative colitis. One patient had crohn ileitis which was diagnosed by IE and ileum biopsy. We also found colon polyps in 6 patients (17%). These polyps showed adenomatous, tubulovillous or inflammatory changes with the size from 1 mm to 50 mm. Five of them had multiple polyps.

Conclusions: Our Results showed that patients with celiac disease may have IBD, even severely active ulcerative pancolitis or Crohn ileitis. So, we recommend a lower GI tract examination with deep IE and ileal and colonic biopsies in patients with celiac disease to early diagnosis of IBD.

P287
Serologic responses to microorganisms in IBD patients - a prospective longitudinal study

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Background: Inflammatory bowel diseases (IBD), specifically Crohn's disease (CD) are characterized by loss of tolerance towards intestinal microorganisms that may be reflected by serologic responses such as the anti-glycan antibodies. Patients with ulcerative colitis (UC) undergoing large bowel resection and ileal pouch anal anastomosis (pouch surgery), tend to develop small intestinal inflammation resembling CD. We hypothesized that pouch and CD patients have serologic similarities, and aimed to evaluate their serologic responses over time compared to unoperated UC.

Methods: IBD patients were prospectively recruited. Disease phenotype was determined clinically. Sera were tested for anti-glycan antibodies (anti-Saccharomyces cerevisiae, anti-laminaribioside, anti-chitobioside, and anti-mannobioside carbohydrate antibodies, ASCA, ALCA, ACCA, and AMCA, respectively) were assessed by ELISA.

Results: A total of 232 IBD patients (112 CD, 39 UC, 81 pouch) were included. Mean age 38.1, 38.5 and 44.7 years, males 54.5%, 51.3% and 59.3%, Ashkenazi origin 29.5%, 25.6% and 39.5%, smoking 22.3%, 38.5% and 30.9%, disease duration at sampling 10.85, 8.95, 23.2 years for CD, UC and pouch patients respectively (duration for pouch was calculated from UC diagnosis).The mean visit number was 3.5, 4.2 and 2.4 over a period of 262.8, 335.4 and 505.4 days for CD, UC and pouch , respectively ($p<0.0001$ for both). Serum samples (2-14)were obtained during short, intermediate and long (1-3, 3-12, more than 12 months, respectively) follow-up periods. The prevalence of any positive serology upon recruitment was 67.9% ,30.8% and 45.7%, ($p<0.0001$) whereas ASCA positivity was 45.5%, 7.7% and 8.6% ($p<0.0001$) for CD, UC and pouch patients respectively. No significant short-term serologic changes were observed in any phenotype. However, a steady increase in AMCA mean titers was observed in CD and UC (36.2 IU, $p=0.0001$ and 37.4 IU, $p=0.002$, respectively). ALCA titer was modestly increased in the pouch group (mean change 8.4 IU, $p=0.028$). The rate of disease complications was comparable between short vs. long term follow-up groups. While ASCA positivity in CD was associated with surgical interventions, no associations between disease complications or phenotype and serology in UC and pouch patients were found. Male gender was an independent risk for having at least one positive antibody across the entire cohort with an OR of 5 (CI 1.3-19.2, $p=0.02$).

Conclusions: Serologic responses in IBD over time are generally stable, but AMCA tends to increase. Serologic stability after disease diagnosis may suggest that the causative processes are ongoing and that the major serologic changes occur before diagnosis or at its early stages.

P288
Vitamin B12 deficiency in patients with ileal resection for Crohn's disease: Frequency and predictive factors

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Background: Vitamin B12 deficiency is involved in a broad range of hematological, neurological and mucocutaneous disorders. Absorption occurs at the terminal ileum. Patients with Crohn's disease (CD) in whom the terminal ileum (RTI) was removed may suffer from a deficiency in this vitamin.

The aim of the study was to determine the frequency of vitamin B12 deficiency and associated factors in patients followed for CD with RTI.

Methods: We collected prospectively sera from patients followed for CD in clinical remission with RTI from January to September 2014. Patients in which the metabolism of vitamin B 12 is disturbed (total gastrectomy, pernicious anemia or chronic intake of proton pump inhibitors) were excluded.

We performed a descriptive and analytical study to determine the demographic, clinical, biological features of the study population and looking for independent predictive factors of vitamin B12 deficiency.

Results: A total of 51 patients were included. The average age of patients at baseline was 35.56 years [16-77] with a sex ratio M / F= 1.04. Forty-three percent of patients were active smokers at the time of inclusion.

The average time frame between RTI and diagnosis of CD was 58.5 months [1-264] while that between RTI and inclusion was 69.5 months [5-300]. The mean extent of RTI was 39.48 cm [7-110], the mean remaining healthy small intestine was 356.6 cm.

The mean serum vitamin B12, hemoglobin and mean corpuscular volume were respectively 297.86 ng/l [34-501]; 12.4 g/dl [7.5-16.5] and 86.4 fl [61-105.2].Vitamine B12 deficiency was seen in 9 patients (17,6%).

Univariate analysis shows that vitamin B12 deficiency was associated with an age over 40 years at baseline (p=0.015), a folate deficiency (p=0.028), resection of more than 30 cm of the ileum (p<0.030) and a healthy remaining small intestine less than 3 m (p=0.041).In multivariate analysis, only ileal resection upper 30 cm (p=0.046) was found as an independent risk factor for vitamin B12 deficiency.

The mean serum vitamin B12 was significantly higher (312.6 ng/l) in the subgroup of patients who was included within 5 years from RTI [G1] compared with the subgroup of patients [G2] included more than 5 years after RTI (263.5 ng/l); p = 0.046.

The threshold limit for the appearance of a vitamin deficiency was 60.5 months.

Vitamin B12 deficiency was not correlated neither with endoscopic (p=0.606) nor with clinical recurrence (p=0.490).

Conclusions: Our work demonstrated that vitamin B12 deficiency in patients followed for CD with RTI was seen in 17% of patients. It is correlated with extent of ileal resection (>30 cm) and delay after resection (beyond 5 years) probably related to the depletion of liver stocks. These patients should be screened for replacement therapy.

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Poster presentations

OXFORD

Clinical: Therapy & observation

P289
Extracolonic neoplasias in Inflammatory Bowel Disease patients: Data from the GETECCU ENEIDA registry

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Background: Aims: a) To know the prevalence and distribution of ECNs in IBD patients; b) To estimate the incidence rate of ECNs; c) To evaluate the association between ECNs and the treatment with IMM and anti-TNF agents

Methods: Cohort, observational study. Inclusion criteria: IBD patients included in ENEIDA Project (a prospectively maintained registry) from GETECCU. Exclusion criteria: Patients with ECM before the diagnosis of IBD, lack of relevant information for this study (gender, date-of-birth, information about IMM and anti-TNF treatment, history of neoplasia) and patients that had received IMM other than steroids, thiopurines, methotrexate or anti-TNFs. To estimate the incidence rate of ECNs, only patients diagnosed with IBD after the implementation of ENEIDA in each center (2007 in most of them) were considered (inception cohort).

Results: 11,076 patients met the inclusion criteria (53% male, 50% Crohn's disease, median age 44 years) with a median follow-up of 99 months. 48% of patients had been exposed to IMM or anti-TNFs (46% thiopurines, 5% methotrexate, 20% anti-TNFs). The prevalence of ECN was 4.3% The prevalence of non-melanoma skin cancer and lymphoma was similar among patients exposed and non-exposed to thiopurines. The prevalence of cervical cancer was higher (but without reaching statistical significance) among women exposed to IMM (0.8 vs. 0.4%, p=0.1). In the multivariate analysis, age was the only variable associated with the risk of ECN (OR=1.03, 95%CI 1.02-1.03). 3,497 patients comprised the inception cohort, with a median follow-up of 27 months (52% male, 49% Crohn's disease, median age 38 years). 44% of patients had been exposed to IMM or anti-TNFs at any time during follow-up (42% thiopurines, 4% methotrexate, 20% anti-TNFs). 42 patients developed ECNs (1.2%), with an incidence rate of 478 and a standardized incidence rate (SIR) of 402 cases/100,000 patient-year (incidence rate in Spanish population=215 cases/100,000 inhabitants/year). Per-tumor incidence rate is shown in table 1. In the multivariate analysis, age was the only variable associated with a higher risk of ECN (HR=1.04, 95%CI 1.02-1.05). The treatment with IMM or anti-TNFs was not associated with a higher risk of ECN.

Conclusions: The standardized incidence rate of ECNs in IBD patients was two-fold the incidence described for the Spanish general population. Older age was the only variable associated with a higher prevalence and incidence of ECNs. Neither thiopurines nor anti-TNF drugs seem to increase the risk of ECNs.

"Incidence rate of extracolonic cancers in the inception cohort"

Cancer	Incidence rate (cases/100,000 patient-years)
Breast	68.3
Lung	68.3
Cervix	56.8
Bladder	45.5
Prostate	34
Melanoma	34
Leukemia	22.7
Basal cell carcinoma	22.7
Seminoma	11.4
Ovary	11.4
Renal	11.4
Thyroid	11.4
Stromal tumor	11.4
Stomach	11.4
Metastasis of unknown origin	11.4
Lymphoma	11.4
Squamous cell carcinoma	11.4
Lips and mouth	11.4
Appendix	11.4

P289a
Intestinal transplantation for Crohn's Disease: A 5-year nationwide follow-up

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Background: Crohn's disease (CD) is a chronic and progressive inflammatory bowel disease. Despite advances in medical therapy, half of patients still require bowel resection 10 years after diagnosis, and a third will require at least another resection within the next 10 years. A progressive reduction in small bowel length may lead to short gut syndrome and need for long-term total parenteral nutrition (TPN). Intestinal transplantation (ITxp) may benefit these patients who develop TPN-associated liver failure, loss of vascular access, and recurrent catheter-associated sepsis. However, published data on post-transplant outcomes are sparse and limited to small groups of patients. Our primary aim is to characterise long-term risk of rejection, graft failure, and death among CD patients in the largest available ITxp cohort in the United States.
Methods: The study included all adults who underwent ITxp between May 1990 and November 2013, as recorded in the U.S. Scientific Registry of Transplant Recipients. Data were collected on patient demographics, body mass index (BMI), waitlist time, and transplant indications. Outcomes included allograft rejection, graft failure, TPN resumption, and survival. Cox proportional hazards analyses were used to evaluate time to events, comparing CD with non-CD ITxp patients. Multivariable analyses were adjusted for age at transplantation, sex, race, BMI, and time on waitlist.
Results: There were 976 adults who underwent 1069 ITxp from 1990 through 2013; 134 (12.5%) were for CD (Table). Patients were followed for a median of 36 months and a maximum of 60. At transplantation, CD patients had a mean age of 44.7 years, mostly normal or overweight BMI (73.9%), and <6 months on the waitlist (76.8%). Actuarial risk of acute rejection was 22.4% at 1 year, 38.1% at 3 years, and 42.7% at 5 years, while risk of graft failure was lower at 5.6%, 16.8%, and 19.2%, respectively. Patient survival was 69.2%, 62.0%, and 62.0% at 1, 3, and 5 years, respectively. In multivariable analyses, CD patients had a similar risk of acute rejection (hazard ratio [HR] 0.85; 95% confidence interval [CI] 0.59-1.24; P=0.40), graft failure (HR 1.70; 95% CI 0.91-3.17; P=0.09), resumption of TPN (HR 1.48; 95% CI 0.93-2.35; P=0.10), and death (HR 1.07; 95% CI 0.70-1.64; P=0.77) as non-CD patients.
Conclusions: In the largest reported cohort of CD patients undergoing intestinal transplantation, long-term outcomes were similar for CD and non-CD indications. Intestinal transplantation should be considered for CD patients with intestinal failure.

Characteristics of patients undergoing intestinal transplantation for Crohn's disease and other indications.

	Crohn's Disease (N=134)	Other Indications (N=935)	P Value
Age at transplantation (SD)	44.7 (9.8)	40.2 (13.4)	<0.01
Male (%)	63 (47.0)	440 (47.1)	0.99
Race, Caucasian (%)	129 (96.3)	821 (87.8)	<0.01
Body mass index (%)			0.03
- Underweight	17 (12.7)	143 (15.3)	
- Overweight or obese	28 (20.9)	251 (26.9)	
Waitlist time, < 6 months (%)	103 (76.8)	735 (78.7)	0.81
Deceased donor (%)	132 (98.5)	917 (98.1)	0.53

P290
Impact of induction therapy with 3 doses of infliximab on deep remission in paediatric patients with active Crohn's Disease

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Background: The clinical efficacy of infliximab (IFX) for induction of remission in both adults and children with active Crohn's disease (CD) has been well documented. Recently, so-called "deep remission" defined as mucosal healing has become the ultimate endpoint of the most recent therapeutic advances for CD. However, endoscopic evidence of mucosal healing is not necessarily associated with histological evidence of suppression of inflammation. Since data on that issue are limited, especially in pediatric population, the aim of this study was to assess the impact of induction therapy with IFX on deep microscopic remission in pediatric patients with CD.
Methods: Fifty-six children (32 boys and 24 girls) aged 13.0 ± 9.3 years with moderate to severely active CD diagnosed at the mean age of 5.5 ± 0.83 years were included into the study. Colonoscopy and gastroscopy with sample collection were performed in all patients before and after three injections of IFX. Clinical activity of the disease was assessed using the Pediatric Crohn's Disease Activity Index (PCDAI), and the endoscopic activity was scored using the Simple Endoscopic Score (SES-CD). Histological changes were evaluated by a previously described numerical scoring system.
Results: Thirty-nine patients (69.6%) reached clinical remission (PCDAI below 10). When comparing data at baseline and at week 10, significant decrease was observed in median PCDAI, and in SES-CD score between the initial and control colonoscopies. We also reported a decrease in histological scale. However, the difference was not statistically significant (p=0.63). Three (5.4.%) patients had a score of 0 in the control histological examination. The correlation was found only between histological score and SES-CD score. Clinical remission correlated better with mucosal healing expressed by a decrease in SES-CD score than with microscopic changes.
Conclusions: Biological therapy with infliximab enables mucosal healing in pediatric patients with CD, which is not necessarily associated with histological evidence of suppression of inflammation. Mucosal healing correlates better than microscopic healing with clinical remission

P291
Association between Inflammatory Bowel Disease activity and therapeutic drug monitoring of azathioprine and infliximab comparing free and total antidrug antibody measurement

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Background: Therapeutic drug monitoring (TDM) of infliximab (IFX) is useful in patients with inflammatory bowel disease (IBD). Therapeutic cut-offs to predict active disease and the influence of thiopurines on drug levels (DL) according to 6-thioguanine nucleotide (TGN) are not defined. There is limited data on the utility of free

"Table 1"

Kit	Outcome	Optimal DL (μg/mL)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	+LR	AUC	95%CI
LT	FCP>250 μg/g	5.7	96	51	45	96	1.5	0.73	0.62-0.84
LT	FCP>59 μg/g	5.7	85	64	75	75	2.3	0.73	0.61-0.85
LT	CRP>5	3.0	70	76	55	85	3.0	0.70	0.56-0.84
LT	HBI>4	1.5	56	89	42	93	4.8	0.75	0.61-0.90

anti-drug antibodies (ADAb) against total ADAb. We assessed the utility of TDM of IFX in IBD using a commercially available ELISA and investigated the influence of TGNs on DL and free/total ADAb.
Methods: Prospective evaluation of trough DL and ADAb using Lisa-Tracker,((LT),Theradiag, France) and Immundiagnostik ELISA, ((IM), Germany) in 79 IBD patients (male=40) between January and May 2014. Only free ADAb is detected with LT assay, whereas IM assay measures total ADAb (semiquantitative). Total ADAb Results were calculated using the cut off control. Results of TDM were assessed with respect to faecal calprotectin,(FC), C-reactive protein (CRP) and clinical activity (Harvey Bradshaw Index,(HBI) <5 remission). The relationship between TGN and DL/ADAb was also assessed. LT kits were provided by Theradiag at no cost.
Results: Higher DL were observed amongst patients in remission (HBI;<5 DL 4.7 vs 1.7μg/mL, p=0.01, CRP<5mg/L DL 5 vs 2.5μg/mL,p=0.007, FC<250μg/g DL 5.6 vs 2.9μg/mL, p=0.001, FC<59μg/g DL 5.8 vs 3.3μg/mL, p< 0.001. ROC curve analysis including thresholds to detect active disease are shown in Table 1. ADAb were detected in 3 (4%) patients using LT vs 19 (24%) using IM assay. All patients with ADAb with LT had undetectable DL and had active disease on FC59. Total ADAb with IM assay did not correlate with outcomes. Concomitant immunomodulation use was associated with absence of ADAb using IM assay (p=0.03), however a therapeutic TGN (>245pmol/8×10^8) was not associated with ADAb (p=0.5). TGN quartile analysis did not identify a value associated with DL, (p>0.5), nor was a therapeutic TGN associated with higher DL(p=0.7).
Conclusions: IFX DL were inversely related to disease activity. A cut-off of 3.0-5.7μg/mL was associated with active disease depending on the definition used. The presence offree ADAb was associated with active inflammation, whereas the presence oftotal ADAbwas not. There was no relationship between TGN and DL or ADAb, although most patients were adequately dosed. This study highlights the limitations and utility of TDM in IBD.

P292
Immunogenicity of 13-valent pneumococcal conjugated vaccine in pediatric patients with inflammatory bowel disease

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Background: There are only a few studies on immune response to pneumococcal vaccines in patients with inflammatory bowel disease (IBD); all of them assessed polysaccharide vaccines only. The aim of the study was to evaluate the immunogenicity and safety of 13-valent pneumococcal conjugated vaccine (PCV13) in IBD pediatric patients compared with healthy controls.
Methods: This was a multi-center, prospective and controlled study on children and adolescents aged 5-18 years with IBD with no history of pneumococcal immunization or documented pneumococcal infection. The subjects for the study belonged to one of the following groups: patients with IBD on no immunosuppressive therapy (Group A), those on TNF agents or immunomodulators (Group B) and healthy controls (Group C). The study population received one intramuscular injection of PCV13. The primary outcome measure was adequate vaccine response defined as post-vaccination titer greater than or equal to 0.35 μg/mL to all 13 serotypes. Geometric mean titers and geometric mean titer rises (GMTRs) were measured for all serotypes. The evidence of local and systemic adverse effects for five days after the vaccine was registered.
Results: A total of 178 subjects (122 patients and 56 controls) completed the study course. There was no significant difference in the rate of adequate vaccine response between IBD patients and controls measured 4-8 weeks after vaccination (90.4% vs. 96.5%, p=0.5281). Children in group A had higher GMTRs than children in group B (p = 0.0369). There were no serious adverse events related to PCV13 during the study.
Conclusions: PCV13 is both immunogenic and safe in pediatric patients with IBD.

P293
The sooner, the better: Early treatment of Crohn's Disease precludes a bad outcome

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Background: Early stages of Crohn's disease (CD) are supposed to be predominantly inflammatory, and it is thought that early treatment of the disease could be one of the keys to change the natural history of the disease. We aimed to confirm this concept in our own experience.
Methods: We retrospectively reviewed the clinical records of all CD patients in our database with a stable follow up in our centre. Dates of diagnosis, of starting immunosuppressive therapy (either thiopurines or biologics), and of the first surgery when appropriate were considered. Patients lacking any of those data on our database were excluded from the analysis.
Results: 467 CD patients were included; 71% males, mean age 45yrs (range 18-82 yrs).
We found 422 CD patients with thiopurines. 189 had undergone surgery along the follow up. Those operated patients started thiopurines after a median of 117 months, interquartile range (IQR) 44-196 months since diagnosis, while non-operated CD patients started thiopurines after a median of 30 months IQR 6-128 months; p<0,001. The Odds ratio for undergoing surgery was 1,006 (CI95% 1,004-1,008) for each month of delay in starting thiopurines.
We found 272 CD patients with biologics. 137 had undergone surgery along the follow up. Those operated patients started biologics after a median of 166 months IQR 90-233 months since diagnosis, while non-operated CD patients started thiopurines after a median of 59 months IQR 14-162 months; p<0,001. The Odds ratio for undergoing surgery was 1,008 (CI95% 1,005-1,010) for each month of delay in starting biologics.

We found 467 CD patients with thiopurines and/or biologics. 210 had undergone surgery along the follow up. Those operated patients started any immunosuppressant after a median of 120 months IQR 48-197 months since diagnosis, while non-operated CD patients started thiopurines after a median of 30 months IQR 6-126 months; p<0,001. The Odds ratio for undergoing surgery was 1,008 (CI95% 1,005-1,010) for each month of delay in starting immunosuppressants. **Conclusions:** Early treatment of CD is associated with a better outcome and could be useful to change the natural course of the disease since avoids surgery in our experience. Each month of delay (since diagnosis) add risk of surgery and should be taken into account.

P294
Is the tuberculin skin test alone accurate in modeate-to-severe BCG vaccinated patients with Inflammatory Bowel Disease treated with immunosuppressives to test for latent tuberculosis?

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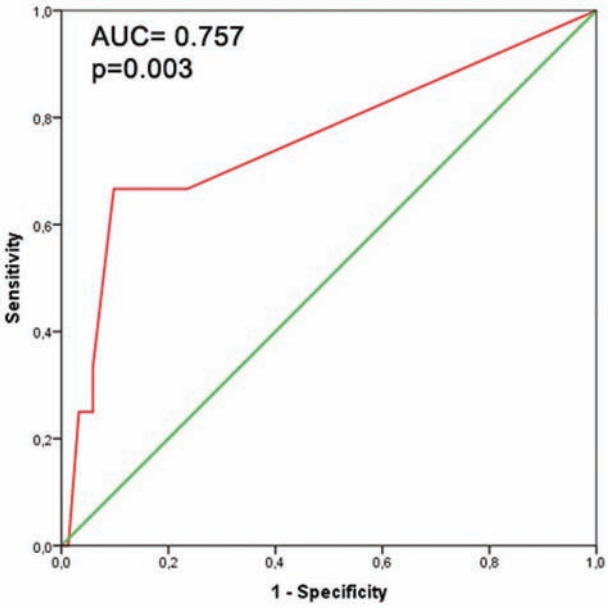
Background: There are few data available on effect of immunomodulator/biological therapy on the accuracy of tuberculin skin test (TST, Mantoux skin test) and interferon-gamma release assay (IGRA) in BCG vaccinated immunosuppressed IBD patients. Our aim was to define the accuracy of the TST and IGRA tests in a BCG vaccinated referral IBD cohort treated with immunosuppressives and/or biologicals.

Methods: Data of 166 consecutive moderate-to-severe IBD (122 CD, 44 UC) patients were analyzed (male/female: 86/80, median age at diagnosis: 24.0; IQR: 18-31 years, duration: 7.0; IQR: 4-13 years). Patients were treated with immunosuppressives (azathioprine, steroids) and/or anti-TNF therapy. Blood samples for IGRA were collected during routine laboratory testing parallel with TST. The result of TST was determined according to international guidelines. Both in- and outpatient records were collected and comprehensively reviewed.

Results: TST positivity rate was 23.5%, 21.1%, 14.5% or 13.9% with cut-off values of 5, 10, 15 and 20mm. IGRA positivity rate was 8.4% with indeterminate result in 0.6%. Chest X-ray was suggestive in only 2 patients. The correlation between TST and IGRA was significant, with moderate-to-good kappa values if TST Results were >15mm (kappa: 0.39-0.41, p<0.001). In addition, a TST of 14 and 17mm was also identified as best cut-off value in a ROC analysis (AUC: 0.76, p=0.003). There was no association between the type and number of medications (szteroid, immunosupressives, aTNF or combination) used or any disease phenotype characteristics and the TST or IGRA results. Importantly, smoking was identified as a risk factors for TST but not IGRA positivity in the full cohort (OR: 2.70, 3.14, 5.02 and 4.62, p<0.007, for TST cut-off 5, 10, 15 and 20mm) and in CD (OR: 4.07, 4.84, 9.92 and 9.05, p<0.001, for TST cut-off 5, 10, 15 and 20mm).



"Figure 1 Association between tuberculin skin test and Quantiferron positivity"

Conclusions: The TST and IGRA are partly complimentary Methods and accuracy is acceptable also in BCG vaccinated and immunosuppressed IBD patients. A TST of >15mm should be used as a cut-off to identify patients at risk for latent TB in these patients. Smoking is a risk factor for TST positivity.

P295
Preliminary assessment of efficacy and safety of switching between originator and biosimilar infliximab in paediatric Crohn disease patients.

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Disease activity (PCDAI) and laboratory values at the beginning of originator INF treatment, before switch and after first dose after switch are presented as mean (median; range).

	At the start of originator INF treatment	At last but one originator INF infusion	At last originator INF infusion	At switch (1st biosimilar INF infusion)	At 2nd biosimilar INF infusion
Week	-	W -16	W -8	W 0	W +8
No. of patients	32	25	31	32	25
PCDAI Mean (median; range)	48 (53; 2.5–65)	7 (3.8; 0–30)	5.9 (2.5; 0–30)	8.5 (5; 0–35)	7.5 (5; 0–23)
CRP	5.1 (1.1; 0–65)	1.5 (0.3; 0,1-20)	1.2 (0.4; 0–23)	1.2 (0.35; 0–19)	0.6 (0.4; 0–2.1)
ESR	28 (23; 3–80)	13 (7; 2–66)	15 (10; 2–59)	14 (9; 2–63)	13 (8; 1–55)
Platelets	391 (298; 169–630)	306 (298; 156–543)	302 (294; 171–654)	304 (282; 183–804)	305 (309; 175–529)
Hb	12 (12.3; 10.3–14.4)	13.3 (13.1; 11.6–16.7)	13.2 (12.8; 10.3–15.6)	13.1 (13.4; 10.4–16.4)	13.3 (13.3; 11.4–15.1)

Background: A steady increase in number of paediatric patients requiring biological therapy in Crohn's disease (CD) is observed. Recently, biosimilar infliximab (INF) was authorized in European Union. With quality, efficacy and safety claimed to be equivalent to the originator, biosimilar infliximab may increase the access to biologicals due to cost reduction. The authorization covers CD, despite the lack of formal clinical studies in both adult and paediatric population. Moreover, the safety of switch between originator and biosimilar infliximab was shown only in rheumatology.

Methods: Thirty-two paediatric patients with diagnosis of CD from 3 academic hospitals who were switched from originator to biosimilar infliximab (CT-P13) were included in the study. Patient characteristics, disease history, disease severity (PCDAI), laboratory values (CRP, ESR, platelet count, haemoglobin level) were recorded. Mean, median and range values were calculated. Adverse events were recorded before and after the switch.

Results: Mean age of patients at diagnosis of CD was 11.1 years (range 2.7-15.3). Six patients had been previously treated with a biologic: infliximab (5) or adalimumab (1). Mean time from CD diagnosis to the start of current biological treatment was 1.8 years (range: 1 week - 5 years). Mean number of originator INF infusions before the switch to biosimilar was 9.9 (median 8.0; range 4-29). Disease activity (PCDAI) and laboratory values at the beginning of originator INF treatment, before switch and after first dose after switch are presented in the Table as mean (median; range). Number of patients may vary due to lack of data at given time point.

There were no infusion reaction after originator of biosimilar INF treatment. The occurrence of sporadic mild adverse events did not differ significantly when were measured before and after switching and was consistent with INF molecule safety profile. Additionally, at weeks 16, 24, 32 after switch 16, 5 and 4 patients were evaluated with no disease flare or unexpected adverse events.

Conclusions: Switching form originator to biosimilar infliximab in children with CD seems to be safe.

P296
Isoniazid prophylaxis may not prevent tuberculosis reactivation during anti-TNF treatment

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Background: Treatment with tumour necrosis factor antagonists(anti-TNF) has been recognized as a risk factor for tuberculosis(TB) reactivation. Isoniazid(INH) prophylaxis is recommended according to baseline TB screening tests(tuberculin skin test, QuantiFERON®-TB Gold test) and chest X-Ray. However, the effectiveness of the chemoprophylaxis in the long term period is not clear, especially in the high prevalence countries for TB.

Methods: In this retrospective study, it was reviewed the medical records of 1263 patients with inflammatory bowel disease(IBD), and 1 rheumatoid arthritis and 1 hidradenitis suppurativa patients who attended for exudative ascites. Baseline TB screening tests including purified protein derivative(PPD) test and/or QuantiFERON®-TB Gold test were performed in all patients before starting anti-TNF therapy. PPD >5 mm and/or patients with positive QuantiFERON®-TB Gold test received INH prophylaxis for 9 months. We analyzed the data of patients diagnosed with TB reactivation during the anti-TNF treatment despite INH chemoprophylaxis.

Results: Anti-TNF treatment rate was 13.9% (n=175) among IBD patients (137 patients [117 infliximab, 20 adalimumab] with Crohn's disease(CD), and 38 patients [34 infliximab, 4 adalimumab] with ulcerative colitis(UC). Six patients (4 males, mean age: 44.5 ± 18.6 years) on anti-TNF treatment (3 CD, 1 UC, 1 rheumatoid arthritis and 1 hidradenitis suppurativa) were enrolled in this study for developing TB reactivation despite INH prophylaxis. TB reactivation was occurred in 6.6% (n=4/60) of IBD patients who received INH prophylaxis beside anti-TNF treatment. Patients' PPD tests were positive in 4 and anergic in 2 patients. Anergic patients were positive for QuantiFERON®-TB Gold test. All these 6 patients received INH therapy(300 mg/day) for 9 months. Active TB was diagnosed at 33 ± 26 (range: 12-84) months of the anti-TNF treatment. Four of them received adalimumab and the others infliximab. Only one patient used also azathioprine during the anti-TNF therapy and that patient was diagnosed with disseminated TB. In 3 patients, we detected mycobacterium species as Mycobacterium bovis, M. tuberculosis and M. genavense, respectively. In 2 TB patients, we diagnosed TB according to compatible findings of peritoneal biopsies. In one patient, TB was diagnosed according to clinical and laboratory findings.

Conclusions: Isoniazid chemoprophylaxis may not prevent reactivation of TB in the long term period of anti-TNF treatment. It should carefully and periodically screen the patients during the anti-TNF therapy for TB reactivation.

P297
Utility of post-induction trough level measurement in planning infliximab maintenance therapy for pediatric IBD

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Background: Multicenter clinical trial data in adults and children with IBD demonstrate that efficacy of infliximab correlates with drug levels at trough. Trough levels of 3-7 µg/ml are targeted. We measured infliximab levels early following 3rd induction dose in pediatric patients with Crohn's disease (CD) and ulcerative colitis (UC), aiming to optimize individual maintenance regimens.

Methods: Beginning September 2013 at SickKids Hospital, Toronto 51 children and adolescents (median age 14.9 yrs; 30 CD; 21 UC) initiating infliximab therapy via a 3-dose induction regimen were given first maintenance dose earlier than the conventional 8 weeks following 3rd induction dose. Infliximab trough levels, measured by ELISA at time of first maintenance infusion were compared between CD and UC. Influence of disease activity (assessed by physician global assessment and PCDAI or PUCAI), serum albumin and hsCRP at baseline on post-induction early trough levels were assessed. Response to induction regimen was assessed using PGA and PCDAI/PUCAI at time of first maintenance infusion.

Results: 30 CD patients infused in standard fashion (weeks 0,2,6) with mean dose of 5.3 mg/kg across the 3 doses had week 12 median trough levels of 9.7 (IQR 4.8 -12.8). All but one received concomitant immunemodulation during induction. Nine (30%) CD patients had week 12 trough level of <5.0µg/ml, suggesting that standard q8 weekly maintenance regimen beginning at week 14 would have been suboptimal. 21 UC patients (9 steroid dependent;12 steroid refractory) received higher infliximab doses (mean of 3 doses 6.2mg/kg, p=0.001 vs CD),often given more intensively (3 doses within 4 weeks in 17). UC patients were given first maintenance dose 4 weeks following 3rd induction dose, but median trough levels of 10.2 (IQR 4.8-14.0)

were similar to those achieved among CD patients 6 weeks post 3rd infusion (Wilcoxon p=0.80).
Although similar in age, gender and baseline disease activity, CD and UC patients differed with respect to concomitant steroid therapy (CD:40%; UC:100%, Fisher's exact p<0.0001) and immunomodulation (CD:96.7%; UC:4.8%, Fisher's exact p< 0.0001) during induction. 24/28 children treated for CD, excluding those with a primary indication of perianal disease, compared with 7/21 treated for UC achieved steroid-free clinical remission post induction. 9/12 of the UC patients with continuing active disease had adequate trough levels (>3).
Conclusions: Early post-induction trough level testing is useful in assessing primary non-response to infliximab and in planning of optimal maintenance regimen. In this pediatric cohort, patients with UC cleared drug more rapidly, requiring higher per kg dosing and a more intensive regimen to achieve comparable drug levels post induction.

P298
Validation of the mobile Health Index (mHI) for remote monitoring of IBD disease activity

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Background: Mobile health technologies are increasingly used to monitor patients remotely in chronic disease management such as diabetes mellitus and congestive heart failure. In IBD several monitoring systems have been studied but the use of mobile devices is still limited. We developed two 4-question indices to monitor disease activity using a smartphone in Crohn's disease (CD) and ulcerative colitis (UC) patients; the mobile Health Index (mHI) -CD and mHI-UC. The aim of this study was to validate the mHI in an independent cohort of IBD patients.
Methods: Patients with a diagnosis of CD or UC were included in 3 specialized IBD centers. During clinic visits, clinical disease activity indices (Harvey Bradshaw index for CD, partial Mayo score for UC) were completed by the physician, and patients filled out the mHI and the short-IBDQ for quality of life (QoL) assessment. During endoscopic visits the physician also completed an endoscopic score (Mayo for UC, SES-CD for CD). Spearman rho was calculated to assess correlation of the mHI with clinical and endoscopic disease activity indices. Patients were followed over time to assess responsiveness to change; a Spearman rho was calculated to estimate the correlation between changes in scores. A subset of patients filled out a second mHI within 24 hours after the clinic visit, and the intraclass correlation (ICC) was calculated to assess test-retest reliability.
Results: In total 194 UC patients (19% active) and 217 CD patients (19% active) were included. The correlation of the mHI with clinic scores was 0.73 (p<0.001) for CD and 0.70 (p<.0001) for UC. Sensitivity and specificity to detect active disease were 93% and 66% for CD and 67% and 93% for UC, respectively. Both scores were responsive to change with a correlation of 0.37 (n=46) for CD and 0.65 (n=27) for UC between the change in scores. Test-retest reliability was good with an ICC of 0.91 (n=28) for the UC mHI and 0.95 (n=23) for the CD mHI. The CD mHI did correlate with endoscopic healing, though predictive values were poor (sensitivity 69%, specificity 51%, rho=0.31 (p=0.0062)). For UC the mHI correlated strongly with mucosal healing (rho=0.57 (p<0.0001), sensitivity 56%, specificity 88%). Furthermore, both scores have a strong inverse correlation with QoL (rhoi=-0.78 for CD and rho=-0.80 for UC, p<.0001)
Conclusions: The developed mHI scores for CD and UC have excellent test characteristics to monitor patients' symptoms remotely. Because the scores consist of 4 simple questions answered by patients, the score is ideal for implementation in a mobile smartphone app for home monitoring. As previously shown CD symptoms do correlate poorly with mucosal healing, while UC symptoms are strongly correlated with mucosal lesions.

P299
Ulcerative colitis and paediatric liver transplantation for primary sclerosis cholangitis - multi-case report

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Background: Primary sclerosing cholangitis (PSC) is strongly associated with ulcerative colitis (UC) and may enhance the risk of colorectal dysplasia and cancer. Liver transplantation (LTx) for PSC and immunosupressive regiments, especially those including steroids, may alter the outcome of UC but up-to-date evidence in children is scarce. The aim of the study was to analyze the influence of pediatric LTx on the course of UC.
Methods: We retrospectively analyzed the data of children with PSC and UC who underwent LTx in our institution between 2000 and 2013. In all patients PSC was confirmed by endoscopic retrograde cholangiopancreatography (ERCP) and/or magnetic resonance cholangiopancreatography (MRCP) and liver biopsy. UC diagnosis was based on clinical presentation, endoscopy and histology.
Results: Seven patients (4 male/3 female) with PSC and UC underwent LTx from deceased donors at the median age of 15,6 years (11,5-17,5). In 6 patients UC was diagnosed before LTx at the median age of 11 years (5-12), and one patient developed UC six months after LTx. Six patients (85%) had pancolitis at presentation and 1 proctosigmoiditis. Severe macroscopic inflammation was present in 5 (71%) cases. Initial treatment consisted of mesalazyne or sulfasalazine in combination with steroids and azathioprine. All patients received ursodeoxycholic acid once PSC was diagnosed and it was continued after LTx. None of the patient received biological treatment.
At the moment of transplantation (median 4 year after onset of UC, range 5-11) clinical activity according to PUCAI was remission in 4, mild in 2 and moderate in 1 case. All patients received deceased donor, AB0 compatible, whole liver grafts. Biliary anastomosis was hepaticojejunostomy in 6 and duct-to-duct anastomosis in 1 patient. Post transplant immunosuppressive regiment consisted of tacrolimus (n=4), cyclosporine (n=3), mycofenolate mofetil (n=5), azathioprine (n=1) and steroids (n=6). Neither of the patients developed colorectal neoplasia/cancer, nor underwent colectomy within median post-transplant follow-up of 7,3 years (1,3-13). Currently full remission is maintained in 4 (57%). One patient has moderate UC activity and another one with severe endoscopic inflammation was recently switched from tacrolimus to cyclosporine. Recurrence of PSC after LTx was not observed. One patient developed antiphospholipid syndrome with severe thrombosis requiring re-transplantation 7 years after the first LTx. One patient was deceased due to chronic rejection as a result of non-compliance. Up-to date overall patient and graft survival is 85% and 71% respectively.
Conclusions: The course of UC is not worsened by liver transplantation for PSC and likewise UC does not adversely affect patient or graft survival.

P300
Effect of vedolizumab on health-related quality of life (HRQoL) in patients with Crohn's disease

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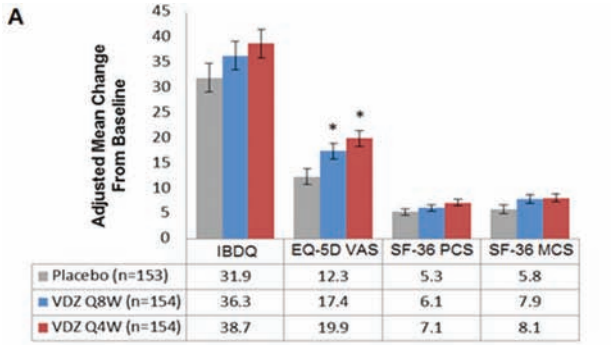

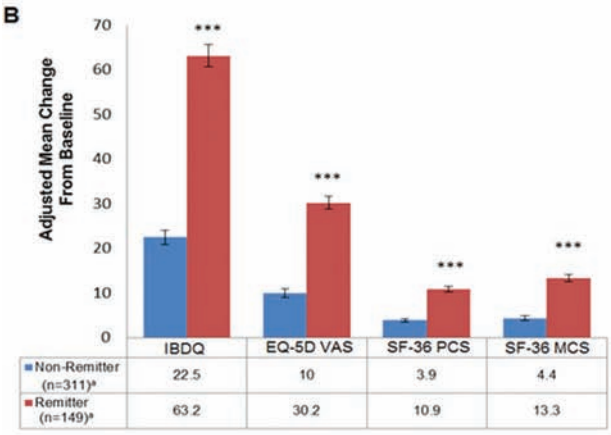

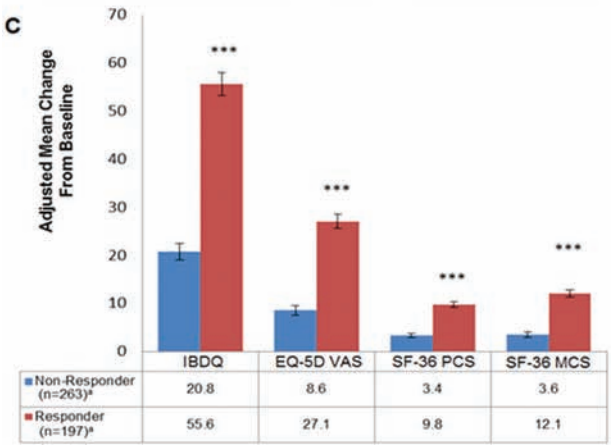

Background: Vedolizumab (VDZ) is an α4β7 integrin antagonist for the treatment of Crohn's disease (CD). In the GEMINI 2 trial (NCT00783692),[1] VDZ resulted in statistically significant improvements in clinical endpoints versus placebo (PBO). Here, the effect of VDZ on health-related quality of life (HRQoL) at week (wk) 52 and its relationship with response and remission are analysed.

Methods: In GEMINI 2, responders to VDZ induction therapy at wk 6 were re-randomised to PBO or VDZ every 8 or 4 wks (Q8W or Q4W) (maintenance ITT population). Exploratory endpoints included the change from wk 0 to 52 in the European Quality of Life-5 Dimension (EQ-5D) visual analogue scale (VAS), Inflammatory Bowel Disease Questionnaire (IBDQ), and 36-item Short-Form Health Survey (SF-36) physical/mental component score (PCS/MCS). In post hoc analyses, the mean changes were stratified by baseline disease severity and prior tumour necrosis factor antagonist (anti-TNF) failure. Percentages of patients (pts) with a clinically meaningful improvement (CMI) in IBDQ total score (≥16-point increase from wk 0) or score >170 and improvements in HRQoL by responder or remission status at wk 52 were assessed. All pts in these analyses received 2 VDZ doses (half-life 25 days) during induction.

Results: Mean changes in IBDQ and SF-36 PCS and MCS from wk 0 to 52 were numerically greater with VDZ than with PBO; EQ-5D VAS scores were significantly greater with VDZ (Figure 1A). Similar trends were observed in pts stratified by disease severity or prior anti-TNF failure. In pts without prior anti-TNF failure, the differences between VDZ Q4W and PBO in IBDQ, EQ-5D VAS and SF-36 PCS were statistically significant. Rates of CMI in IBDQ total scores and of IBDQ scores >170 were generally higher with VDZ than with PBO (CMI: 64% Q8W, 74% Q4W, 63% PBO and score >170: 39% Q8W, 47% Q4W, 35% PBO). Responders and remitters showed statistically significant improvements in all scores (vs non-responders and non-remitters, respectively; Figure 1B,C).

Conclusions: These data indicate that HRQoL benefits accompanied the clinical improvement experienced with VDZ treatment. Treatment differences appear modest because of VDZ exposure during induction and potential carryover effect in pts re-randomised to PBO during maintenance.

The clinical studies were funded by Millennium Pharmaceuticals, Inc. (d/b/a Takeda Pharmaceuticals International Co.). Medical editing was provided by inVentiv Medical Communications and supported by Takeda Pharmaceuticals International, Inc.

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[1] Sandborn WJ, (2013), Vedolizumab as induction and maintenance therapy for Crohn's disease, N Engl J Med, 711-721

P301
Vedolizumab for induction of remission in Crohn's disease in adults, a systematic review and meta-analysis

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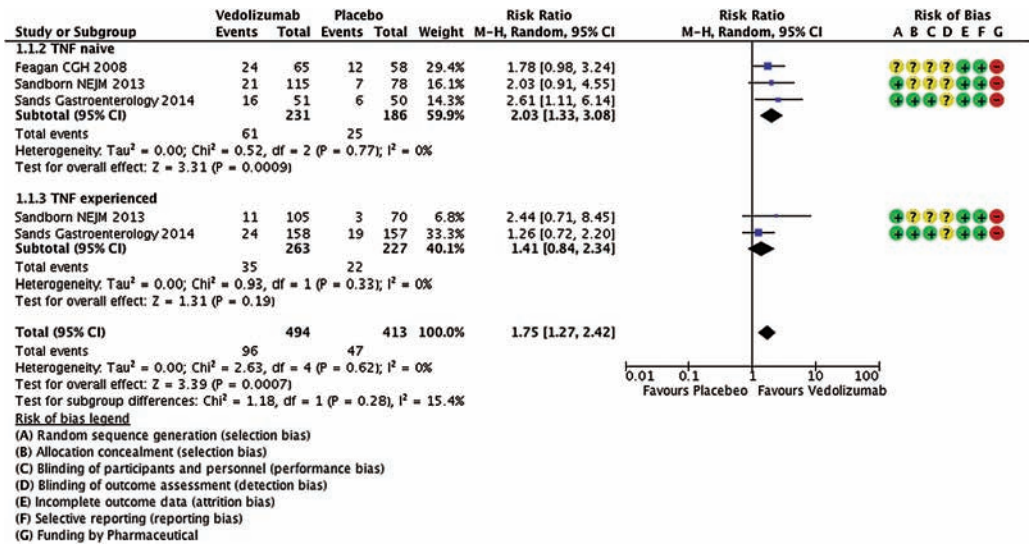
Background: Vedolizumab (VDZ) is a humanized monoclonal IgG1, specific to the alpha4beta7 integrin. Several studies have evaluated the efficacy of VDZ in Crohn's disease (CD). We systematically reviewed and analyzed published clinical trial data assessing the efficacy VDZ for the induction of remission and clinical response in moderate to severe CD in adults.

Methods: Electronic bibliographic databases of the Cochrane Central Register of Controlled Trials (CENTRAL)(1991 to October 2014),



MEDLINE (1946 to 11/26/2014), EMBASE (1974 to 11/26/2014), International Pharmaceutical Abstracts (IPA)(1970 to 11/26/2014), BIOSIS Previews (1969 to 2008), PubMed, clinicaltrials.gov, and Drugs@FDA (http://www.accessdata.fda.gov) was searched. MeSH terms Entyvio, LDP 02, LDP-02, LDP02, MLN0002, MLN02, UNII-9RV78Q2002 were used for VDZ. Hand searches of abstracts from scientific proceedings and reference lists of primary articles were also performed.

Controlled trials of VDZ in treatment of moderate to severe CD were selected for review. Two independent reviewers (ML and NF) evaluated article titles and abstracts to determine the need for detailed review and eligibility for inclusion. Disagreements were resolved by consensus or majority vote with a third reviewer (GR). The review authors extracted data independently. Study bias was assessed using the Cochrane Risk of Bias tool.

The primary outcome was proportion of patients achieving induction of clinical remission within 8 weeks of therapy, defined as CDAI of < 150. The secondary outcome was proportion of patients achieving induction of clinical response within 8 weeks of therapy, defined as a drop of CDAI >100. Subgroup analysis based on anti-TNF-alpha exposure was performed to assess confounding. Adverse events (AE) and serious AE were also evaluated.

Results: A total of 668 studies were identified using the search strategy. Three studies involving 1716 participants were included in the final analysis. The risk ratio (RR) for induction of clinical remission and response was 1.75 (95% CI: 1.27, 2.42) and 1.42 (95%CI: 1.17, 1.73) respectively. Subgroup analysis of induction of remission and response in anti-TNF-alpha naïve was 2.03 (95% CI: 1.33, 3.08) and 1.36 (95%CI: 1.05, 1.76) respectively, and in anti-TNF-alpha experienced was 1.41 (95% CI: 0.84, 2.34) and 1.42 (95% CI: 0.85, 2.35) respectively. (Figure 1) The RRs of AE and serious AE were 1.01 and 1.06 respectively. Moderate heterogeneity among studies was due to different VDZ dosing and schedule.

Conclusions: Vedolizumab is effective for induction of remission and clinical response for patients with moderate to severe CD. Most benefit is seen in anti-TNF naïve patients.

P302
Pharmacoszintigraphic investigations of a high-dose mesalazine tablet with a new coating

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Background: Mesalazine has been used for several decades for induction of remission and maintenance of remission of mild to moderate ulcerative colitis (UC). Doses recommended for induction and maintenance of remission require several gastro-resistant tablets to be taken each day. Commonly used are polymer coatings, which disintegrate in a pH dependent manner (pH ≥ 7). The tested formulation (TP05) uses a double trigger, double layer coating technology: an outer polysaccharide and polymer coating, whose degradation is triggered by either ph or intestinal bacterial enzymes and an inner layer for faster dissolution of the active constituent at the ileo-caecal target region. We investigated the influence of this novel formulation on the delay and site of release of Mesalazine.

Methods: Design: Open-label, single-center study.

Number of participants using a specific formulation of TP05: 9 (3 patients, 6 healthy volunteers).

Inclusion: Healthy subjects or patients with mildly active UC, between 18 and 55 years old.

Test product, dose and mode of administration: A single dose TP05 tablet containing 1600 mg mesalazine with double layer coating radiolabelled with 1 MBq Sm-153 was administered orally.

Duration of treatment: 1 single tablet was administered in the morning (fasted condition).

Repeated gamma-scintigraphy pictures were taken to determine the anatomical site of initial tablet disintegration (ITD) and the release of the study drug.

In parallel blood samples were collected for a PK profile (data not shown).

Results: The anatomical site of ITD was determined to be within the ileocaecal junction (ICJ) or ascending colon (AC) in 8 out of 9 participants. One was in the transverse colon (TC). The location of complete tablet disintegration (CTD) is also within the right colon in 89% of subject/patients.

For all subjects combined, the median gastric rention time (Q1, Q3) (min) that was 30 (30, 30) and the small intestine transit time (SITT) was 150 (120, 210).

The median (Q1, Q3) colonic arrival time of TP05 occurred after 270 (240, 360) minutes and ileocaecal junction residence time was 30 (30, 60) minutes.

Initial and complete tablet disintegration occured 270 (240, 450) and 400 (270, 600) minutes (median, Q1, Q3) post-dosing.

No serious adverse events occurred.

Conclusions: The scintigraphic Results demonstrate that this new coating technology allows reliable delivery of mesalazine from a high-dose mesalazine tablet in fasted subjects to the site in which it is most needed for a maximal therapeutic effect.

TP05 was found to be well-tolerated.

P303
Real life effectiveness of Adalimumab for the treatment of ulcerative colitis: comparison between anti-TNF-naïve and non-naïve patients. Results from the Spanish ENEIDA Registry.

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Background: The benefit of adalimumab (ADA) in anti-TNF naïve vs anti-TNF-exposed patients in active ulcerative colitis (UC) has been evaluated in the placebo-controlled trials (ULTRA-2) and in short cohorts. Objective: To evaluate the efficacy of ADA in UC comparing patients previously treated with anti-TNF(non-naïve) and anti-TNF naïve patients (naïve) in the clinical practice.

Methods: Retrospective cohort study based on data obtained from the ENEIDA registry. Demographic data, concomitant therapy, Mayo score (MS) and/or Mayo UC endoscopic score (MES) and cause for anti-TNF discontinuation (non-naïve) were collected at the beginning of the treatment. Clinical response, clinical remission, endoscopic remission, range of adverse events, need for intensification, colectomy and hospitalizations were also evaluated.

Results: Two hundred and forty-five patients were included (163 non-naïve and 82 naïve). Patient demographics and rates of response and remission are summarized in Table1. Adverse events occurred in 11% naïve y 6% non-naïve group. Intensification, hospitalization and colectomy during the first year were required in 26, 21 and 11% of naïve patients and in 40, 43 and 27% of no-naïve patients, respectively. In the multivariate analysis, patients with primary failure and intolerance to the first anti-TNF and severe disease were associated statistically with worse clinical response (p=0.015, p=0.042 and p=0.049). Primary non-response to prior anti-TNF treatment and severe disease were predictive factors of poorer clinical remission (p=0.04 and p=0.026). Endoscopic remission did not show statistical associations.

Conclusions: In real life experience ADA seems an effective treatment in moderate UC especially in anti-TNF naïve patients.

"RESULTS"

	Naïve	Non-naïve
Male sex	66%	59%
Age at diagnosis (years)	42.23 (13.98)	42.99 (14.4)
Smoker	12%	4%
No-smoker	60%	70%
Ex-smoker	28%	26%
Proctitis	24%	17%
Left-sided colitis	14%	21%
Pancolitis	62%	62%
Disease duration (months)	105.81 (94.48)	98.34 (89.77)
Indications for therapy		
Induction of remission	78%	81%
Maintenance of remission	6%	14%
EM	10%	2%
Perianal disease	4%	0.6%
Others	2%	2.4%
Reason to discontinue first anti-TNF		17%
Primary non-response		44%
Loss of response		24%
Intolerance		15%
Others		
Concomitant GC	38%	59%
Concomitant IS		
No	49%	51%
Tiopurines	46%	42%
Other	5%	6%
Mild (MS 3-5 and/or MES≤1)	8 (11%)	32 (22%)
Moderate (MS 6-10 and/or MES=2)	44 (65%)	74 (55%)
Severe (MS>10 and/or MES=3)	15 (24%)	34 (23%)
Clinical Response		
No	15 (20%)	49 (34%)
Yes	60 (80%)	97 (66%)
-at week 12	45 (60%)	66 (45%)
-at week 24	9 (12%)	16 (11%)
-at week 52	6 (8%)	15 (10%)
-2 years maintenance	27 (39%)	47 (33%)
Clinical Remission		
No	25 (36%)	74 (52%)
Yes	44 (64%)	69 (48%)
-at week 12	25 (36%)	33 (23%)
-at week 24	11 (16%)	21 (15%)
-at week 52	8 (12%)	15 (10%)
Endoscopic Remission		
No	22 (50%)	65 (64%)
Yes	21 (50%)	36 (36%)
-at week 12	10 (24%)	12 (12%)
-at week 24	4 (9.5%)	13 (13%)
-at week 52	7 (16.5%)	11 (11%)

Data are expressed in percentage, absolute number (percentage) or mean (standard deviation).
GC: glucocorticoids, IS: inmunosupressants, EM: extraintestinal manifestations.

P304
Crohn Disease localization does not contribute to the course of maintenance therapy with infliximab in children.

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Background: The primary and secondary loss of efficacy are major problems during anti TNF-alpha maintenance therapy. It's documented that complete remission, concurrent immunomodulators, are the predictors of prolonged remission. It is questionable if ileal or colonic localization can contribute the CD flare. The aim of the study was to explore the contribution of CD gut localization to the course of maintenance therapy with infliximab in children.

Methods: This is a per protocol subanalysis of CIMIT study. 77 patients with PCDAI>30 pts and endoscopic evaluation (using Simple Endoscopic Score for Crohn's Disease (SES-CD), based on 4 endoscopic variables (ulcer size, ulcerated and affected surfaces, stenosis) in 5 ileocolonic segments (ileum, right colon, transverse colon, left colon, rectum) and the endoscopic parameters are scored from 0-3)

performed, who finished one year maintenance therapy with infliximab 5 mg/kg were involved to the study. Clinical (PCDAI score) remission (PCDAI<10) were assessed at Week 52. Scorings in each ileocolonic segment were used as five independent variables in analysis of discrimination between: groups with clinical remission (with or without rescue therapy n=57) vs. no remission (n=20) and groups with CD flare during maintenance therapy present (n=34) vs. absent (n=43).

Results: None of the analyzed variable had significant impact on discrimination between group with clinical remission vs. no remission - all partial Wilks' Lambda > 0,97. The optimal model of discrimination had sensivity 0,98 and specifity 0,17.

None of the analyzed variable had significant impact on discrimination between group with CD flare during maintenance therapy present vs. absent - all partial Wilks' Lambda > 0,99. The optimal model of discrimination had sensivity 0,78 and specifity 0,42.

Conclusions: Crohn Disease localization does not contribute to the course of maintenance therapy with infliximab in children.

P305
Infliximab serum levels do not predict remission after the induction phase in Crohn's Disease patients

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Background: The correlation between IFX serum levels and remission achievement after the induction phase in Crohn's disease (CD) patients has not been studied.

Aims: 1) To evaluate the correlation between IFX levels and remission after the induction phase in CD patients. 2) To assess the accuracy of IFX serum levels to predict short-term remission.

Methods: CD patients with active disease (CDAI>150) naïve to anti-TNF treatment were included. Patients received IFX 5 mg/kg at weeks 0, 2, 6 and 14. Remission was defined as a CDAI score < 150, and response as a decrease of >70 points after 14 weeks of treatment. Clinical evaluation was assessed and blood samples were obtained at baseline and weeks 4, 8 and 14. IFX and antibodies to IFX (ATI) were measured using a homogeneous mobility shift assay (HMSA; Prometheus Lab, San Diego, Unites States). Correlation between IFX levels during the induction phase and response at week 14 was calculated. Receiver operating characteristic (ROC) curves were constructed and the area under the ROC curves (AUC) was calculated. Determination of predictive IFX concentration thresholds were based on the choice of the corresponding sensitivity and specificity pair determined from the ROC curves

Results: Twenty-nine patients were included (58% female, 76% ileal or ileocolonic involvement, 48% inflammatory behaviour, 41% with previous surgery and 65% on concomitant immunosuppressants). At week 14, 72% of patients achieved remission, 14% partial response and 14% non-response. Female gender was more frequent among responders, CDAI score was lower, and time of evolution of the disease was shorter among patients that reached remission. Mean IFX concentration was similar between patients that reached remission at week 14 and those who did not: 35 vs. 42 µg/mL at week 4, 33 vs. 34 µ g/mL at week 8, and 5 vs. 8.4 µ g/mL at week 14, respectively. In the multivariate analysis adjusted by age, gender and time of evolution of the disease, IFX trough levels at week 14 were not associated with remission (odds ratio=0.75, 95% confidence interval=0.5-1.1). The AUCs for the IFX concentration to predict remission at week 14 were: 0.38 at week 4, 0.52 at week 8 and 0.37 at week 14. The corresponding figures for response instead of remission were 0.2 at week 4, 0.23 at week 8 and 0.15 at week 14. No concentration threshold was predictive of remission in any visit.

Conclusions: There was no association between IFX serum levels at weeks 4, 8 or 14 and clinical response or remission after the induction phase in CD patients. Therefore, IFX threshold concentration that predicts clinical response or remission at week 14 could not be determined

P306
Embedding pharmaceutical care into the multidisciplinary team

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Background: Pharmacists traditionally do not get involved in the long-term management of patients with chronic disease.

This service development aimed to integrate pharmacy-lead IBD medication optimisation into the IBD Multi Disciplinary Team (MDT).

We report our experience of extending our specialist pharmacist's remit.

Methods: 1. A weekly pharmacist outpatient clinic was established, to initiate immunomodulating drugs and undertake biochemical monitoring. The pharmacist optimised therapy according to blood levels, adverse drug reactions (ADRs) & concordance.

2. Strategic and operational management of the biologics infusion clinic was transferred to the pharmacist.

3. A new blood & therapeutic drug monitoring (TDM) service for immunomodulators & biologics was introduced to optimise therapy decisions.

4. The rapid access (helpline) service was reviewed to see whether the pharmacist could add value.

5. The pharmacist facilitated MDT-approved pathways to initiate and review immunomodulators.

6. A workload and prescription audit was conducted over four months with financial impact assessment.
7. Patient & anonymous colleague feedback was sought.
Results: 1. In the four months analysed, 14 pharmacist clinics were held, serving 138 patients. 382 patients had blood monitoring, ensuring clinical governance.
2. The biologics infusion clinic expanded to include a cross-speciality services.
3. 65 patients had their immunosupressant therapy adjusted in the TDM service. The pharmacist is gatekeeper for testing and is responsible for optimising therapies (as a non-medical prescriber).
4. The advice sought from the rapid access service was primarily nurse-orientated and the service remains nurse-lead, with pharmacist deputising to maximise resources. In 4 months 142 of 1032 queries were answered by the pharmacist.
5.The MDT reviewed 42 patients on biologics according to the new pathways.
6.The TDM service resulted in a minimum of £60,000 savings for the health economy.
7. 6 of 6 peer-assessors returned overwhelmingly positive reviews of the service and patient feedback was favourable.
Conclusions: Involving the pharmacist in all aspects of the long-term care of patients with IBD enhanced patient safety and standardised treatment & monitoring protocols, whilst individualising therapy.
The focus of the MDT shifted to early medicines optimisation, realising considerable cost savings. Interprofessional relationships profited from working closely together / deputising for each other.
Embedding pharmaceutical skills into the multidisciplinary team influenced therapeutic decision making, ensuring that services incorporated good medicine management and medicine optimisation principles at conception to guarantee high-quality, compassionate care and strong governance.

P307
Clinical outcome of adalimumab therapy in patients with ulcerative colitis previously treated with infliximab: a Danish single center cohort study

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Background: Controlled trials have shown that anti-TNF-alpha inhibitors are of proven value in the treatment of active ulcerative colitis. Adalimumab (ADL), a fully humanized TNF-inhibitor, is increasingly used both as primary anti-TNF agent and in patients switching from another TNF-inhibitor due to loss of response or side effects. This study investigated clinical outcomes of ADL therapy in an everyday clinical setting, where infliximab (IFX) had been used as first choice of anti-TNF agent, and followed by ADL as second line agent.
Methods: Retrospective, observational single-center cohort study including all ulcerative colitis patients treated with ADL at a tertiary Danish IBD center until 2014. Clinical outcomes were assessed after 12 and 52 weeks and classified according to physicians' global evaluation and supported by endoscopy.
Results: The study population comprised 33 patients. All patients had previously received IFX. Main reasons for switching to ADL were infusion reactions to IFX (45%) or IFX treatment failure (33%). Short-term efficacy of ADL after 12 weeks revealed 15 patients (45%) with clinical response, and 6 (18%) in clinical remission. Twenty-three patients continued ADL for more than 12 weeks, and at long-term follow-up after one year of ADL treatment, 8 of these (34%) had clinical response (24% of the entire cohort), and 6 (26%) were in clinical remission (18% of the entire cohort). A total of 5 patients (15%) were colectomized during the study, and this was generally caused by primary ADL treatment failure (4 of 5 patients).
Conclusions: Long term efficacy of ADL therapy in ulcerative colitis patients previously treated with IFX appears to be modest in clinical practice and associated with a more than 3 fold higher colectomy rate than reported in the pivotal ULTRA registration trials. [1] The Results raise interest in introduction of biologic drugs with a different therapeutic target, such as cell migration inhibitors, as an alternative to switching between TNF-inhibitors in patients with chronic active ulcerative colitis.

References:

[1] Feagan BG et al, (2014), Adalimumab therapy is associated with reduced risk of hospitalization in patients with ulcerative colitis, Gastroenterology

P308
Interobserver agreement in assessment of Rutgeerts' score of endoscopic recurrence of ileal Crohn's disease: a substudy of the TOPPIC trial

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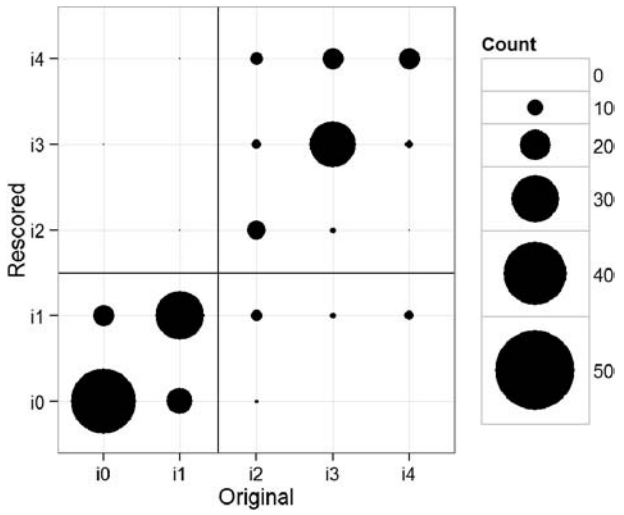
Background: Rutgeerts' score is widely used for the assessment of endoscopic recurrence following ileocaecal (IC) resection for Crohn's disease (CD). Higher scores have been shown to be associated with an increased risk of clinical recurrence. TOPPIC is a double-blind randomised, placebo-controlled trial of mercaptopurine for the prevention of post-operative recurrence after IC resection for CD and includes a secondary endpoint of endoscopic recurrence. Few published data are available on interobserver agreement of Rutgeerts' score. This study aimed to assess the interobserver agreement of



"Figure 1 Comparison of original Rutgeerts' scores with those when rescored. The number of scopes is indicated by the size of the circle. Lines indicate endoscopic recurrence (>=i2) vs no recurrence"

Rutgeerts' score on images from endoscopies carried out as part of the TOPPIC trial.

Methods: Five TOPPIC trial investigators were shown endoscopic images taken from 43 colonoscopies performed in Edinburgh as part of the TOPPIC trial. The investigators were blinded to the original report and were shown only the images with a description of the anatomical location from which each image was taken. Each investigator was independently asked to score each colonoscopy using the Rutgeerts' score and a custom-designed application. Statistical analysis was performed using R and the psych package. The five scores for each colonoscopy were compared with each other and the score made by the original endoscopist. Shrout and Fleiss' intraclass correlation and pairwise weighted Cohen's kappa were calculated.

Results: The original scores for the colonoscopies were spread across the possible scores, with 11 i0, 10 i1, 7 i2, 10 i3 and 5 i4. Intraclass correlation for single ratings (ICC3) was 0.82 (95% confidence interval 0.74-0.88). The weighted Cohen's kappa when assessed for each possible pair of scorers ranged from 0.72 to 0.88. A graphical representation of the agreement between the original score and the rescores is shown in figure 1.

When scores were stratified into endoscopic recurrence or not, as defined by a score of i2 or greater, all five scorers agreed with the original score in 34/43 (79%). There was no significant difference in this agreement between those procedures with an original score ≥i2 or <i2.

Conclusions: Interobserver agreement for Rutgeerts' score of endoscopic recurrence was generally good in this cohort of patients. Despite the limitation of using still images, agreement with the score of the original endoscopistwas also good. However, there was some variation in assessment, even when assessing the presence/absence of endoscopic recurrence. These findings are important when considering the reliability of outcome data in multicentre clinical trials.

P309
The effects of preoperative adsorptive leukocytapheresis on inflammatory cytokines and septic complications after restorative proctocolectomy for ulcerative colitis: a prospective randomized study

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Background: Granulocyte, monocyte/macrophage adsorption (GMA) has produced significant clinical efficacy together with down modulation of specific inflammatory cytokines in patients with ulcerative colitis (UC). This study was to investigate if preoperative GMA produces immunosuppressive effect on dysregulated immune activity and septic complications after restorative proctocolectomy (RPC) in patients with UC.

Methods: Forty patients requiring RPC were included. Twenty randomly selected patients received 5 GMA sessions over 2 consecutive weeks prior to RPC (GMA group). RPC was performed within 2 weeks after the last GMA. The other 20 patients did not receive GMA prior to RPC (non-GMA group). Interleukin (IL)-1β, IL-6 and tumour necrosis factor (TNF)-α in plasma and peritoneal fluid from a drainage tube were measured on postoperative days 0, 1, 3 and 7. Incidence of septic complications (anastomotic leak, fistula, intra-abdominal abscess or wound infection) and cytokine levels were monitored. Leukocyte and platelet counts, and C-reactive protein (CRP) levels were also measured perioperatively.

Results: Between the two groups, patients were matched with respect to age, sex, UC duration, severity, extent and the dose of prednisolone at surgery. Septic complications occurred in 3 patients (15%) in each group. IL-1β, IL-6 and TNF-α levels in plasma and peritoneal fluid were not significantly different between the two groups during the entire study period. Similarly, leukocyte and platelet counts, and CRP levels were not significantly different between the two groups during the study period.

Conclusions: Based on the assays of IL-1β, IL-6 and TNF-α levels in the plasma and the peritoneal fluid, this study did not show any immunosuppressive effect on these cytokines by preoperative GMA in patients with UC who underwent RPC. Likewise, GMA did not affect the incidence of septic complications.

P310
Systematic review: The financial burden of surgical complications in patients with ulcerative colitis

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Background: Patients undergoing colectomy for ulcerative colitis (UC) may experience complications associated with reduced patient quality of life (QoL) that Results in a considerable economic burden to healthcare systems. Appreciation of this burden is important when evaluating the cost-effectiveness of newer interventions for UC versus colectomy. A systematic review was conducted to identify studies reporting resource utilisation, costs of complications and the related QoL burden (presented as health state utility values [HSUVs]) arising from colorectal surgery procedures in patients with UC.

Methods: Embase, MEDLINE and The Cochrane Library were searched for studies (1995-2014) reporting resource use/costs of surgical complications, and HSUVs data in adult patients with UC, undergoing colorectal procedures. Conference proceedings from January 2011-January 2014 were searched manually. Costs were inflated to the 2013 price year using the Consumers Price Index (CPI) and Purchasing power parity (PPP) exchange rates. Quality assessment was conducted alongside extraction of each individual study.

Results: The systematic review identified 15 studies (retrospective observational, n=11). Resource use/costs were reported in 12 studies and three studies reported HSUVs data in patients with UC experiencing postoperative complications. Costs of postoperative complications ranged from $18,650/patient at a six-month follow-up to $35,000/patient over a five-year period. The main cost drivers were reoperations, physician fees, additional inpatient hospital stays and infertility treatment as a result of complications. Pouchitis, pouch failure and small bowel obstruction were the postoperative complications associated with the greatest burden. Across three studies, marked reductions in HSUVs were observed for patients with UC experiencing surgical complications compared with patients with UC in a remission state.

Conclusions: There is a paucity of well-reported studies on resource use/cost, and QoL burden of surgical complications in patients with UC. However, surgical complications represent a substantial burden both in terms of cost and patient QoL. A better understanding of the extent of the burden of surgical complications on healthcare systems

and the impact on patient QoL is required to provide accurate cost estimates to inform health technology appraisals for newer UC therapies.

P311
Measurement of functional blocade of TNF-alpha by anti-TNF agents is a stronger predictor than trough levels and anti-drug antibodies: 2-year prospective clinical data

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Background: In case of loss of response (LOR) to anti-TNF agents in inflammatory bowel disease (IBD) patients, interventions, such as dose increase and shorten the interval, lead only to a transient improvement and a majority patients will eventually loss response. Patients could also be successfully switch within class following antibodies development. However, the LOR in some patients is due to a non anti-TNF driven pathway of inflammation. A functional in vitro test (CD-62L shedding) measuring TNF functional blockade should help us identified those specific situations.

Methods: An in vitro test was used to predict the response to the drug: the shedding of the L-selectin (CD62L) quantified by flow cytometry on the surface of granulocytes before and after the anti-TNF agent administration. In a subgroup of patients trough level of the drug (TL) and antibodies against the drug (ADA) have been performed in order to compare both tests. The treatment strategy during the 2 years of the study was blinded to the Results of the CD62L shedding, TL and ADA and followed clinical symptoms-based interventions or switch by IBD specialists.

Results: From June 2012 to October 2014, 33 IBD treated with anti-TNF agents at Bern University Hospital were followed prospectively (clinicians blinded) to correlated clinical outcome with their response profile tested at baseline. The 22 responders (R) and 11 non responders (NR) had similar clinical characteristics. During a median follow up of 22 months (range 7- 26; 53 patient-years), 17 medico- surgical events occurred (3 adverse events, 1 CMV colitis, 9 flares, 3 intestinal resections and 1 de novo fistula) 5 in R and 12 in NR, which means 11% vs. 60% (p< 0.001) of the patient-year follow up. The delta of calprotectin between year 1 and year 2 of follow up was 261 for NR and 1.3 for R. ADA and TL measurement could be performed in 15 patients (45%; 9 R and 6 NR). Only 2 patients developed ADA (one in each group). There was no significant difference in trough levels between R and NR (2.8 vs. 4.8; p=0.4) and 62% had a therapeutic level (>1.5).

Patients stable without need for intervention were 16/20 (84%) in R vs. 1/11 in NR (p<0.001). In the NR group all the dose optimisation failed, whereas in the responders group, interventions that would have been suggested on the basis of TL and ADA have not been performed (clinicians blinded), but were finally not required, based on the favourable clinical outcome.

Conclusions: Testing the in vitro functional blockade of TNF alpha (CD62L shedding) in anti-TNF treated IBD patients seem to be a better long term predictor than trough levels and antibodies against the drug measurements.

This could certainly minimize interventions and therefore reduce costs and risk of adverse events.

P312
Evolution of the Lemann index in Crohn's disease: a retrospective study

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Background: The development and the first validation of the Lemann index (LI), the first global Crohn's disease (CD) damage index assessing cumulative structural bowel damage in CD, has recently be published. The aim of the present study was to assess the evolution of the LI over time.

Methods: We conducted a retrospective observational study. All the patients underwent two digestive damage evaluations (E1 and E2), at two different times separated for at least 12 months. At each evaluation (E1 and E2), examinations were performed according to the investigational protocol of the LI, including clinical evaluation abdominal-magnetic resonance imaging (MRI) for all patients. Further investigations were based on the disease location: upper endoscopy for upper digestive tract, colonoscopy for colorectal disease, and pelvic-MRI for perianal disease. As defined in the protocol, all examinations were performed within a delay less than 4 months, at each evaluation.

Results: Thirty CD patients were included. Among them, 2/30 (6.6 %), 29/30 (96.6%), 5/30 (16.6%), and 2/30 (6.6%) patients had upper digestive tract, small bowel, colonic, and anal CD respectively. At E1, median disease duration was 7 years (range: 0 - 25), 10/30 (33.3%) and 1/30 (3.3%) patients had underwent small bowel and colonic surgical resections respectively, and 10/30 patients (33.3%) and 18/30 patients (60.0%) had received immunosuppressive and anti-TNF therapies respectively. At E1, median LI was 2.5 (range: 0.0-29.0). Median time between E1 and E2 was 23 months (range: 13-56 months). Between E1 and E2, three patients had surgery (two intestinal resections and one colectomy), immunosuppressive therapy was introduced in two patients and anti-TNF therapy in 6 patients. At E2, median LI was 2.5 (range: 0.0-29.2). An increase of LI was observed in 11/30 patients (36.0%) and a decrease in 5/30 patients (16.0%). LI did not change in 14 (46.7%) patients. Median time between E1 and E2 was significantly longer in patients with an increase of LI compared to patients with no change of LI (30.0 and 19.5 months respectively, p < 0.05).

Conclusions: In this retrospective study, LI increased in more than one third of the patients. Importantly, increase of the LI was significantly related to disease duration, suggesting that digestive damage evaluations should not be performed within short delays.

P313
Medication use and its perception by female inflammatory bowel disease patients.

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Medication	% Number of patients
5-ASA	66%
Steroids	6.44%
Azathioprine	22.3%
Infliximab	20.2%
Adalimumab	7.30%
Methotrexate	1.29%
6-Mercaptopurine	1.29%
Sulfasalazine	1.29%

Background: Medication use in females with IBD of child-bearing age is challenging and has to be dealt with individually. Patients are young and want to take an active role in their own management. Some tend to stop medications before or during pregnancy. However, they fail to realize that most drugs are considered low risk for congenital anomalies. Maintaining remission with medical treatment outweighs the potential risks of adverse drug effects. Stopping medications carries the risk of flair ups during pregnancy.
Methods: This was a retrospective study were patients were recruited from 5 European centres. Female IBD patients were recruited and they were interviewed through a purposely designed questionnaire.
Results: 233 patients were recruited (mean age 40 SD±11.9). The mean age of diagnosis was 31.4 years (SD±11.2). 85.5% of patients with ulcerative colitis (UC) had a Montreal classification of E2 or E3. 64.7% of Crohn's disease (CD) patients, had non-stricturing and non-penetrating disease.
4.3% were not compliant to treatment. Reasons given included, well-being, long standing remission, fear of medications, problems with employers and suppositories and enemas being uncomfortable. 15.0% thought that all medications should be stopped during pregnancy. 63.1% of patients were unsure and 12% claimed that only some medications should be stopped. 5-ASA was considered as a very safe medication by more than 99% of patients.
Medications were stopped by the patient's doctor in 13.9%. This consisted of biologics stopped in the third trimester (2.7%), 5-ASA (9.4%), methotrexate (0.9%) and prednisolone (0.9%). Medications were added by the doctor in 3.9% mainly by adding 5-ASA, folic acid, azathioprine and prednisolone. Dose of steroids and 5-ASA were increased in 2.6%. There was no reported reduction in dose of medications. 1.7% stopped medications on their own accord. Reasons given included fear of harm to the baby and being in remission.
26.6% patients were uncertain if patients with IBD could breast feed. 40.8% thought that they could not breast feed. 54.5% breast fed their babies. In those who did not breastfeed, only 10.7% did not do so because of the medications that they were having. The rest did not breastfeed due to fear and misconceptions about IBD and breastfeeding.
Conclusions: Unfortunately, 5-ASA is still regarded as unsafe during pregnancy by some physicians. There is still lack of awareness amongst patients about why patients should continue medications during pregnancy. More awareness is needed about breast feeding in patients with IBD.

P314
Biosimilar infliximab in inflammatory bowel diseases: first interim Results from a prospective nationwide observational cohort

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Background: Biosimilars are biologic medicines that enter the market subsequent to an original reference product whose patent has expired. Biosimilar infliximab received EMA approval in June 2013 and entered the Hungarian market in May 2014. Few data is yet available on the safety and efficacy of biosimilar infliximab in extrapolated indications, such as inflammatory bowel diseases.
Methods: A prospective, nationwide, multicentre, observational cohort was designed to examine the safety and efficacy of CT-P13 infliximab biosimilar in induction and maintenance of remission in Crohn's disease (CD, 108 weeks follow-up) and ulcerative colitis (UC, 54 weeks follow-up). Demographic data were prospectively collected at inclusion and a harmonized, tight monitoring strategy was applied in terms of clinical scores (CDAI, PDAI, MAYO/pMAYO each visit), biochemical markers (incl. CRP, at least every 3 months) and endoscopic/imaging (at least every 12 months) as requested by the National Health Fund. Sera is collected for drug through and antibody measurement at 0, 12, 24 and 52 weeks. Safety data was meticulously registered during follow-up
Results: 90 consecutive IBD patients were included in the present cohort (57 CD patients (27 males) and 33 UC patients (16 males)) Age at disease onset was 26.0 (SD:10.9) years in CD and 30.5 (SD:14.1) years in UC. In CDileocolonic and perianal disease was present in 40.4% and 37.5%, respectively. 55.2% of UC patients had extensive colitis. 21.4% of CD patients had previous surgery. In CD and UC, 60.4%/50% and 55.2%/74.2% of patients received concomitant immunosuppressives and steroids, while 30.4% of CD and 16.1% of UC patients received previous anti-TNFs. At induction, mean CDAI was 289(SD:107), while MAYO/pMAYO scores were 8.8(SD 3.1) and 6.4(SD 2.6) in UC. There was a significant decrease in CDAI after 2 and 6 weeks of treatment compared to baseline p<0.001, ANOVA-Scheffe). In addition there was a numeric decrease in the mean CRP level(from 23.5mg/L to W2:11.3mg/L and W6:15.3mg/L). There was a significant decrease also in the mean pMAYO score(from 6.4 to (n=16) W2:3.7 and W6:3.6) with a numeric decrease in CRP level during induction therapy in UC . 4 allergic reactions occurred, all in patients who had received previous anti-TNF medication.
Conclusions: This is the first prospective nationwide cohort examining the safety and efficacy of the biosimilar infliximab in IBD. A significant decrease of disease activity (CDAI and pMAYO) was observed coupled with a decrease in CRP levels during induction

with the infliximab biosimilar. A complete analysis of the induction data will be available at the time of congress.

P315
Remission induction therapy in patients with remitting-relapsing ulcerative colitis dependent and refractory to corticosteroids or intolerant to thiopurines

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Background: Ulcerative colitis (UC) is a chronic remitting-relapsing inflammatory bowel disease, requiring remission induction therapy during an active phase. Corticosteroid is often administered to achieve remission of moderate to severe UC, but UC in many patients may become refractory to corticosteroids at a subsequent remission induction therapy. This study was to investigate the success of remission induction therapy in patients with remitting-relapsing UC who were dependent and refractory to corticosteroids or intolerant to thiopurines.

Methods: In a retrospective single centre setting, from January 2008 to September 2014, 103 patients with remitting-relapsing UC dependent and refractory to corticosteroids or intolerant to thiopurines were monitored for the efficacy of remission induction therapy with corticosteroid (n=31), granulocyte/monocyte apheresis (GMA, n=44), tacrolimus (Tcl, n=13), and infliximab (IFX, n=15). Assessment of UC activity level was according to the Mayo clinical activity index (CAI); <3 meant remission, and a decrease of at least 30% in the CAI score meant significant response to therapy.

Results: Induction therapy sessions were 90 times in the steroid group, 75 times in the GMA group, 13 times in the Tcl group and 15 times in the IFX group. The average CAI before treatment was 6.91, 7.14, 8.60 and 8.67, respectively in the 4 groups. Remission induction rates were 8.88%, 22.3%, 15.4%, 0%, respectively in the 4 groups. In the same order, response rates were 33.3%, 60.3%, 30.8%, and 13.3%. The response and the remission induction rates for GMA were higher than for steroid (P=0.00045), Tcl (P=0.045) or IFX (P=0.00081).

Conclusions: In this setting of patients with remitting-relapsing UC and intolerant to thiopuries, the number of patients was not well balanced in the 4 groups for adequate statistical analyses. However, our observational judgment indicated that in this setting, IFX, corticosteroid and Tcl had very low efficacy. In contrast GMA appeared to be very much better than the other three interventions.

P316
Impact of anti-TNF therapy in the number of hospitalizations and surgeries - Overview of clinical practice in a tertiary referral center

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Background: Anti-TNF therapy has represented a major breakthrough in the medical treatment of moderate to severe Ulcerative Colitis (CU) and Crohn's Disease (CD). Hospitalization and surgery are important outcomes and drivers of healthcare costs in these patients.

Our aim was to evaluate the impact of anti-TNF therapy in the number and length of hospitalizations and surgical procedures in patients with inflammatory bowel disease (IBD).

Methods: Retrospective study including patients with IBD assigned to start anti-TNF therapy (infliximab [IFX], adalimumab [ADA] or golimumab [GM]). Patients were evaluated in two different time cohorts: before anti-TNF therapy (A), after starting anti-TNF therapy (B). Period of observation comprehended 25 years (July 1989-October 2014). Endpoints included number and length of hospitalizations and surgeries. Statistical analysis was performed with SPSS v 20.0 IBM statistics.

Results: 164 patients met our inclusion criteria, 131 with CD, 33 with UC.

Anti-TNF therapy included IFX (127), ADA (35) and GM (2). The average age of diagnosis was 29 years. Mean age of starting anti-TNF was 37 years. Over 50% of patients were diagnosed before 24 years and were started on biologics before 35 years old.

The average age at anti-TNF induction was significantly lower in patients with CD than in UC (34.3 ± 11.2 years versus 41.3 ± 13.1 years, p=0.0001).

During our follow-up time a total of 870 hospitalizations occurred, 739 (85%) in patients with CD. Anti-TNF therapy was also associated with both a reduction in the number of admissions (60.0% versus 40.0%, p=0.0001) and in the length of hospitalizations (8.2 ± 15.7 days versus 4.3 ± 8.3 days, p= 0.0001).

In patients with CD, IFX was associated with shorter hospitalizations than ADA (6.3 ± 14.3 days versus 9.7 ± 13.2 days, p=0.034). Disease behavior also influenced the number and length of hospitalizations with penetrating or stricturing disease being associated with more hospitalizations (182 versus 535, p=0.003) and longer lengths of stay (4.6 ± 10.2 days versus 7.4 ± 15.5 days, p=0.023).

During the study period 98 surgeries were performed in these patients; 94 in patients with DC and 4 in patients with UC. The majority of surgeries were performed before patients were started on anti-TNF therapy (72.4% versus 27.6%, p=0.0001). The length of hospitalizations was not significantly different between the two times cohorts.

Conclusions: Our series clearly demonstrate a trend for reduction in hospitalizations and surgeries since introduction of anti-TNF therapy. These findings reinforce the dramatic role of anti-TNF therapy in the progression of both CD and UC.

P317
Clinical value of routine therapeutic anti-TNF drug monitoring (TDM) in Inflammatory Bowel Disease (IBD) patients in clinical practice

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Background: In light of emerging data demonstrating that therapeutic anti-Tumour Necrosis Factor alpha (anti-TNF α) levels are

"Patient Demographics"

Mean age (years) sd	39 ± 14
Male	52%
Mean Disease Duration (years ± SD)	7 ± 6
Crohns's disease n. (%)	71 (70%)
Ulcerative Colitis n. (%)	29 (29%)
Current immunomodulator n (%)	11 (11%)
Mean duration current immunomodulator (months ± SD)	3 ± 2
Length of follow up n=55 (months ± SD)	11 ± 3
Mean duration of biological treatment (months ±SD)	66 ± 238
Previous Biological agent n. (%)	28 (27%)
Pre medication with steroids n. (%)	12 (12%)
Indication drug assay n. (%) Routine medical follow up Post induction Therapeutic failure Reaction/Intolerance	 81 (79%) 9 (9%) 8 (8%) 2 (2%)

associated with better clinical outcomes, various treatment algorithms incorporating TDM have been proposed. Many studies have focused on the utility of TDM in the management of non-response or loss of response to TNF α - inhibitors, fewer on the use of routine assay. Our primary objective was to evaluate routine use of TDM for three TNF α inhibitors and observe physician response in clinical practice.

Methods: A retrospective study was conducted on all IBD patients treated with TNF α -inhibitors who attended two IBD referral centres (2013-2014). Infliximab, adalimumab or certolizumab pegol trough levels and anti-drug antibody (ADA) were measured using a commercially available ELISA (Lisa Tracker Premium Kit). Patient demographics, details of disease, subsequent clinical management and outcomes were retrieved from patient records.

Results: 180 anti-TNF α and ADA assays were performed in 103 patients. Patient demographics are reported in Table 1. 88% of patients were treated with infliximab, 8% adalimumab and 4% certolizumab pegol. A change in management as a result of TDM occurred in 29% of the patients. 41% of the total numbers of assays were in the subtherapeutic range. The prevalence of ADA was 10%. Focusing on the sub therapeutic subgroup (n=73), 55% had no change in management, 15% had an increase in dose while 3% had an increase in frequency. 14% of the subtherapeutic group had detectable ADA. 80% of the ADA positive assays lead to change TNF inhibitor, 10% ceased due to anaphylaxis and 10% resulted in the addition of azathioprine. In the assays performed for routine medical follow up, 40% were in subtherapeutic range. Modification in management as a result of routine TDM occurred in 34% of cases.

Conclusions: This is the first study to evaluate utility of anti-TNF α TDM in Switzerland. In this cohort TDM altered management in 29% of cases. TDM ordered for routine medical follow up revealed subtherapeutic levels in 41% of cases and led to a change in clinical management in one third of cases. The approaches to subtherapeutic levels and presence of ADA varied between physicians. Further studies are required to develop consensus on approaches to subtherapeutic levels and presence of low level ADA and further evaluate the use of TDM in routine clinical care.

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P318
Management of loss of response to infliximab. Results of a descriptive study of a cohort of inflammatory bowel disease patients.

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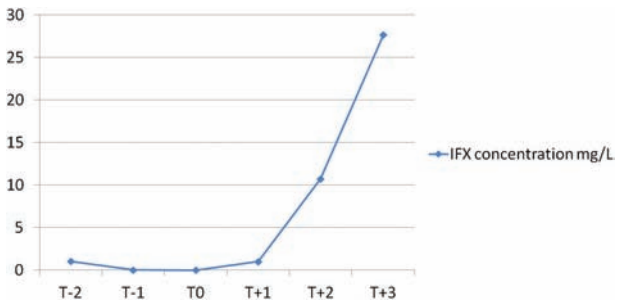
Background: Infliximab has profoundly modified the treatment of inflammatory bowel disease. Nevertheless, 30 to 50 % of patients present loss of response, and treatment alternatives are limited. Understanding the mechanism of loss of response and defining its management is essential.

Methods: We report the Results of a retrospective study in a cohort of patients treated by infliximab for inflammatory bowel disease, between January 2009 1st and December 2012 31th. Patients following an episodic or induction treatment only were excluded. The data collected was: demographic data, disease characteristics, initial albumin and C-reactive protein sera concentrations, corticoresistance at the start of the treatment, week 14 infliximab serum concentration. For patients presenting loss of response we also collected: infliximab serum concentration at the time of loss of response (T0), 2 infusions (T-1, T-2) before loss of response and 4 infusions (T+1 to T+4) after. Infliximab serum concentrations were measured by ELISA test. Anti-drug anti-bodies were tested by ELISA double antigen.

Results: Eighty-one patients were included. Thirty-four patients presented loss of response to infliximab (42%) and forty-seven maintained clinical remission. All patients presenting loss of response were firstly optimised by a dose increase or interval shortening. Fourteen patients (41%) did not respond to the first optimisation. They were treated either by adding or switching immunomodulator (n=8), by switching for another anti-TNF (n=5), or by surgery (n=1).



"Example of infliximab concentration evolution after adding methotrexate."

A significant correlation was found between initial corticoresistance and ulterior loss of response (OR=2,9 [1,1-7,9], p=0.035). Week 14 infliximab serum concentration was significantly associated to albumin serum concentration (p=0.003).

Methotrexate was used in 6 patients as a second optimisation and helped in 5 out of 6 patients to regain clinical response and a quick increase in infliximab serum concentrations (fig.1).

Conclusions: Our study confirms the high frequency of loss of response to infliximab in inflammatory bowel disease. It helps us to identify several high-risk situations, especially severe clinical and biological diseases, which would benefit from early pharmacological monitoring. Adding methotrexate seems to be a good strategy to regain clinical and biological response.

P319
Adalimumab long-term effectiveness in adults with Crohn's Disease: Observational data from the PYRAMID registry

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Background: To evaluate the long-term effectiveness of adalimumab (ADA), an anti-tumour necrosis factor agent approved for the treatment of moderate to severe Crohn's disease (CD).

Methods: Five years of interim data from PYRAMID, an ongoing, global, observational registry initiated in 2007, were used to evaluate the long-term effectiveness of ADA as measured in the change from baseline in Physician's Global Assessment (PGA; a composite of the Harvey-Bradshaw Index and a rectal bleeding score); Short Inflammatory Bowel Disease Questionnaire (SIBDQ); and 4 components of the Work Productivity and Activity Impairment Questionnaire (WPAI): absenteeism, presenteeism, total work productivity impairment (TWPI), and total activity impairment (TAI). A score increase indicates improvement for SIBDQ; a score decrease indicates improvement for all other effectiveness measures. ADA was prescribed according to local product labels. Effectiveness Results were summarised with descriptive statistics for patients naïve to ADA at enrolment. Only observed effectiveness parameters were to be analysed. No missing data imputations were to be performed.

Results: As of December 2013, 5,061 patients have been enrolled. Of these, 41% (2,092/5,061) were ADA-naïve at enrolment. The mean age for ADA-naïve patients was 37 years, mean CD duration was 10 years, 58% were female, and 96% were white. Mean PGA scores improved from baseline and were maintained through year 5. Clinically meaningful improvements in mean scores for SIBDQ and WPAI (absenteeism, presenteeism, TWPI, and TAI) were maintained over 5 years (**Table**).

Conclusions: This international observational study of ADA use in routine clinical practice demonstrated that clinically meaningful improvements in disease activity, work productivity, and activity impairment were achieved in patients with CD 1 year after initiating ADA. These improvements were maintained over a 5-year period.

P319a
Deep clinical remission in patients with Ulcerative Colitis: Evaluating the effects of vedolizumab on various combinations of endoscopic and patient-reported outcomes

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Background: The evolving concept of *deep clinical remission* in the treatment of ulcerative colitis (UC) involves both endoscopic outcomes and patient-reported outcomes (PROs). The purpose of the current post hoc analyses of data from the GEMINI 1 induction and maintenance phases [1] was to evaluate the effects of vedolizumab (VDZ) on deep remission using various combinations of endoscopic outcomes (Mayo Clinic endoscopy subscore [ES]) and PROs (Mayo Clinic symptom subscores).

Methods: At wks 0 and 2 of the GEMINI 1 induction phase (wks 0-6), patients in cohort 1 received randomly assigned, blinded VDZ 300 mg or placebo (PBO), and patients in cohort 2 received open-label VDZ 300 mg. At wk 6, VDZ responders were randomly assigned to receive VDZ 300 mg every 8 wks (Q8W) or every 4 wks (Q4W) or PBO in the maintenance phase (wks 6-52). At wks 6 and 52, the following 4 post hoc deep remission end points, defined using endoscopic outcomes and PROs, were evaluated: (1) endoscopic remission (ES = 0) and symptomatic improvement (rectal bleeding subscore [RBS] = 0, stool frequency subscore [SFS] decrease or no change from baseline); (2) endoscopic improvement (ES ≤1) and symptomatic remission (RBS = 0, SFS = 0); (3) total score (ES + RBS + SFS) ≤1 with endoscopic and symptomatic improvement (ES≤ 1, RBS = 0, SFS decrease or no change from baseline); and (4) endoscopic and symptomatic improvement (ES ≤1, RBS = 0, SFS ≤1).

Results: At wk 0, mean UC duration was 6.2 y (Q8W), 7.6 y (Q4W), and 7.8 y (PBO); mean complete Mayo Clinic scores were 8.4 (Q8W), 8.3

Effectiveness Measures for ADA-naïve Patients

Measure	Baseline	1 year	2 years	Change From Baseline	4 years	5 years
	Mean (SD)			Mean (SD)		
				3 years		
PGA	8.1 (5.6) n=2,004	-3.6 (5.4) n=1,336	-3.7 (5.5) n=1,124	-4.2 (5.3) n=1,032	-4.1 (5.1) n=847	-4.4 (5.1) n=232
SIBDQ	40.5 (12.7) n=1,457	11.6 (13.0) n=723	10.8 (14.3) n=526	11.8 (13.6) n=441	12.3 (13.3) n=361	13.2 (13.0) n=108
Absenteeism	21.9 (33.3) n=825	-11.9 (34.9) n=330	-10.6 (32.7) n=227	-15.0 (34.7) n=186	-11.4 (36.7) n=154	-12.3 (31.4) n=40
Presenteeism	41.4 (29.9) n=855	-19.6 (32.5) n=353	-20.1 (35.2) n=259	-22.4 (33.2) n=208	-17.8 (37.1) n=167	-22.9 (28.9) n=42
TWPI	50.2 (33.3) n=823	-23.8 (35.1) n=326	-23.7 (38.9) n=224	-27.3 (35.6) n=181	-22.2 (37.8) n=153	-21.9 (30.4) n=39
TAI	50.7 (30.0) n=1,421	-23.0 (31.7) n=698	-23.3 (34.3) n=513	-23.6 (32.8) n=422	-22.6 (34.0) n=345	-26.6 (29.3) n=97

Table

Deep Remission End Point[a]	Week 6		Week 52		
	VDZ n=225	PBO n=149	VDZ Q8W n=122	VDZ Q4W n=125	PBO n=126
Endoscopic remission and symptomatic improvement[b]	8 (3.6)	4 (2.7)	33 (27.0)	35 (28.0)	11 (8.7)
P value[c]	0.633	-	0.0001	<0.0001	-
Endoscopic improvement and symptomatic remission[b]	27 (12.0)	6 (4.0)	40 (32.8)	39 (31.2)	17 (13.5)
P value[c]	0.008	-	0.0002	0.0006	-
Total score ≤1 with endoscopic and symptomatic improvement[b]	28 (12.4)	8 (5.4)	44 (36.1)	45 (36.0)	19 (15.1)
P value[c]	0.023	-	0.0001	0.0001	-
Endoscopic and symptomatic improvement[b]	60 (26.7)	16 (10.7)	53 (43.4)	54 (43.2)	20 (15.9)
P value[c]	0.0002	-	<0.0001	<0.0001	-

[a] Post hoc analyses of GEMINI 1 data.
[b] Data are No. of patients (%).
[c] *P* values vs PBO are from Cochran-Mantel-Haenszel chi-square test, adjusting for baseline stratification factors.

(Q4W), and 8.4 (PBO); and 36% (Q8W), 32% (Q4W), and 30% (PBO) of patients had prior tumor necrosis factor antagonist failure. Rates of deep remission were significantly higher with VDZ than PBO (Table 1) for all end points at wks 6 and 52 (except endoscopic remission and symptomatic improvement at wk 6). Safety data from the GEMINI 1 induction and maintenance phases have been previously described. [1]

Conclusions: In patients with UC, VDZ led to statistically significant and clinically meaningful improvements at wk 6 for 3 of 4 deep remission end points, defined using various combinations of endoscopic outcomes and PROs, and at wk 52 for all 4 end points.

Clinical study was funded by Millennium Pharmaceuticals, Inc. (d/b/a Takeda Pharmaceuticals International Co.). Medical writing assistance was provided by Stefanie Dorlas of MedLogix Communications, LLC, and supported by Takeda Pharmaceuticals International, Inc.

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P320
Clinical relevance of faecal calprotectin variability in Inflammatory Bowel Disease

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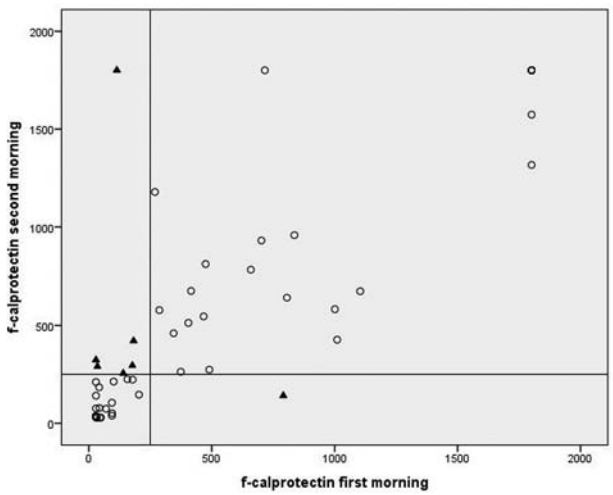
Background: Faecal (f-) calprotectin is a biomarker of intestinal inflammation. Former studies have described intra-individual day to day variability of this biomarker in patients with inflammatory bowel disease (IBD) http://planner.smart-abstract.com/ecco2015/submission/en/abstract/400110/content# http://planner.smart-abstract.com/ecco2015/submission/en/abstract/400110/content#. The variability is however of uncertain clinical relevance. With this project we aimed to investigate if day to day variability was clinically relevant, and if this variability differed from diurnal variability.

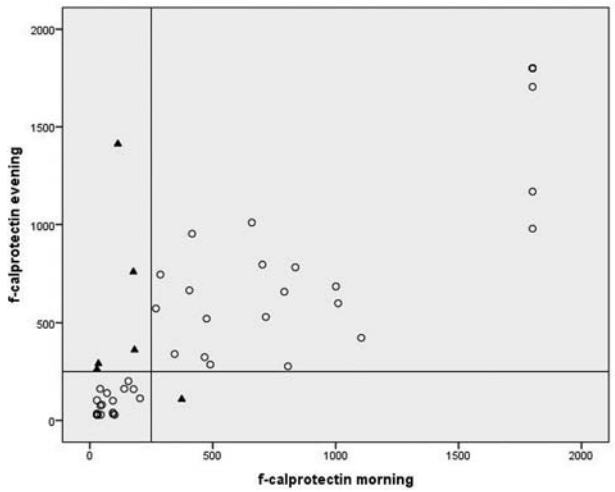
Methods: 51 patients with IBD submitted three faecal samples taken successively morning - evening - morning on two consecutive days. The faecal samples were analysed for f-calprotectin (ELISA, Bühlmann Laboratories AG, Switzerland) in duplicates. Coefficient of variation (CV) was calculated for all three f-calprotectin values for each patient, representing intra-individual variability. CV was also calculated for the duplicated f-calprotectin levels, representing variability within the assay. Wilcoxon signed ranks test was used to compare the different values of calprotectin. For case reliability measure, kappa statistics were applied.

Results: The mean CV of the duplicated f-calprotectin analyses was 3.4% (95% confidence interval 2.5%-4.3%). In contrast, there was a large intra-individual variation in the three f-calprotectin samples, with a mean CV of 39% (95% confidence interval 31%-48%). There were no significant diurnal variation (p=0.97) or day to day variation (p=0.07). The kappa statistic for the two morning samples` reliability of detecting mucosal inflammation as defined by a f-calprotectin level > 250 µ g/g, was substantial at 0.73. The kappa statistic for the reliability of the two samples from the same day (morning - evening) was also substantial at 0.77.

Conclusions: Although considerable intra-individual variation in f-calprotectin values within IBD patients, this variation seem to be of low clinical relevance. The reliability of morning samples is equal to the reliability of evening samples.



"Scatterplot of the f-calprotectin values from the first and the second morning, with the 250 microgram/gram cut-off levels marked. Triangles represent patients with values on both side of this cut-off"



"Scatterplot of the f-calprotectin values from morning and evening on the same day, with the 250 microgram/gram cut-off levels marked. Triangles represent patients with values on both side of cut-off"

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P321
Postoperative complications after ileo-caecal resection for Crohn's Disease: a prospective multicentre study.

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Background: Most of the data investigating postoperative complications after ileocaecal resection for Crohn's Disease (CD) come from retrospective studies or monocentric cohort. We aimed to determine the frequency and risk factors for early post-operative complication after ileocaecal resection in a well-characterized mutlicentric prospective cohort of CD.

Methods: The REMIND group conducted a nationwide study in 9 French academic centres. Patients undergoing ileocaecal resection between 1st September 2010 and 31th September 2014 were included in a prospective cohort. Clinical, biological, surgical data and medical therapies within the 3 months before surgery were prospectively collected. Early postoperative complication was defined by a medical or surgical event within 30 days after surgery. Factors associated with early post-operative complication were searched by univariate and multivariate regression analysis.

Results: 211 patients were included. 50% were male with a median age at surgery of 29 years (IQR 25-39). Indications for ileocecal resection were stricturing disease (n=110, 52%), penetrating disease (n=66, 31%), both stricturing and penetrating disease (n=21,10%), and inflammatory disease with failure of medical therapy (n=14, 7%). Seventy-two (34%) patients were exposed to corticosteroids within 3 months before surgery. Ninety-five (45%) and 41 (19%) patients were treated with anti-TNF within 3 and 1 months before surgery. Median duration between the last anti-TNF administration and surgery was 18 days (14-50). Laparoscopy was performed in 115 (70%) patients; 14 (12%) of them needed conversion to laparotomy. Initial stoma was performed in 32 (15%) patients. There was no postoperative death. Forty-three (21%) patients had a total of 56 early post-operative complications after a median time of 5 days (4-12): wound abscess (n=17), intra-abdominal collection (n=16), anastomotic leakage (n=10), extra-intestinal infections (n=9), and haemorrhage (n=5). Reoperation was necessary in 16 patients and stoma in 7. Median duration of temporary stoma was 3.4 months (3.2-6.3). Multivariate analysis found that corticosteroids therapy within 3 months before surgery was the only factor associated to postoperative complications (p=0.04, HR 2.0, IC95%[1.01-4.0]).

Conclusions: In this large multicentre prospective cohort, early post-operative complications after ileocecal resection were observed in 21% of patients. Corticosteroids therapy was the only factor associated to postoperative complications.

P322
Cost per clinical outcomes with biologics for the treatment of moderately to severely active ulcerative colitis

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Background: To compare cost per clinical outcomes of vedolizumab (VDZ) with approved biologics over one year period for the treatment of anti-tumour necrosis factor (TNF) naïve and anti-TNF experienced patients with moderately to severely active ulcerative colitis (UC) from a UK perspective.

Methods: With a systematic literature search, currently available randomized controlled trials for approved biologics (infliximab [IFX], adalimumab [ADA], golimumab [GOL], and VDZ) for treatment of UC were identified. Outcomes of interest included response and remission defined according to the Mayo score as reported in the individual trials. Due to differences in study designs, recalculation of GOL and VDZ outcomes was done to ensure valid comparisons with ADA and IFX trials. The odds ratios for sustained response and remission at 52 weeks of biologic treatment relative to placebo were estimated using network meta-analyses and were transformed into number-needed-to-treat (NNT) using the average placebo Results across all trials. For the cost per outcomes analyses, we assumed that responders to induction treatment with ADA and VDZ continue with maintenance treatment at 8 and 10 weeks respectively, based on the respective labels. For IFX and GOL, we assumed that in the absence of response at respectively 8 and 6 weeks, treatment was

discontinued in line with clinical trial design. The acquisition and administration costs for the biologics were calculated based on the labeled dose and frequency of administration.

Results: The NNT and cost per patient with sustained response and remission at 52 weeks for anti-TNF naïve UC patients was estimated to be the lowest for VDZ followed by IFX, ADA and GOL (Table 1). For the anti-TNF experienced UC patients, the NNT for sustained response for VDZ and ADA was 4.0 (2.2; 9.7) and 13.3 (5.0; 82.2) respectively; and for sustained remission was 9.2 (4.1; 27.8) and 41.4 (11.7; 303.9) respectively. The cost per anti-TNF experienced UC patient with sustained response was £49,912 (95%CI 27,535; 122,364) with VDZ and £69,736 (95%CI 26,176; 431,971) with ADA; and the cost per patient with sustained remission was £116,100 (95%CI 51,233; 349,433) with VDZ and £217,457 (95%CI 61,237; 1,597,033) with ADA.

Conclusions: VDZ had a lower NNT and cost per patient for sustained response and remission potentially providing better clinical and economic value compared to other biologics licensed for the treatment of patients with moderately to severely active UC.

P323
Risk factor analysis for therapy related adverse events and infections in elder patients with Inflammatory Bowel Disease; An analysis from the IG-IBD aged study

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"Table 1 Number needed-to-treat and cost per clinical outcomes of biologics among anti-TNF naïve patients with UC"

	Estimate	95% confidence interval	Estimate	95% confidence interval	Estimate	95% confidence interval	Estimate	95% confidence interval
	Probability of induction response		Probability of sustained response at 52 weeks		NNT for sustained response at 52 weeks		Cost per sustained responder at 52 weeks in GBP	
Placebo	0.34	(0.31; 0.37)	0.12	(0.09; 0.15)	Reference		Reference	
INF 5mg/kg[1]	0.69	(0.62; 0.76)	0.34	(0.23; 0.47)	4.5	(2.9; 8.9)	58,685	(37,664; 116,829)
ADA 160/80/40 mg[2]	0.49	(0.42; 0.56)	0.22	(0.14; 0.31)	10.2	(5.0; 45.4)	67,529	(32,931; 300,539)
GOL 200/100/100 mg[3]	0.57	(0.49; 0.65)	0.31	(0.22; 0.41)	5.2	(3.4; 9.5)	77,851	(51,421; 142,299)
VDZ 300mg[4]	0.63	(0.51; 0.75)	0.40	(0.26; 0.59)	3.6	(2.2; 7.5)	53,130	(33,210; 111,482)
	Probability of induction remission		Probability of sustained remission at 52 weeks		NNT for sustained remission at 52 weeks		Cost per patient in sustained remission at 52 weeks in GBP	
Placebo	0.09	(0.07; 0.11)	0.04	(0.03; 0.05)	Reference		Reference	
INF 5mg/kg[1]	0.34	(0.27; 0.41)	0.16	(0.09; 0.24)	8.5	(4.8; 18.9)	111,435	(63,789; 249,642)
ADA 160/80/40 mg[2]	0.17	(0.13; 0.22)	0.08	(0.04; 0.14)	22.4	(9.7; 108.8)	148,087	(63,884; 719,599)
GOL 200/100/100 mg[3]	0.23	(0.17; 0.29)	0.13	(0.08; 0.21)	10.2	(6.0; 20.7)	153,213	(90,593; 309,873)
VDZ 300mg[4]	0.28	(0.18; 0.40)	0.19	(0.11; 0.32)	6.5	(3.5; 15.4)	95,833	(51,855; 228,719)

Abbreviations: ADA, adalimumab; CI, confidence interval; GOL, golimumab; IFX, infliximab; NNT, number needed to treat; VDZ, vedolizumab.
[1]infliximab 5mg/kg induction treatment (week 0, 2, and 6) followed by every 8 weeks as maintenance treatment;
[2]adalimumab 160 mg at week 0, 80 mg at week 2 for induction treatment followed by 40mg every other week as maintenance treatment;
[3]golimumab 200mg at week 0, 100 mg at week 2 for induction treatment followed by 100mg every 4 weeks maintenance treatment;
[4]vedolizumab 300mg induction treatment (week 0,2, and 6) followed by every 8 weeks maintenance treatment.

Infections, Hospitalizations and AEs in the different age groups

	Group 1 n=433	Group 2 n=450	Group 3 n = 840	p-value
INFECTIONS Infections total, %	9.0	5.6	8.9	0.058
Hospitalization due to infections, %	38.5	36	16	0.529
HOSPITALIZATIONS IBD-related, %	37	37.1	35.9	0.442
Length of stay; days mean ± SE	13.7 ± 0.7	12.1 ± 0.6	12.2 ± 0.4	0.031
IBD-unrelated, %	9.0	5.1	3.3	0.000
AE from steroids, %	2.1	3.7	1.5	0.122
AE from IMM; %	28.8	26	21.1	0.348
Ae from BIO,%	8	7	11	0.127
Moderate permanent damage from AE	12.8	4.4	0.8	0.003

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Background: Elder people with inflammatory bowel disease present problems related to concomitant pathologies and to a worse outcome compared to younger patients in case of infections. The AGED study (Assessment of IBD in the Geriatric patients and Evolution of Disease) is based on a retrospective data collection on the first 3-years period following diagnosis in different age groups.

Methods: The database includes 1723 patients with 433 diagnosed over age 65 years (group 1: UC 280, CD 153, males 231), 450 patients between 40 - 65 years (group 2: UC 289, CD 161, males 271), and 840 patients diagnosed before age 40 years (UC 523, CD317, males 438); data on therapy steroids, S, immunomodulators, IMM, and biologics, BIO), adverse events (AEs) and their outcome (mild or moderate permanent damage), IBD-related and -unrelated hospitalizations and on infections were extracted together with the Charlson comorbidity score (CCS), and concomitant therapies (antihypertensives, AH, proton pump inhibitors, PPI, antidiabetics, AD, antithrombotics, AT).

Results: therapy with 5-.ASA and S was similar in all groups; significantly more IMM (p<0.001) and BIO (p<0.001) were used in group 3; the number ofr AEs were similar in the 3 groups;

reports Aes related to different therapies, as well as AEs requiring hospitalizations. Mild (p<0.045) or moderate (p<0.003) permanent damage from AEs was more frequently observed in group 1 and 2. IBD-related hospitalizations in the first 3 years were not significantly different in the 3 groups, whereas IBD-unrelated hospitalizations were more frequent in group 1 and 2.

Univariate analysis identified CCS (OR: 1.418; 95%CI 1.053-1.909; p<0.021), the use of 2 (OR: 1.738; 95%CI 1.185-2.550; p<0.005) or 3 (OR: 3.065 (95%CI 1.665-5.645, p< 0.000) immunosuppressants (IMSs), PPI use (OR: 1.727; 95%CI 1.005-2-967, p<0.048), and AT use (OR: 2.143; 95%CI 1.272-3.611; p<0.004) as risk factors for infections.

Risk factors for AEs were the use of 2 (OR: 3.880; 95%CI 2.857-5.270; p<0.000) or 3 (OR: 4.231 (95%CI 2.556-7.004, p< 0.000) IMSs; interestingly the use of a single IMS represented a protective factor against AEs (OR: 0.443; 95%CI 0.317-0.619; p<0.000).

Conclusions: Although numerically not different from younger age groups AEs leading to permanent damage were more frequently observed in the older age groups of IBD patients. The length of hospital stays due to infections was significantly increased in elder patients. Risk factors for infections were the association of 2 or more IMSs, as well as concomitant pathologies, PPI and AT use.

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Biomarkers predict lack of response to anti-TNF in Moderate to Severe Ulcerative Colitis

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Background: It is still poorly understood why certain patients with moderate to severe ulcerative colitis do not respond to anti-TNF antibody therapy. The availability of serum biomarkers allowing prediction of response would be of great clinical value.

Methods: We studied consecutive patients with moderate to severe ulcerative colitis (endoscopy Mayo grade ≥ 2) started on infliximab after failure of conventional treatment and collected serum samples at 10 serial time points between week 0 and week 6. IFX serum concentrations and ATI were measured with a homogeneous mobility shift assay (Prometheus Laboratories, San Diego, CA). In addition, serum TNF- α , IFN- γ , IL-6, IL-8, IL-10 and IL-12p40 levels were measured at baseline, week 2 and 6. Serum TNF- α was measured by a Collaborative Enzyme Enhanced immuno-Reactive (CEER) Assay, Interleukins by a high sensitive ELISA. The primary outcome was endoscopic response defined as improvement by at least 1 Mayo point at week 8.

Results: Twenty patients were included, 19 of which completed a standard IFX induction regimen (5mg/kg at week 0,2,6). 11/19 patients had an endoscopic response at week 8. Antibodies to IFX (ATI) were detected in 7 patients as early as a median of 28 days (18-42 days) into treatment. 6/8 patients without endoscopic response tested ATI+ compared to 1/11 with response (P<0.01, OR:30, 95%CI:2.2-406.2) without clear impact of immunomodulators. Lower median levels of IFX at one hour after the end of the first infusion were associated with consecutive development of ATI after the second infusion: 93 (83-102) ug/ml in ATI+, versus 126 (106-155) ug/ml in ATI- patients (P<0.01). The ratio serum TNF/IFX one hour after the end of the first infusion was also associated with ATI formation(P<0.05). (TABLE 1.)

Patients with higher week 2 IL12/23 p40 and IL-8 levels were less likely to have an endoscopic response at week 8 (P=0.03 and 0.06).

Conclusions: Low IFX levels and higher TNF/IFX ratio one hour after the end of infusion were associated with early ATI formation and treatment failure. High IL12/23 p40 and IL8 levels at week 2 also predicted lack of response, suggesting early diversion of inflammation towards the IL12/23 pathway and enhanced recruitment of neutrophils, respectively. Further validation of this data in larger samples is warranted.

Day 0 cytokines, chemokines and infliximab concentration in relation to ATI formation (up to week 6)

Day 0 cytokines, chemokines, IFX	ATI- (N=13), Median (IQR)	ATI+ (N=7), Median (IQR)	P-value
IFN- γ (pg/mL)	9.83 (6.93–25.64)	19.81 (8.70–29.87)	P=0.52
IL-6 (pg/mL)	1.48 (0.21–3.13)	7.55 (0.71–8.05)	P=0.25
IL-8 (pg/mL)	75.9 (15.1–501.1)	49.9 (22.1–600)	P=0.98
IL-10 (pg/mL)	1.73 (0.81–3.47)	1.67 (1.13–2.31)	P=0.70
IL12p40 (pg/mL)	61.88 (28.38–160.8)	36.35 (14.81–63.05)	P=0.22
Infliximab [µg/mL]	126 (108–155)	88 (83–102)	P=0.002
TNF- α (pg/ml)	0.46 (0.31–0.65)	0.55 (0.34–1.69)	P=0.26
TNF- α /IFX	0.0031 (0.0026–0.0048)	0.009(0.004–0.017)	P=0.048

P325
Unfavorable initial thiopurine response does not reduce anti-drug antibody formation compared to thiopurine responders in Crohn's disease patients treated by thiopurine & infliximab co-therapy

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Background: Previous studies demonstrated that combination thiopurine-Infliximab (IFX) therapy reduced the appearance of anti-drug antibodies (ADA) compared with IFX monotherapy. Whether the nature of past clinical response to thiopurine therapy affects this effect is unknown.
Methods: A retrospective multicenter cohort analysis of CD patients treated by at least four scheduled IFX infusions who had a documented response to past/ongoing thiopurine treatment and serial ADA measurements was conducted. Patients with combined therapy were grouped according to past response to thiopurine therapy (primary failure, past response and de-novo combination) and compared to IFX monotherapy. The primary end-point was ADA appearance. Kaplan-Meier (KM) analysis was used to compare ADA free survival between the groups.
Results: 342 patients with serial ADA measurements were reviewed. 206 patients were excluded due to ineligibility to the study protocol: 73 received episodic IFX therapy, 25 received Methotrexate co-therapy, 16 did not have Crohn's disease, 32 did not receive IFX maintenance therapy and 60 had insufficient data. 136 were eligible for final analysis: 61 received IFX monotherapy, 33 responded to thiopurines, 22 failed thiopurines and 20 received de-novo combination therapy. No statistical significant differences were found between study groups in most demographic and clinical parameters (Table 1). However, Montreal B1 disease behavior was significantly more frequent in the primary failure group (p=0.015), patients on monotherapy were older at diagnosis (p=0.009) and IFX was started later during the disease for past responders (p=0.03). Median follow-up time was 272 days.
KM analysis revealed 2 year cumulative risk of ADA development of 31.8% in the thiopurine failures, 32.9% in the de-novo group, 24.4% in thiopurine responders and 62.0% in monotherapy group (p=0.013, p=0.012 and p=0.01 for the difference between each of the first 3 groups compared to monotherapy in Wilcoxon test, relatively) (Figure 1).
Conclusions: Thiopurines-IFX co-therapy in CD patients is associated with reduced ADA formation relative to IFX monotherapy regardless of past response to thiopurines.
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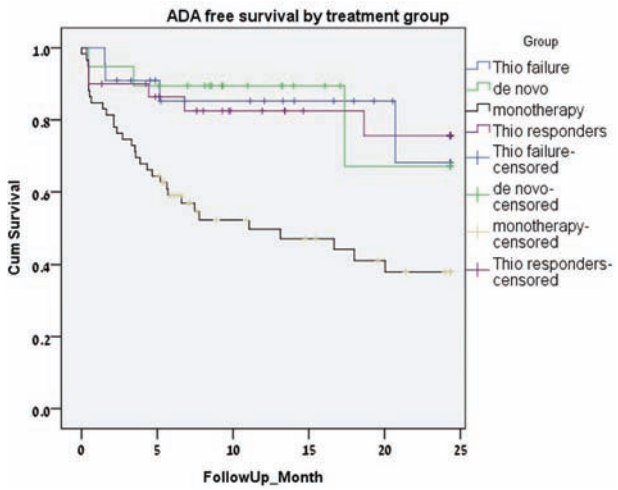

"ADA-free survival curves between study groups"

P326
Three-year steroid free remission and safety of azathioprine treatment in inflammatory bowel disease patients.

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Background: Purine analogue azathioprine (AZA) is widely used for induction and maintenance of remission in steroid dependent patients with inflammatory bowel disease (IBD). The treatment must be withdrawn in 5-30% of patients due to the occurrence of adverse events. We investigated its efficacy and safety in maintaining steroid-free remission in steroid dependent IBD patients three year after the institution of treatment.
Methods: Data from consecutive IBD outpatients referred in our Institution, between 1985-2012, were reviewed and all patients treated with AZA were included in this retrospective study. AZA was administered at the recommended dose of 2-2.5 mg/kg.

Table 1 Clinical and demographic parameters - all parameters were not significantly different between study groups except age at diagnosis (p=0.009)* and time of disease till IFX therapy (p=0.03)**

	Monotherapy (n=61)	Primary failure (n=22)	Past responders (n=33)	De-novo combination (n=20)
Female (%)	49.2	45.5	36.4	55
Smoking (% never smoked)	69.8	81.8	70	68.4
BMI (Mean)	22.4	21.4	20.9	21.4
Age at diagnosis (Median in years)*	22.1	17.6	17.5	23.1
Time of disease till IFX therapy (Median)**	5.6	5	9.3	2.8
Perianal disease (%)	46	63.6	42.4	45
Extra-intestinal manifestations (%)	42.6	40.9	40.6	36.8
Past surgery (%)	26.2	31.8	36.4	35

Results: Out of 2472 consecutive IBD outpatients visited in the index period, AZA was prescribed to 360 patients, 189 (52.5%) were affected by Crohn's disease (CD) and 171 (47.5%) by ulcerative colitis (UC). Seventy-eight patients with a follow-up <36 months were excluded from the study. Two hundred and eighty-two patients were evaluated, 152 (53.9%) with CD and 130 (46.1%) with UC. One hundred and fifty-four (54.6%) were male and 128 (45.4%) female (average age of 33.75 ± 13.82 SD years, range 14-76 y.). Three year after the institution of treatment, 170 (60.3%) patients still were in steroid-free remission (101 CD vs 69 UC, 66.4% and 53.1%, respectively, p=0.0279), 62 (22%) had a relapse requiring retreatment with steroids (38 UC vs 24 CD, 29.2% and 15.8%, respectively, p=0.0091), 50 (17.7%) discontinued the treatment due to side effects (27 CD vs 23 UC, 17.8% and 17.7%, respectively). Loss of response from 1st to 3rd year of follow-up was low, about 12%.

Conclusions: Three year after the onset of treatment 60% of patients did not require further steroid courses. After the first year loss of response was low in two subsequent years. In the present series the maintenance of steroid-free remission was significantly higher in CD than in UC patients. The occurrence of side effects leading to the withdrawal of AZA treatment has been low.

P327
Colorectal cancer in IBD patients treated or untreated with anti-TNFs: A retrospective matched-pair study in a 14 years follow up

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Background: In murine models, blocking TNF-alpha showed efficacy in colitis-associated colon cancer. Chronic inflammation in Inflammatory Bowel Disease (IBD) colitis has been associated with colorectal cancer (CRC). In a retrospective matched-pair study, the frequency of CRC was compared in a cohort of Inflammatory Bowel Disease (IBD) patients treated or not with anti-TNFs. In a matched-pair study, the role played by clinical characteristics of IBD in determining the frequency of CRC was evaluated.

Methods: Clinical records of all IBD patients followed up from 2000 to 2014 at our tertiary IBD center developing cancer of the lower GI tract (IBD-K)(small intestine, appendix, CRC, anal canal) were reviewed. Each IBD-K patient was matched with 2 IBD patients with no cancer of the lower GI tract (IBD-C) for IBD type (Crohn's Disease,CD/Ulcerative Colitis, UC), gender,age (±5yrs). Anti-TNFs (Infliximab or Adalimumab, at least 1 administration) and immunosuppressors (IS) use was reported. Statistical analysis: data were expressed as median (range), Student's T test, Chi square test.

Results: IBD population included 2387 patients: 384(16%) used anti-TNFs. Cancer of the lower GI tract developed in 15/2387 (0.62%) IBD patients (9 CD,6 UC), including 12 CRC (6 UC,6 CD),1 ileal carcinoma (1CD),1 appendiceal carcinoid (1CD),1 anal canal carcinoma (1CD). In the 15 IBD-K patients, age at diagnosis of cancer was 51 yrs (28-73), IBD duration 19 yrs (1-47). IBD-K patients included; 9 CD of the ileum (I)(n=4), colon (C)(n=2), ileum-colon (IC)(n=3), 6 UC distal (n=3), left-sided (n=1), pancolitis (n=2). Among the 15 IBD-K patients, 3 (20%) received anti-TNFs and/or IS (combined in all 3). In these 3 IBD-K patients, cancer included CRC (n=2), carcinoid (n=1) in 2 CD (2F,age 40,54yrs, CD duration 28,26 yrs; I-C,fistulizing), 1UC (1F,CRC, age 30, duration 19yrs; pancolitis). Among the 384/2387 (16%) IBD treated with anti-TNFs, CRC developed in 3 (0.78%) (combined IS in 3).Among the 2003/2387 (84%) IBD patients anti-TNFs naïve, 12(0.6%) developed cancer of the lower GI tract: CRC in 10 (0.5%)(p=ns vs patients treated with anti-TNFs). IBD-C included 30 patients (18CD, 12UC;14 M,age 54 [37-75]), with CD (13 I;2 C;3 I-C) or UC (distal 11,left-sided 1). Anti-TNFs were used in a comparable proportion of matched IBD patients developing or not cancer (IBD-C n=6/30; 20% vs IBD-K n=3/15;20%). In IBD-C controls, IS were used in 10 (33%)(combined with anti-TNFs in 2; 6.7%).

Conclusions: In a retrospective matched-pair study, a comparable low frequency of colorectal cancer was observed in IBD patients treated or untreated with anti-TNFs.

P328
P-glycoprotein 170 (P-GP) functional activity in peripheral blood lymphocytes (PBL) of IBD patients during treatment with anti-TNFs

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Background: Pgp, encoded by the MDR1 gene is a transmembrane, ATP-dependent, efflux pump, expressed in cells with barrier function and PBL. IBD share drugs Pgp influenced (as steroids, 6MP in leukemia cells) with other diseases. Pgp overexpression was implicated in highly active resistant RA (Tsujimura, Ann Rheum Dis 2008) induced by IL2 and TNF α, influencing steroid efflux from lymphocytes, reporting that a single infliximab (IFX) infusion overcame refractoriness with elimination of Pgp high expressing CD4+lymph, and recovery of dexametasone in PBL with Ppg marked decrease. Pgp measure in PBL could be an early marker of AntiTNFs efficacy and Pgp activity could modify the efflux of concurrent Pgp substrates drugs. AIM: to study Pgp activity in PBL of IBD pts. treated with antiTNFs.

Methods: Pgp functionality was evaluated in PBL of IBD and healthy contr (HC: n30)- IBD: n123 recruited (CD 59, UC 64)in 5 groups - Before and after 20 days of AntiTNF (IFX/ADA) in steroid refractory (Group 1) or thiopurine refractory (Group 2), - Before and after 3mo of 6MP in steroid refractory (group 3), - In Thiopurine sensitive (Group 4) and Steroid sensitive (Group 5). Response criteria: at 45 days of AntiTNFs or 3 mo. of 6-MP (CDAI: 70 points drop, Mayo Sc.3 points+30% drop) categorized in: remission (CDAI ≤150, Mayo Sc. ≥ ≤2) and partial response. Rhodamine123 (fluorescent Pgp substrate) efflux was studied by flow cytometry, expressed by the behaviour of 2 markers (according % of cells with different fluoresc. levels: M1 (high fluoresc./low Pgp pump activity), M2 (low fluoresc./Pgp high activity, used for the Results).

Results: (mean±SD): Major finding was a significant decrease of Pgp after AntiTNFs in total PBL (M2) in most of responder IBD. (Δ-difference in refractory vs remission p: 0.030018, and 0.0023 for Groups 1 and 2, and vs. partial response p: 0.014 in group 2, Mann Whitney). Basal (pre AntiTNFs) Pgp values of pts. with available post AntiTNFs measures according response (remission, partial response, refractory) were: Group 1 (n 20) 38.0 ± 17.7, 44.6 ± 8.4, 38.6 ± 21.0 and Group 2 (n 23) 35.9 ± 16.0, 34.8 ± 9.9, 23.1 ± 7.1. Post AntiTNF (same criteria): 26.2 ± 16.0, 29.0 ± 12.1, 47.0 ± 19.3 (Group 1) and 21.0 ± 11.6, 22.3 ± 11.5, 36.0 ± 11.7 (Group 2). Pts. in 6MP monotherapy (n23) did not show signif. changes. Pgp dropped after AntiTNFs in CD3 lymph. in remission vs. refractory (group 2 p<0.003, B lymph. of

responders showed a trend for lower values post AntiTNFs (Group 1). Post-treatment values were lower in IBD vs HC ($p<0.04$).
Conclusions: We found that AntiTNFs decreased Pgp activity in PBL of IBD pts, significantly associated with treatment response. It is possible that the transport of Pgp substrates can be modified by antiTNFs. MDR1 polymorphism typing is ongoing

P329
Intermittent vancomycin and gentamicin as exclusive therapy for severe very early onset Inflammatory Bowel Disease

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Background: Very Early Onset Inflammatory Bowel Disease (VEO-IBD) is a unique subtype of IBD and many patients are resistant to standard therapy. VEO-IBD is more often associated with monogenic etiologies, particularly those with infantile onset. While children with both PSC and IBD treated with vancomycin have been reported to incidentally show improvement in IBD as well, vancomycin has never been studied as exclusive therapy for VEO-IBD.
Methods: We report here our experience using oral vancomycin and gentamicin (V&G) to successfully treat two patients with VEO-IBD refractory to standard treatments.
Results: Patient 1, with severe Crohn's colitis, presented at 5 months with hematochezia and subsequent diarrhea, failure to thrive and elevated inflammatory markers. Colonoscopy revealed aphthous ulcerations in the rectosigmoid and cecum with granulomas. Investigation for immune deficiency and interleukin-10 defects was negative. Treatment with corticosteroids, exclusive enteral nutrition, sulfasalazine and infliximab was unsuccessful; he had an allergic rash on azathioprine. At the age of 14 months he fully responded (PUCAI=0) within 5 days to oral V&G following 6 months of chronically active disease (PUCAI 20-85). Over the next 14 months he received no maintenance treatment; he had 2 exacerbations which were successfully treated with 2 week courses of V&G. Seven months after completing the third course, he continues to be in complete clinical remission with no medications.
Patient 2 had intermittent hematochezia starting at 8 months of age. At 2.5 years she presented with bloody diarrhea along with elevated transaminases and GGT. Colonoscopy demonstrated pancolitis and liver biopsy was consistent with PSC. Investigation for immune deficiency and interleukin-10 defects was negative. She was refractory to 5-ASA. Over the next 7 months she received three courses of oral V&G with prompt and complete remission each time of both her colitis symptoms and her liver markers, including normalization of CRP. At last follow-up she is in complete clinical remission with normal transaminases and GGT without any maintenance treatment.
Conclusions: We have reported the first two cases of VEO-IBD successfully treated with only oral antibiotics, using intermittent courses of vancomycin and gentamicin. The treatment also resulted in normalization of liver enzymes in a patient who had concurrent PSC. Both antimicrobial and immunomodulatory effects, including stimulation of regulatory T cells, may play a role in the mechanism of action. As VEO-IBD is often difficult to treat, our findings represent a potential treatment and should be further investigated in controlled trials.

P330
Efficacy and safety of vedolizumab with advancing age in patients with Crohn's disease: Results from the GEMINI 2 study

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Background: Vedolizumab (VDZ) is a gut-selective monoclonal antibody to α4β7 integrin for the treatment of patients (pts) with Crohn's disease (CD). The efficacy and safety of VDZ have been demonstrated in the phase 3 placebo (PBO)-controlled GEMINI 2 study (NCT00783692).[1] Here we report post hoc analyses of data from GEMINI 2 that evaluate the effects of VDZ with advancing age in pts with CD.
Methods: In GEMINI 2, pts received double-blind (DB) VDZ or PBO (induction intent-to-treat [ITT] population) or open-label VDZ at weeks 0 and 2. At the end of the induction period (week 6), VDZ responders were re-randomised to receive DB VDZ every 8 or 4 weeks (Q8W or Q4W) or PBO up to week 52 (maintenance ITT population). Efficacy endpoints and adverse events (AEs) were described by baseline (week 0) age category (<35, 35-55, and >55 years).
Results: At baseline, 178 (48%), 161 (44%), and 29 (8%) pts in the induction and 246 (53%), 179 (39%), and 36 (8%) pts in the maintenance ITT populations were aged <35, 35 to 55, and >55 years, respectively. At week 6, there were 31 (28%) VDZ-treated pts aged <35, 32 (33%) aged 35 to 55, and 6 (50%) aged >55 years with response (≥100-point reduction in CD Activity Index [CDAI] score from baseline). Remission (CDAI total score ≤150) was achieved by 16 (14%), 15 (16%), and 1 (8%) VDZ-treated pts in each age

	Age <35 years		Age 35-55 years		Age >55 years	
	PBO/PBO[a] (n=67)	VDZ/VDZ[b] (n=442)	PBO/PBO[a] (n=64)	VDZ/VDZ[b] (n=317)	PBO/PBO[a] (n=17)	VDZ/VDZ[b] (n=55)
Event	**Number of Patients (%)**					
Any AE	58 (87)	374 (85)	46 (72)	282 (89)	14 (82)	50 (91)
Any SAE	14 (21)	118 (27)	5 (8)	71 (22)	4 (24)	10 (18)
Infections and infestations (SOC)	26 (39)	193 (44)	23 (36)	142 (45)	8 (47)	24 (44)

Abbreviations: AE, adverse event; CD, Crohn's disease; PBO, placebo; SAE, serious adverse event; SOC, system organ class; VDZ, vedolizumab.

[a] Patients received PBO during induction and maintenance periods.

[b] Patients received VDZ during induction and maintenance periods.

category, respectively. At week 52, remission was achieved by 65 (38%), 42 (37%), and 9 (41%) pts treated with VDZ aged <35, 35 to 55, and >55 years, respectively. AEs occurred at similar rates across the ages (Table). Three malignancies were reported in VDZ-treated pts aged 20 years (carcinoid tumour of the appendix), 45 years (breast cancer), and 52 years (squamous cell carcinoma [skin]). Five deaths were reported: 3 VDZ-treated pts aged <35 years (myocarditis; CD and sepsis; septic shock), 1 VDZ-treated pt aged 46 years (intentional overdose), and 1 PBO-treated pt aged 75 years (bronchopneumonia).

Conclusions: These data suggest that the safety and efficacy of VDZ were generally similar in CD pts across all ages. Interpretation of data is limited by the small pt population aged >55 years; these findings should be further evaluated in prospective studies.

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P331
Endoscopic Balloon Dilation Delays the Need for Subsequent Surgery in Patients With Strictures In Crohn's Disease Even In Ileocolonic Anastomotic (ICA) Localization ?

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Background: There are relatively published data comparing endoscopy and surgery in treating CD-related ICA in the literature. The aim was to compare the long-term outcome between endoscopic dilation and surgery for ICA stricture.

Methods: Eligible patients with ICA stricture treated with either endoscopic dilation vs. surgery between December 1998 and May 2013 were evaluated. Patients were divided based on the initial treatment at the inception point (endoscopic balloon dilation vs. restorative surgical resection). Patients with concurrent enterocutaneous fistula or abdominal abscess were excluded.

Results: We included 96 patients (dilation, n=46 and surgery, n=40). The total number of dilations was 125 with a median of 2(1-7) per patient in the endoscopy group. There was no difference in the need for the subsequent surgery between the two groups (p>0.05). However, patients in the surgery group had a longer time interval from the inception to the subsequent surgery than those in the endoscopy group. Eight patients in the surgery group even underwent subsequent dilation for recurrent stricture. In univariate analysis, the need for subsequent surgery was associated with current smokers,corticosteroids or anti-TNF use. Kaplan- Meier analysis showed that the average time to surgery delayed by dilation was 4.25 years in the endoscopy group. In a subgroup analysis of the endoscopy group, patients with bowel dilation proximal to ICA stricture had a higher rate of need for surgery than those without.

Conclusions: Endoscopic dilation is an effective approach for ICA stricture in CD patients. The long-term need for subsequent surgery appeared to be comparable between the two groups, although the interval to the subsequent surgery in the surgery group was longer. Endoscopy dilation of ICA stricture is shown to space out the need for the second surgery and may be attempted first when feasible.

P332
Impact of Inflammatory Bowel Disease on Japanese patients' lives: International comparison of patients' views

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Background: Inflammatory bowel disease (IBD) has a substantial negative effect on quality of life; however, little is known about the impact of IBD on patients' lives. The European Federation of Crohn's and Ulcerative Colitis Associations (EFCCA) conducted the European Crohn's and Ulcerative Colitis Patient Life Impact Survey (IMPACT survey) for 2010-2011 to obtain an international perspective on the impact of IBD on patients' lives. We conducted the IMPACT survey in Japan and compared our Results with those of the European survey.

Methods: The Japanese version of the IMPACT survey questionnaire was provided to IBD patients through patient advocacy groups, either online or by postal mail. The questionnaire comprised 52 questions on patients' experiences and treatment of IBD, and the impact of IBD on their lives. Participation was voluntary, and data collection preserved patient anonymity.

Results: Between June 2013 and January 2014, 172 Japanese IBD patients completed the questionnaire (ulcerative colitis, 84 patients; Crohn's disease, 83 patients; unclassifiable, 1 patient; no response, 4 patients). The Japanese and European survey Results slightly differed in terms of patient background, complications, and treatment. The major differences included the fact that most of the Japanese patients went to an emergency clinic or department before receiving a definitive diagnosis (Japan vs. Europe: 95.9% vs. 67.3%), fewer Japanese patients received corticosteroids (16.3% vs. 20.5%), more Japanese patients received aminosalicylates (76.2% vs. 47.4%), the Japanese patients' satisfaction of operative outcome was lower (52.9% vs. 72.9%), and fewer Japanese patients were hospitalised within the last five years (58.1% vs. 84.6%). Both patient groups answered gastroenterologist as the professional who best understands the impact of IBD on their lives (both > 60%), but the proportions of patients who selected family physician (18.6% vs. 28.1%) and counsellor (2.9% vs. 8.2%) differed between the groups. Meanwhile, the responses to most of the questions were similar between the two groups; many of the Japanese patients were concerned about communication with their physicians and experienced inconvenience in daily life and work due to IBD.

Conclusions: Despite the differences in race, living environment, and medical service system between Japan and Europe, the impact of IBD on patients' lives was similar between the two groups. Information on the unmet needs of Japanese patients with IBD may help provide sufficient medical and administrative support, improve working and educational environments, and increase the awareness of health care providers in order to bridge communication gaps between patients and physicians.

P333
Safety of fecal microbiota transplantation in patients with chronic colitis and immunosuppressive treatement.

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Background: Alterations of the gut microbiome, termed dysbiosis, are postulated in patients with recurrent Clostridium difficile colitis (CDI) as well as inflammatory bowel diseases as ulcerative colitis (UC). In these diseases fecal microbiota transplantation (FMT) is supposed to reestablish a normal microbiota. The aim of the present study was to investigate short- and long-term side effects and safety of FMT.
Methods: Between 02/2011 and 06/2014 30 patients received FMT due to various indications such as UC (n= 21), CDI (n=7) and cryptogenic or antibiotic associated colitis (n=2). All patients were nonresponsive to standard medical therapy. 22/30 of our patients received one (n=13) or more (n=9) immunosuppressive drugs due to their underlying diseases at the time of FMT. Short-term side effects and laboratory parameters were compiled during the observation period of 90 days in UC patients and 3 days in the non UC patients. Long-term safety data referring to de novo occurred diseases or persisting symptoms after FMT were collected via questionnaire.
Results: 13/30 patients showed elevated CRP values one day after FMT: before FMT 9,31 mg/l (0,6 - 82,6mg/l), after FMT 15,9 mg/l (0,6 - 103,1 mg/l). There was no correlation between CRP increase and immunosuppressive therapy. Minor adverse events like temperature increase (n=3) up to 38,1 °C, abdominal pain (n=5) and flatulence (n=3) were described up to 7 days after FMT. During the long term observation period intermittently gluten sensitivity (n=1), joint pain (n=1) and post-infectious irritable bowel syndrome (n=1) occured. 2 UC patients, Non-Responders to FMT, developed a colonic stenosis in chronic active disease with the consequence of colectomy 18 month after FMT, one of them appeared with an histological verified low grade DALM. 1 patient presented with a benign thyroid nodule, another one developed a multilevel thrombosis within 12 month after FMT.
Conclusions: Colonoscopically applied FMT is well tolerated and shows high safety despite ongoing immunosuppressive therapy. There were no immediate severe adverse events observed. A temporary increase of CRP levels after FMT was noticed without any need of therapeutic intervention. The development of intestinal stenosis and DALM is a known complication in chronic active UC patients, the role of FMT as an additional risk factor has to be further investigated.

P334
Level of education and knowledge about female health issues in patients with inflammatory bowel disease.

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Background: Female health issues such as fertility, breastfeeding, pregnancies, HPV vaccination and cervical cancer screening can be causes of concern and anxiety in inflammatory bowel disease (IBD) patients. The aim of this study was to assess the patient's knowledge about these issues.
Methods: This was a prospective study were patients were recruited from 5 European centres. Female IBD patients were recruited and they were interviewed through a purposely designed questionnaire.
Results: 233 patients were recruited (mean age 40 SD±11.9). The mean age of diagnosis of IBD was 31.35 years (range 4 - 65 years; SD±11.2). 43.3% of pregnancies were planned. A younger age at diagnosis was associated with a higher number of pregnancies ($p<0.006$).
Only 57.9% of patients were counseled by health care professionals on IBD and fertility. This was done by gastroenterologists (46.8%) and gynaecologists (7.30%). Considering not having children was positively correlated with lack of counseling delivered by health care professionals (coefficient 1.147).
37.8% were uncertain about whether mode of delivery could be influenced by underlying IBD. Most of the patients who experienced uncertainty had been to high school or had had a better level of education.
26.6% were uncertain if patients with IBD could breastfeed their babies. They all had gone to college or had had a better level of education.
Only 15.9% were counseled by health care professionals to undergo regular pap smears. This was done by a gastroenterologist (6.87%) and by a gynaecologist (9.44%). 61.8% received information about the HPV vaccine. Most information was given by a gastroenterologist (38.2%) and by a gynaecologist (15.5%). 1.72% had received information from both. 24.9% were using contraception. There was a statistical correlation with a higher level of education ($p<0.003$).
1.7% of patients stopped medications on their own accord during pregnancy. They all had finished secondary school or had a higher level of education. Reasons given included fear of harm to the baby and being in remission.
Conclusions: A higher level of education can influence decisions such as planning a pregnancy and number of pregnancies. However, this data demonstrates the need for a lot more of appropriate counseling of female IBD patients with regards to pregnancy, breast feeding, cervical smear testing and IBD drugs during pregnancy.

P335
Screening for enteric infection in inflammatory bowel disease patients contacting the IBD helpline and presenting with disease flares

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Background: We participated in the UK National Audit of inflammatory bowel disease service provision (Royal College of physicians, 2014). This recommends that >90% of inflammatory bowel disease (IBD) patients with diarrhoea, have a stool sample sent for culture and Clostridium difficile (CDT) testing on admission. ECCO guidelines recommend stool testing in both outpatient and inpatient disease flares. To date a national audit reviewing stool testing of patients contacting IBD Helplines for advice with diarrhoea has not

Level of Education	Percantage
Primary School	03.4%
Secondary School	20.2%
High school / sixth form / college or equivalent	39.1%
Diploma	04.7%
Trade / technical / vocational training	04.7%
University degree	04.7%
Post-graduate degree	03.9%

been performed; therefore we reviewed the Results from our clinical practice of both inpatients and out-patients.

Methods: We searched the IBD telephone helpline electronic records from September 2011 to October 2014 to identify patients presenting with diarrhoea. Electronic records were reviewed to determine if stool samples for standard stool culture and CDT were requested before escalating therapy, and the Results of that testing.

By searching hospital admission data we identified all patients admitted for >24 hours with a diagnosis of Crohn's disease or ulcerative colitis with symptoms of loose stool and increased frequency during the same time period and reviewed the same data.

Results: 357 patients contacted the IBD Helpline complaining of diarrhoea. 357 (100%) were sent stool pots for standard stool culture and CDT by post. Results were reviewed before deciding on further management. 300 (84%) patients completed the tests. Of these 15 (5%) were positive. 8 showed CDT, 6 Campylobacter and 1 Blastocystis hominis.

179 (99 male) IBD patients were admitted during the same 3 year period with symptoms of a flare. 122 patients had diarrhoea on admission. 96 (79%) underwent stool testing. 2 (2%) were positive for infection: 1 for campylobacter, 1 for CDT.

Conclusions: These Results demonstrate that enteric infection is a relatively common cause of disease flares and underlines the importance of screening for this. Unfortunately frequency of stool testing in our inpatient population falls below recommended standards. In contrast testing undertaken by our nurse-led IBD helpline met the standard.

P336
Intestinal transplantation for Crohn's Disease: The Cambridge experience since 2008

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Background: Intestinal transplantation (either alone or part of a cluster of organs) is indicated in patients with Crohn's disease and intestinal failure who develop complications associated with parenteral support (PS) including recurrent line sepsis, loss of vascular access, or intestinal-failure associated liver disease (IFALD). Some may require other organs (e.g. liver, kidney) which cannot be undertaken without simultaneous bowel transplantation.

Methods: We retrospectively reviewed case notes for all patients with Crohn's disease who were transplanted at our institution between January 2008 and August 2014.

Results: Pre-transplant, median Body Mass Index (BMI) was 21.0kg/m2 (range 17.8–23.5), median handgrip strength 62% (range 22–78%), and 3 patients had low bone density (2 osteoporosis, 1 osteopenia). At latest follow up BMI had improved to median 22.0kg/m2 (range 19.4–29.9). Assessment of handgrip strength in those at least 1 year post-transplant showed improvement (n=3) as did bone density (n=2). Pre-operatively, 6 patients had developed complications of PS but currently no patients require ongoing PS. 6 patients are alive at a median 30.5 months post-transplant (range 7–76). Case 4 died at 15 months from invasive fungal infection and cerebellar haemorrhage. Overall 5-year survival following intestinal transplantation at our institution (41 patients) is 64% (100% isolated small bowel, 65% modified multivisceral, 58% multivisceral).

Conclusions: All patients had ileocolonic, stricturing and/or fistulising disease and were diagnosed at a median age of 17 years. They commenced PS at a median of 18 years from diagnosis and continued for a median 10 years before transplantation. Survival following intestinal transplantation in our cohort is good. Nutritional status (assessed by BMI, bone density, and handgrip strength) of these patients improved following transplant. No histological recurrence of Crohn's disease was seen in 229 specimens over 213 patient months of follow up.

Summary of cases

Case	1	2	3	4	5	6	7
Gender	Male	Female	Female	Female	Female	Male	Male
Age at transplant	35	64	37	52	61	60	50
Montreal classification	A1L3B3p	A2L3B3p	A1L3B2	A2L3B3p	A2L3B3	A1L3B2	A2L3B2
Anatomy from DJF	50cm to end jejunostomy, and left colon (not in continuity)	60cm to colon with end colostomy	120cm to full colon	20cm to jejunostomy	100cm to ileostomy	120cm to ileostomy	70cm to colon with end colostomy
Years from diagnosis to commencing PS	18	26	11	10	34	42	13
Years on PS pre-transplant	3	13	10	22	10	3	11
Indication	Short gut with IFALD	Loss of vascular access	Loss of vascular access	Short gut with IFALD	End stage renal failure; SB/colon needed for enteral fluid management	NAFLD cirrhosis with short gut	Recurrent line infections
Organs transplanted	St, SB, liver, pancreas	SB	1) SB; 2) SB, kidney	St, SB, liver, pancreas, kidney	SB, colon, kidney	SB, liver, pancreas	SB, colon, pancreas
Year of transplant	2008	2010	Both 2010	2011	2013	2013	2014

Key to table: DJF = duodenojejunal flexure, NAFLD = non-alcoholic fatty liver disease, SB = small bowel, St = stomach Case 3: 2nd transplant performed for rejection (non-compliance with immunosuppression)

P337
Profile and outcomes of mercaptopurine therapy in inflammatory bowel disease

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Background: Mercaptopurine (MP) is less used in Spain than azathioprine (AZA). Our aim was to determine the main situations in which MP is used as immunomodulatory therapy in inflammatory bowel disease (IBD), either as first choice thiopurine or as a second choice after AZA, as well as describing its efficacy and safety
Methods: Retrospective observational study in which all cases of patients treated with MP in a total cohort of 1598 patients with IBD were included: 851 patients with Crohn's disease (CD), 676 ulcerative colitis (UC) and 47 colitis non-classified (CNC). Demographics and clinical data regarding IBD and its treatment were collected
Results: Out of 1598 patients, 60.1% (n = 961) had been treated with thiopurines at some time. Of these, 151 patients received MP (98 CD, 51 UC, 2 CNC, 51% female, 25.9% smokers, mean age 49 ± 15 y); this represents 9.4% of all patients with IBD, and 15.7% of patients treated with thiopurines. The median time from diagnosis of IBD to the start of MP was 81 months (IQR: 20-109) and the mean dose used 80 ± 29 mg/d. MP was the initial thiopurine chosen in 14.1% of patients; in 4.5% it was indicated after AZA failure, and in 80.5% it was prescribed as continuation thiopurine following AZA intolerance: 36.9% (n = 48) digestive intolerance, 35.4% (n = 46) hepatotoxicity , 2.3% (n = 3) myelotoxicity, 1.5% (n = 2) pancreatitis and 23.8% (n = 31) other adverse effects. In 80/151 patients (53%; 47 EC, 33 CU), adverse effects of MP appeared, resulting in withdrawal in 50 of them; in one third, the adverse effect was identical to the one suffered after AZA. MP treatment was effective in 39% of cases (95%CI 31-47%), 41% efficacy in EC, 35% in CU. In the remaining, failure was due to withdrawal due to side effects (49.5%), need for therapeutic step increase (35.9%), need for surgery (12.4%) or supply problems (1.1%). The average total time of MP treatment was 36 months (IQR: 2-60), during which 31 patients (20.5%) required hospitalization and eventually almost half discontinued treatment with MP (47.7 %, of which 11.1% later resumed treatment)
Conclusions: In our setting, MP is primarily used as rescue therapy in patients with AZA adverse effects, which could explain its modest efficacy and the high rate of adverse effects. However, this drug is still an alternative in this group of patients, before a therapeutic step-up to biologics is considered

P338
Serologic profile and reactivation of Hepatitis B in rheumatic and Inflammatory Bowel Disease patients treated with TNF inhibitors bowel disease

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Background: TNF inhibitors (TNFi) are widely used in rheumatologic diseases (RD) and inflammatory bowel disease (IBD). However, these drugs have been associated with an increased risk of reactivation of latent infections. The specific risk of hepatitis B (HB) reactivation remains unclear since the low incidence of that infection in the majority of European countries. Our study aims to evaluate the serologic HB profile of patients with RD and IBD who had undergone TNFi therapy in a single centre; and to assess the incidence of HB reactivation in patients with a serological pattern of past HB infection.
Methods: Retrospective study of HB baseline serologic profile in patients with IBD and RD who have started TNFi therapy at our institution. Clinical signs of liver injury and liver injury blood tests were analysed during the treatment in order to identify cases with reactivation. Reactivation was defined as the detection of AgHBs or DNA-VHB.
Results: We analyzed 484 patients with available data on HB serologic profile, 210 men (43.4%) with a mean age of onset of biological therapy of 38 ± 15 years. 258 patients were diagnosed with RD (100 rheumatoid arthritis, 76 ankylosing spondylitis and 82 other RD); 226 patients suffered from IBD (180 Crohn's disease, 41 ulcerative colitis and 5 indeterminate colitis); 273 patients were simultaneously submitted to immunosuppressive treatment with azathioprine, 6-mercaptopurine, corticosteroids or methotrexate, for at least 1 month. At the beginning of the treatment, the HB serologic profile variations were: negative in 63.4%, 31.0% AbHBs+/AbHBc- and 5.8% AbHBc+ (with or without AbHBs+). The 28 AbHBc+ patients did not differ significantly from the overall population in terms of demographic characteristics, diagnosis, follow-up interval and biological therapy. No patient received prophylactic antiviral therapy during the follow-up period (median 8 years and 80 days) and there was only one case of HB reactivation, a Crohn's disease patient treated with infliximab and azathioprine.
Conclusions: In our cohort, there was one case of HB reactivation, corresponding to 3.5% of AbHBc+ patients treated with TNFi. This study highlights the importance of assessing HB serologic profile at the beginning of immunosuppressive therapy. This strategy allows not only the vaccination of serologic negative patients but also the identification of patients at risk of HB reactivation.

P339
High dose intravenous iron isomaltoside 1000 in subjects with inflammatory bowel disease - the PROMISE trial

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Background: Patients with inflammatory bowel disease (IBD) often suffer from iron deficiency anaemia (IDA), and have a high annual iron need which can be difficult to replace orally. Also, due to the IBD disease as such oral iron is most often not suitable for these patients. An

Treatment Group	Haemoglobin (Hb)	Body Weight < 70 kg	Body Weight ≥ 70 kg	Study Duration
A	Women: 10 ≤ Hb < 12 g/dL and men: 11 ≤ Hb < 13 g/dL	1,500 mg Monofer	2,000 mg Monofer*	8 weeks
B	Women: Hb < 10 g/dL and men: Hb < 11 g/dL	2,500 mg Monofer*	3,000 mg Monofer*	16 weeks

intravenous (IV) iron which is possible to administer as a high dose infusion in a single visit would offer the best pharmacoeconomic profile and optimal convenience for patients. The present trial evaluates high single and total doses of iron isomaltoside 1000 (Monofer®) in patients with IBD.

Methods: In this prospective, open-label, multi-centre GCP regulated safety trial iron isomaltoside 1000 was administered to subjects with IBD and IDA. The subjects were divided into two treatment groups:

*Dose given in two visits - 1500 mg at the first visit, remainder at the second visit. All doses were infused over approximately 15 min. Outcome measures were safety parameters and Hb measurements.

Results: 21 subjects were enrolled.

Hb increased from a mean of 10.8 (±1.0 SD) g/dL at baseline to 13.3 (±0.6 SD) g/dL at week 8 in group A ($p < 0.0001$, n = 11) and from 8.5 (±1.3 SD) g/dL to 11.6 (±3.5 SD) g/dL at week 16 in group B ($p = 0.0755$, n = 5). No serious adverse drug reactions (ADRs) were observed. 9 mild to moderate ADRs were observed in 4 subjects (1 subject had 4 events (feverish, vomiting, constipation, palpitations and dyspnoea), 1 subject had 2 events of eye allergy, 1 subject had 1 event of abdominal pain, and 1 subject had 2 events of chest pain with dyspepsia) and they were all reported as recovered.

Phosphate was (mean±SD) 3.7 (±0.4) mg/dL at baseline and 3.6 (±0.5) at week 8 in group A and 3.9 (±0.6) mg/dL at baseline to 3.8 (±0.3) mg/dL at week 16 in group B. No ADRs of hypophosphatemia were reported.

Conclusions: Rapid infusions of high dose iron isomaltoside 1000 administered as single doses up to 1,500 mg and cumulative doses up to 3,000 mg were completed without safety concerns and were efficacious in increasing Hb in IBD patients. This treatment algorithm represents are promising alternative to current routines.

The trial was sponsored by Pharmacosmos A/S.

P340
Adalimumab treatment in Ulcerative Colitis patients who are naïve to anti-TNF: Week 8 of our pilot study

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Background: Adalimumab has proved its efficacy in Ulcerative Colitis (UC) treatment in controlled studies. Nevertheless, we have little information on the response of adalimumab in clinical practice. Aim: Learn the response to Adalimumab treatment in UC patients and the related factors.

Methods: We carried out a multicentric, prospective and observational study in steriod-resistant and steroid-dependant UC patients who were naïve to anti-TNF treatments. They were treated with Adalimumab at a dosis: 160, 80, 40 mg on weeks 0, 2, 4 and every two weeks, with weekly dose intensification according to the clinician's judgement. We performed an endoscopic study at weeks 0 and 8 that was assessed by Mayo endoscopic scoring system from 0 to 3. We assessed clinical response at weeks 4 and 8. The clinical activity at weeks 0 and 8 was determined with Mayo scoring index (0-12) and at week 4 with Mayo subindex (0-9).

We defined clinical remission (CR) as a Mayo score <2; clinical response as a drop of at least 3 points in this score; and Mucosa Healing (MH) as a subscore of 0-1. The analysis of the Results was performed with intention-to-treat (ITT) (it includes all the patients that had received at least one dose of adalimumab)

Statistical analysis was performed with SPSS 20, using the Chi-square test for univariate analysis and for the multivariate analysis a logistic regression was performed.

Results: Of the 24 patients enrolled in this study, 22 completed the 8 weeks (2 were pulled out because of clinical worsening). UC was severe in 4 (16.7%) , moderate in 19 (79.2%) and mild in 1 patient (4.2%). 5 of them (20.83%) were hospitalized and more than half, 14 (58.33%), were steroid-dependant. Clinical remission was achieved, at weeks 4 and 8, in 8 (33.3%) and 11 patients (45.8%), and clinical response in 11 (45.8%) and 8 (33.3%), respectively. At week 8 of the study, only 1 patient was hospitalized and none suffered a colectomy. Mucosal healing (MH) at week 8 was achieved in 15 cases (78.9%), and a correlation was found with remission ($p<0.025$) and clinical response ($p<0.028$). Among the response factors at week 8, we found a relationship between the absence of blood in the stool, clinical response ($p<0.014$) and clinical remission ($p<0.001$) and between the calprotectine stool levels and Clinical Remission ($p<0.019$).

Conclusions: 1.-Adalimumab is an effective treatment in the induction of clinical response in patients with ulcerative colitis.

2.-Adalimumab is an effective therapy in the induction of early mucosal healing in these patients. There is a relationship between clinical activity and mucosal healing.

P341
Endoscopy Assessment at 1-year Identifies Long-term Responders to Thiopurines Maintenance Therapy in Patients with Crohn's Disease

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Background: When treating Crohn's disease (CD) with thiopurines, achievement of an objective response is essential. We aimed to determine the endoscopic responses of thiopurines monotherapy and to determine the minimal degree of mucosal improvement to alter outcomes of CD.

Methods: One-hundred and thirty CD patients with mucosal ulceration at baseline were included. The endpoints were endoscopic responses at two follow- endoscopies performed at 12 months (M12) and 36 month (M36) from the initiation of thiopurines.

Results: At M12, mucosal healing (MH) and a positive response (PR) were documented in 38% and 46% of patients, respectively. At the second follow-, merely a further 14% (9/65) of patients on monotherapy had a PR and a total of 46% (30/65) presented with MH. In a logistic regression model, both a PR ($P < 0.02$) and MH ($P < 0.001$) at M12 were associated with response at M36 in patients continuing thiopurines treatment. MH at M12 was associated with outcomes of CD at M36, with an area under the Receiver Operator Characteristic curve of 0.54 for predicting clinical remission, 0.69 for hsCRP normalization, 0.69 for MH, and 0.74 for PR, respectively. A PR at M12, defined a decrease in endoscopic activity score by ≥*** 2 points from baseline, yielded similar Results.

Conclusions: Endoscopy at M12 can help to identify long-term responders to thiopurines monotherapy in active CD. A PR could represent the minimal clinically important improvement in endoscopic disease activity.

P342
Meta-analysis: Does aspirin or non-aspirin non-steroidal anti-inflammatory drug use reduce colorectal cancer risk in patients with inflammatory bowel disease?

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Background: Inflammatory bowel disease (IBD) patients are at increased risk of developing colorectal cancer (CRC). Aspirin and non-aspirin non-steroidal anti-inflammatory drugs (NA-NSAIDs) have chemopreventive activity against 'sporadic' CRC.
Aim: To investigate whether aspirin and NA-NSAIDs have chemopreventative activity against CRC in patients with IBD.
Methods: We followed a pre-specified and peer-reviewed protocol; the PRISMA statement, a 27 item checklist deemed essential for reporting systematic reviews and meta-analyses of randomized controlled trials and observational studies. We searched for articles reporting the risk of CRC in patients with IBD related to aspirin or NA-NSAID use. No limits or language restrictions were applied. Pooled odds ratios (OR) and 95% confidence intervals were determined using a random-effects model. Publication bias was assessed using Funnel plots and Egger's test. Heterogeneity was assessed using Cochran's Q and the I2 statistic.
Results: Eight studies involving 14917 patients and 3 studies involving 1282 patients provided data on the risk of CRC in patients with IBD taking NA-NSAIDs and aspirin, respectively. The pooled OR of developing CRC after exposure to NA-NSAIDs in patients with IBD was 0.88 (95% CI 0.62 to 1.25) and after exposure to aspirin it was 0.75 (95% CI 0.27-2.08). There was significant heterogeneity (I2> 50%) between the studies. On meta-regression analysis, the population studied (hospital or population-based) was the only factor that almost reached statistical significance (p=0.06). Grouping studies based on the population studied showed that the OR for developing CRC in NA-NSAID users was lower in hospital-based studies (OR=0.44, 95% CI 0.06-3.07) compared to population-based studies (OR=0.91, 95% CI 0.76-1.08).
Conclusions: There is currently no convincing evidence that NA-NSAID or aspirin use is chemopreventive for CRC in patients with IBD. Whilst not reaching statistical significance, the OR for hospital-based studies was lower than population based studies. Hospital-based patients are likely to have more severe disease and so it is possible that NA-NSAIDs and aspirin only exert a significant chemopreventive effect in patients at higher risk of developing CRC. Further large epidemiological studies using prospective databases are needed to clarify the true effect of aspirin and/or NA-NSAIDs on the risk of CRC in patients with IBD. Chemoprevention remains an attractive option due to the poor uptake of surveillance colonoscopy in this group of patients.

P343
Misconceptions about reproductive issues in female patients with inflammatory bowel disease.

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Background: The quality of life of female patients with inflammatory bowel disease (IBD) has improved such that they are very often considering pregnancy. However, there are still a lot of reproductive issues that are not being addressed. Women with IBD may opt for voluntary childlessness due to certain misconceptions. The aim of this study was to determine the prevalence and type of misconceptions among female IBD patients.
Methods: This was a retrospective study were patients were recruited from 5 different European centres. Female IBD patients were recruited and they were interviewed through a purposely designed questionnaire.
Results: 233 patients were recruited (mean age 40 SD±11.9). The mean age of diagnosis was 31.4 years (SD±11.2). 85.5% of patients with ulcerative colitis (UC) had a Montreal classification of E2 or E3. Most Crohn's disease (CD) patients (64.7%) had non-stricturing and non-penetrating disease.
27.5% considered voluntary childlessness. 52.8% were afraid of harm of IBD to the baby. 61.4% reported fear of IBD medications to the baby. 57.9% were scared of passing on IBD to the baby. 51.5% feared having a complicated pregnancy due to IBD. Only 8.6% were afraid of being incapable of taking care of their child after birth because of IBD. However, another 9% gave other reasons.
19.7% experienced fear of not becoming pregnant at some point in their lives following the diagnosis of IBD. 8.2% were aware that mode of delivery could be influenced by IBD.
15.5% were aware that surgery could influence fertility. Only 36.5% of patients were aware that surgery could influence mode of delivery.
26.6% of patients were uncertain if patients with IBD could breast feed. 36.4% thought that females with IBD could breast feed and the rest (37%) said that they could not. 40.7% thought that females with IBD could not breast feed due to medications crossing into the breast milk and causing harm to the baby.
15.0% thought that all medications should be stopped during pregnancy due to safety to the fetus. 63.1% of patients were unsure. 12.0% claimed that only some medications should be stopped during pregnancy. 5-ASA was considered as a very safe medication by practically all patients.
Conclusions: A significant proportion of patients considered voluntary childlessness or feared infertility. An alarmingly high percentage of patients were not aware that mode of delivery is influenced by past surgery and IBD and that surgery could influence fertility. Misconceptions about breast feeding and medications during pregnancy were evident. This highlights the importance of more patient support groups, leaflets and the need for health care professionals to deliver appropriate information.

P344
Restless-Legs-Syndrome and iron deficiency in patients with inflammatory bowel disease

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Background: Patients with inflammatory bowel disease (IBD) frequently develop deficiency symptoms in addition to their characteristic IBD symptoms. In iron deficiency (ID), a modified cerebral iron metabolism may cause restless legs syndrome (RLS). In a previous study a prevalence of 30% for RLS in patients with Crohn´s disease (CD) was shown (Weinstock et al. 2010). In that study, RLS symptoms in patients with CD were not associated with current iron deficiency. Data for ulcerative colitis (UC) is lacking so far.
This study wants to determine the prevalence of RLS in patients with CD and UC of an IBD tertiary referral center evaluated by a questionnaire and confirmed by a neurologist. Furthermore, we study the effect of iron supplementation in CD and UC patients with RLS and ID.
Methods: Patients were consecutively screened for symptoms of ID and RLS by a self-developed questionnaire and explored for specific RLS-Symptoms by a gastroenterologist/internal medicine specialist. If RLS was suspected, patients were seen by a neurologist for conclusive RLS diagnosis or differential diagnosis, and additional tests (ultrasound with midbrain planimetrics, neuro-psychological tests (SF36, IBDQ-D, International RLS Severity Scale (IRLS), Epworth Sleepingness Scale, Pittsburgh Sleep Quality Index) were performed. Patients with RLS and ID received parenteral iron supplementation and were followed-up on week 4 and 11 after iron substitution.
Results: A total of 315 IBD patients were included in the study. (201 CD, 110 UC, 4 indeterminate colitis IC). RLS was suspected in 11% (n=33) of all patients by a gastroenterologist/internal medicine specialist (MC 10%, n=20; CU 10%, n=11; IC 50%, n=4). Diagnosis was confirmed in 73% of these patients by a neurologist (n=24; MC 70%, n=14; CU 73%, n=8; IC 100%, n=2). 25% of patients (n=6) showed mild, 42% (n=10) moderate, 29% (n=7) severe and 4% (n=1) very severe RLS according to IRLS score. The most common differential diagnosis was polyneuropathy (n=8). Estimated prevalence was 7% in both, CD and UC, respectively. 21% of RLS patients had concurrent ID. Iron supplementation resulted in 3 of 4 patients in improvement of IRLS score
Conclusions: RLS is seen in IBD, although prevalence in our study was much lower than in a previously published study. This may be due to the fact that diagnosis has to be established in close collaboration with a neurologist. CD and UC showed the same prevalence. Especially, sensomotoric peripheral neuropathy has to be considered as a differential diagnosis in IBD patients and can easily be misdiagnosed as RLS. Improvement of IRLS score after iron supplementation indicates a link between ID and RLS. However, further investigations with a larger cohort of RLS patients are necessary.

P345
Rapid weight increase in Infliximab treated Crohn's disease patients is sustained over time

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Background: Infliximab (IFX) is used in moderate to severe Crohn's disease and is effective for induction and maintenance of remission. There are scanty systematic data on weight gain and metabolic changes in IBD-patients under anti-TNF treatment. We have noticed that some, but not all, patients increase their body weight during treatment with IFX. Here we investigated changes in weight and blood chemistry in anti-TNF-naïve patients during their first course of IFX.
Methods: Retrospective analysis of 70 patients (51 men, 19 women) aged 24 years (range 14-33), 42 with luminal CD and 28 with fistulising CD, given at least 3 infusions of IFX (range 3-11). Data regarding body weight, height, C-reactive protein (CRP), haemoglobin and S-albumin before treatment and before the third infusion and at 1 year were collected from the medical records. Of statistical Methods, descriptive statistics, student´s T-test and Pearson´s correlation analysis have been used.
Results: At 6 weeks, 46 (66 %) increased in weight, 18 patients decreased in weight, and 6 had no change. Overall, there was a significant increase in weight (2 kg, IQR=-1-3 kg) and BMI at 6 weeks of treatment (P<0.001 and P<0.001 respectively). Patients with normal BMI at start of treatment had a larger weight gain compared to obese patients (p<0.05). CRP significantly decreased and albumin and haemoglobin increased (P<0,001). The weight gain at 6 weeks correlated to the increase in haemoglobin as well as a decrease in CRP (both P<0.01). There was no difference between men and women.
At 12 months: 57 patients continued IFX treatment for at least one year. Compared to baseline, 39 (68 %) patients had increased in weight, 16 patients decreased weight, 2 had no change. Overall, compared to baseline values treatment was associated with a significant increase in weight (3 kg, IQR=-1-7 kg) and BMI (p<0.001 and p<0.001, respectively). Increased weight correlated with decrease in CRP and increase in albumin and haemoglobin (P<0.001, P<0.01 and P<0.05, respectively). Patients treated with glucocorticosteroids during the induction phase had a larger increase in weight and BMI compared to those without glucocorticosteroids (P<0.04 and P<0.05, respectively). Again, there was no difference between men and women.
Conclusions: Approximately 70 % of infliximab treated Crohn's disease patients experience weight gain within the first 6 weeks. The weight increment correlates with improvements in inflammatory markers. The causes of the weight gain needs to be further explored, and, is probably related to reduction of the inflammatory burden as well as to treatment induced metabolic changes.

P346
Early treatment with infliximab for Crohn's disease patients

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Background: The main therapeutic goal in Crohn's disease (CD) is to suppress mucosal inflammation in order to limit intestinal damages and avoid surgery. The utility of an early treatment with infliximab (IFX) to reach this therapeutic goal is still discussed. The aim of our study was to evaluate the effect of an early treatment with IFX on disease outcomes in CD patients naive from anti-TNFα antibodies.
Methods: We performed a retrospective and comparative study of CD patients naive from anti-TNFα antibodies receiving early or late treatment with IFX from 2007 to 2010 in our center. Early

IFX treatment was defined as a first infusion < 18 months after CD diagnosis while an infusion done >18 months after diagnosis was considered as a late treatment. Clinical activity was evaluated 3 to 6 months after IFX introduction and mucosal healing at the first colonoscopy performed after IFX introduction. Hospitalizations for CD, intestinal resections, modifications and withdrawal of IFX were recorded during the follow-up after IFX introduction. The rate of global surgery was defined as the number of patients with intestinal resection from CD diagnosis to last follow-up visit . The rate of cumulative surgery was defined as the number of surgeries for each patient from CD diagnosis to last follow-up visit.

Results: Among the 153 patients treated by IFX between 2007 and 2010, 36 (24%) received an early treatment and 83 (54%) a late one. The mean follow up from diagnosis was longer in patients with late IFX compared to early IFX (172 ± 98 months vs. 49 ± 21 months, p<0.01) while the mean follow up after IFX introduction was not different in the two groups (42 ± 21 months vs. 44 ± 23 months, p=0.643). Patients with early IFX had fewer surgeries and were less exposed to thiopurines before IFX introduction compared to patients with late IFX (6% vs. 46%, p<0.0001 and 47% vs. 78%, p=0.001). After IFX introduction, rates of hospitalizations (17% vs. 18%, p=0.89), intestinal resections (8% vs. 8%, p=0.98) and IFX withdrawals (47% vs. 49%, p=0.83) were similar in early and late IFX groups. However patients with early IFX had a lower rate of global surgery compare to those with late IFX (14% vs. 52%, p=0.007) and cumulative surgery was also higher in patients with late IFX with more patients that underwent two or more surgeries (20% vs. 0%, p=0.004).

Conclusions: Early treatment with IFX in CD patients seems to decrease surgery in the first years of evolution but once started, IFX seems to have the same efficacy in patients with early or late treatment. These Results need to be confirmed by prospective studies including a follow-up of patients treated with early IFX.

P347
Patient perception towards faecal microbiota transplantation for treatment of Inflammatory Bowel Disease

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Background: Faecal Microbiota Transplant (FMT) is a novel highly effective treatment for Clostridium difficile infection (CDI). Initial clinical trials and case reports suggest that this may be a promising therapy for patients with inflammatory bowel disease (IBD). As part of a patient audit regarding our FMT treatment for CDI we performed a survey to evaluate patient attitudes to potentially receiving FMT as treatment for IBD and gauged attitudes towards participation in a future clinical trial evaluating the effectiveness of FMT in IBD.

Methods: We conducted a structured survey on patients attending gastroenterology clinics to assess perceptions of effectiveness, tolerability, safety and thresholds for considering FMT as a treatment.

Results: We collected 105 responses (M:F 46:59, Median age 36 years) including 80 (76%) from patients with IBD. 91% (96/105) felt that this treatment would be effective and 56% (59/105) did not consider it unpleasant. 96% (101/105) patients perceived it to be safe. 72% (76/105) and 82% (86/105) would be comfortable with having FMT via an NG tube or rectal enema route respectively. 78% (82/105) did not have any concerns regarding the faecal transplant being obtained from a screened unrelated donor. 74% (78/105) of the patients would be willing to have FMT as a first line treatment of CDI. 50% (40/80) of IBD patients surveyed would consider FMT as a first line treatment of their IBD, 85% (68/80) if steroid resistant or dependant, 89% (71/80) if failing on biologics and 94% (75/80) as a salvage treatment option prior to surgery. Importantly 75% (60/80) would consider taking part in a clinical trial evaluating faecal microbiota transplantation for treatment of their IBD.

Conclusions: In this survey of patient attitudes to FMT amongst patients from the UK, we found that patients perceived FMT as a potentially effective, safe, tolerable treatment and were inclined to consider this as part of conventional medical therapy for IBD. In our cohort we did not discover reluctance to take part in a trial of FMT for treatment of IBD.

P348
How could female infertility be reduced after open IPAA

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Background: Ulcerative colitis (UC) and Familial Adenomatous Polyposis (FAP) affect mainly young people of reproductive age and when surgical treatment is indicated proctocolectomy with ileo-anal pouch anastomosis (IPAA) is the treatment of choice. IPAA is highly associated with post-operative infertility due to adhesions at the fallopian tubes and ovaries, especially after hand-sewn open technique compare to laparoscopy.

Aim of this study is to present data from young women operated with IPAA with regard to fertility and to propose surgical measures for prevention of female infertility.

Methods: We retrospectively collected data from young women (15-44 years of age) operated with IPAA for UC or FAP based on structure telephone interview regarding their reproductive behavior and we compared them with those of the general population. We finally present surgical strategies for minimal formation of adhesions into the pelvis.

Results: Over a period of 30 years (1983-2013) 680 patients were submitted to IPAA for UC or FAP. In a total number of 426 patients we selected 104 young female patients (90 UC/14 FAP) of reproductive age. 72 answered to the questionnaire regarding their reproductive status and they were included in the final analysis. Twenty one females (29, 16%) were able to take over 1 or 2 full-term deliveries while 51 (70, 83%) answered negatively including women lacking willingness to deliver a baby. We propose surgical techniques such as wrapping of the ovaries and fallopian tubes, use of adhesion preventing membranes, omental plug and vacuum suction in the pelvis for the prevention of infertility in this group of patients.

Conclusions: This is the largest Greek retrospective analysis of patients operated with IPAA by a single surgeon. Although the limited number of female patients included in this series, it seems that preventing measures perioperatively can reduce infertility in young women of reproductive age and reaching to acceptable fertility levels compare to the general population.

P349
Consensus Statements on the Management of Acute Severe Ulcerative Colitis

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Background: Acute severe ulcerative colitis (ASUC) is a potentially life-threatening condition affecting 15% of UC patients. The mortality rate has improved from 24% prior to corticosteroids to 2.9%. Treatment guidelines assist in timely diagnosis and initiation of treatment. However, there are no current guidelines that exclusively aid the management of ASUC. Our aim was to develop consensus guidelines on the diagnosis and management of ASUC.

Methods: The Delphi method was used in the development of the consensus statements. A steering committee generated the statements of interest. 80% or more agreement without or with only minor reservation determined acceptance of statements. Three rounds of anonymous voting were carried out to achieve the final Results. Evidence level and recommendation grade, according to the National Health and Medical Research Council (NHMRC) guideline, were endorsed following further discussion.

Results: A total of 33 statements were grouped into 16 themes covering definition, treatment targets, investigations, first-line treatment, indications and options for second-line therapy, maintenance therapy, DVT prophylaxis, nutrition, pharmacy, pregnancy, and opportunistic infections. From 22 multi-disciplinary clinicians, there was 100% agreement for 24 out of 33 statements; 80-99% for 6 statements; and 3 statements were rejected. The rejected statements involved prolonged DVT prophylaxis after hospital discharge; infliximab dosing based on trough level; and restricted use of thiopurines in EBV-naive young patients. Important translatable outcomes include the paucity of evidence of occupational health and safety risks from casual anti-TNF exposure and that all ASUC therapies be readily available for prompt emergency dispensing. Dose intensification of infliximab either by shorter dosing interval or higher dosage can be considered, but further studies are needed to definitively establish the benefit of this practice. Management of ASUC in pregnant women should be no different to non-pregnant patients, including the use of infliximab in the third trimester, as the previous concern of increased infant infection has been shown to be absent in the latest large prospective cohort study of pregnant women.

Conclusions: These are the first comprehensive consensus guidelines specific to ASUC, containing the latest evidence of emerging areas of therapy, as well as detailed discussion of areas previously addressed in other major guidelines. The endorsed statements are expected to improve and harmonise management and provide auditable quality assessments.

P350
Mucosal and histologic response to cyclosporin in ulcerative colitis: a cohort study

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Background: Cyclosporine (CsA) has demonstrated its efficacy for treating patients with steroid-refractory acute severe ulcerative colitis (UC). However, little is known about the impact of this drug on endoscopic and histologic responses, which are considered as relevant therapeutic goals in UC. The aim of the present study was to assess mucosal healing (MH) and histological remission (HR) rates under CsA and their predictive value on UC course.

Methods: All consecutive patients admitted in two academic hospitals from January 2008 to January 2014 for steroid-refractory acute severe UC and treated with intravenous CsA were eligible. CsA was given as a bridge therapy to azathioprine in all patients. Only primary clinical responders to CsA who had endoscopic assessments at entry and at the end of the treatment were analyzed. They were followed until relapse or until July 2014 for non-relapsing patients. MH was defined by a Mayo endoscopic subscore 0 or 1. HR was defined by absence of basal plasmocytosis or by a Geboes score < 3.1 (Bitton et al, Am J gastroenterol 2001, Bessisow et al, Am J Gastroenterol 2012). The primary outcome was UC relapse, defined by occurrence of clinical symptoms associated with inflammatory endoscopic lesions leading to systemic therapeutic change (steroids, immunosuppressant or biologic agent) or colectomy.

Results: Among 39 patients who received CsA, 18 were excluded (14 for CsA primary non-response and 4 for absence of endoscopic assessment). Therefore, 21 (54%) patients (11W; median age: 36 [range: 16-69] years) were analyzed. Median duration of CsA treatment was 103 [60 - 145] days. MH was achieved in 81% patients, HR in 85% according to basal plasmocytosis and in 65% according to Geboes score. With a median follow-up duration of 42 [0.3 - 66.1] months after CsA withdrawal, survival rates without UC relapse at 1 and 2 years were respectively 79% and 79% in patients with MH as compared to 50% and 25% to those without MH (p=0.040). They were similar in patients achieving HR and in those without HR whatever the definition used. On multivariate analysis, Mayo endoscopic subscore 0 was the sole prognosis factor associated with absence of relapse with a relative risk of 12 (95%CI: 1.05-136.79).

Conclusions: CsA provided 81% of MH in patients with severe refractory UC responding to this drug and 65-85% of HR. With a long follow-up duration, complete MH was associated with absence

of UC relapse. As observed with other UC treatments, these data with CsA further confirm the high prognostic value of MH.

P351
Does failure to respond to one anti-TNF agent in Ulcerative Colitis predict treatment failure with other anti-TNF agents?

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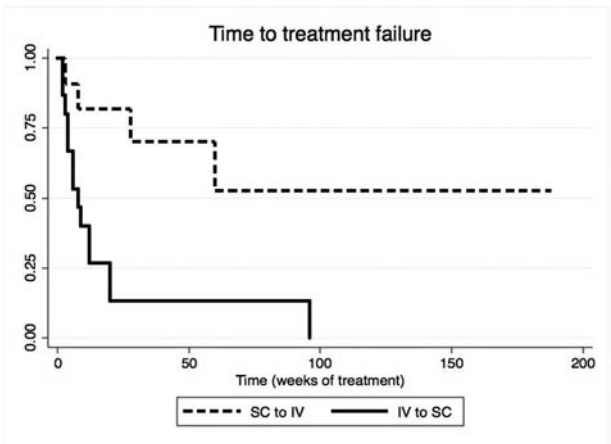
Background: Anti-TNF therapy is an effective maintenance treatment for ulcerative colitis (UC) of moderate severity with inadequate response to standard therapy. In clinical practice, there is uncertain clinical benefit of trying a second biologic in UC patients who failed to respond adequately to the first anti-TNF agent. Our aim is to evaluate the response to a second anti-TNF agent in UC patients who failed to respond to initial biologic treatment.

Methods: A retrospective study was performed using a prospectively maintained electronic database of 3,200 patients with IBD attending a single centre. Patients with histologically confirmed ulcerative colitis who received sequential treatment with two anti-TNF agents were identified. Patients who switched treatment due to secondary loss of response, adverse reaction to the first agent were excluded. The Results were analysed on the basis of whether patients received an intravenous agent (e.g. infliximab) first followed by a subcutaneous agent (IV to SC) or vice versa (SC to IV). Treatment failure is defined as inevitable colectomy, steroid dependence, or enlisting into new clinical trials.

Results: n=63 UC patients were identified who had received at least two biologics over a 10 years period. n=7 patients were excluded as they did not meet inclusion criteria (n=3 were diagnosed with Crohns disease during follow up, n=4 received one or other biologic agent for other indications e.g. arthopathy). Of the remaining 56 patients 30 patients were excluded as they had a response to the first biologic but developed an adverse reaction, lost response or relapsed after discontinuation of treatment. n=26 patients were commenced on anti-TNF to treat UC and received a second agents due to non response (n=15 IV to SC and n=11 SC to IV). There were 18 males and 8 females, and 14 patients had pancolitis. 14/15 (93%) patients in the IV to SC failed treatment during follow up compared to 4/11 (36%) in the SC to IV group (Fishers exact p=0.003). Disease extent was not associated with treatment failure. Time to treatment failure was significantly shorter in the IV to SC group than with sequential SC to IV treatment (log rank p=0.003) See Figure 1



"TIME TO TREATMENT FAILURE"

Conclusions: These Results suggest a high likelihood of treatment futility with use of a SC anti-TNF in patients who fail to respond to initial IV infliximab, however the majority of patients failing to respond to SC biologic treatment can successfully be treated subsequently with IV infliximab.

P352
Unblinded Results from a dose-escalating placebo-controlled study with allogeneic bone marrow-derived mesenchymal stem cells for the treatment of refractory perianal fistulas in patients with Crohn's disease

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Background: Mesenchymal stromal cells (MSCs) have gained interest as potential cellular treatment for perianal fistulizing Crohn's disease (pCD), because of their ability to regenerate damaged tissue and to regulate immune and inflammatory responses.

Methods: In this prospective double blind phase I-II trial 21 patients with 1 or 2 draining perianal fistulas, but without active luminal Crohn's disease and not responding to current therapy modalities, were randomized in a 5:2 fashion to receive either protocolized local injections of 10, 30 or 90x10^6 (resp. cohort 1, 2 or 3) allogeneic bone marrow-derived MSCs (bmMSC) or placebo; collectively called endproduct. Treatment was preceded by MRI- and surgical localization curettage and closure of the internal opening of the fistulous tract. Follow-up visits took place 6, 12 and 24 weeks after bmMSC therapy. Primary endpoints were safety and preliminary efficacy of allogeneic bmMSC treatment. Secondary objectives were the changes in CRP, disease activity (CDAI and PDAI), adapted Vaizey score, quality of life scores (sIBDQ and SF-36), and endoscopic disease severity (CDEIS and SES-CD) from baseline to week 24.

Results: Local infusion of the endproduct was safe as no serious adverse events were detected. In total 32 draining perianal fistulas were observed at physical examination and MRI in the 21 patients included. At week 6, 6/12 of the fistulas in cohort 1, 6/11 in cohort 2 and 2/9 in cohort 3 were completely healed, defined as no discharge upon pressure at physical examination. At week 12 these numbers were 5/12, 6/11 and 3/9, respectively, and 7/12, 6/11, and 3/8 (n=6) at week 24. In cohort 3, 1 inactive fistula at baseline was active at week 24. Reinstalment of seton and/or abscess drainage was needed in 1 patient in cohort 1, 2 in cohort 2 and 1 in cohort 3. Average PDAI of the total cohort decreased from 4.6 at baseline to 3.4 at week 12 and 3.1 at week 24. In addition, mean Vaizey score declined from 3.8 at baseline to 2.6 at week 12 and week 24. Secondary endpoints CRP, disease activity, sIBDQ, SF-36 and endoscopy scores were stable during the study. Important to note that these unblinded data include the patients which received placebo in each cohort.

Conclusions: Local administration of allogeneic bmMSC is safe and feasible in patients with refractory pCD. No serious adverse events were detected during the 24 weeks after cellular treatment. In total 16/31 of the fistulas had completely healed at 24 weeks with the highest cure rate in cohort 1 (10x10^6 bmMSC). Deblinding of the study randomizing bmMSCs will take place the 17th of December 2014.

P353
Are we under-recognizing skewed thiopurine metabolism in IBD patients? Routine thiopurine metabolite measurement yields clinical benefit at 12 months: A retrospective observational study.

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Background: Azathioprine & 6-mercaptopurine (AZA/MP) metabolites, 6-thioguanine nucleotides (6TGN) & 6-methyl-mercaptopurine (6MMP), are measurable with a proposed "therapeutic range". Therapeutic drug monitoring (TDM) has led to the identification of "shunters" (preferential 6MMP producers), affecting ~15% of IBD patients. Allopurinol co-therapy with reduced AZA/6MP doses overcomes skewed metabolism and can improve IBD activity. Existing studies in shunters are short term, small or focused on apparent AZA/MP resistance or hepatotoxicity. Therefore we evaluated patient outcomes ≥12 months after TDM in all "shunters" identified in a large adult IBD population.

Methods: A multi-centre, cross-sectional retrospective study was performed in 3 Australian IBD Services. Data were collected from clinical records of IBD adults, on AZA/MP for ≥4 weeks at index TDM. Patient demographics, disease characteristics, physician global assessment, IBD therapy at index TDM, and again ≥12 months after TDM-led management were collected. Therapeutic 6TGN range was defined as 235-450pmol/8x10^{8}RBC. Shunters were defined as having 6MMP:6TGN ratio ≥11.

Results: Of 343 patients, 135 (39%) shunters were identified- 102 at baseline, 33 on subsequent TDM. 91 (67%) had Crohn's disease, 76 (56%) female, & mean age 42 years. At baseline, 40 (33%) were in clinical remission, 81 (66%) had active disease. TDM was performed for proactive dose assessment (43%), ongoing active disease (27%), flare (22%) & adverse drug reactions (ADR) (7%). 12-month data was available for 122/135 shunters. Overall, TDM led to AZA/MP continuation in 23 (19%), AZA/MP-allopurinol co-therapy in 46 (38%), anti-TNFα therapy in 27 (22%), another medical agent in 9 (7%), surgery in 6 (5%). At 12 months, 90 (74%) were in clinical remission, 5 (4%) clinical improvement, 26 (21%) ongoing activity. Of 95 patients with 12-month clinical remission/improvement, 18 (19%) were managed on AZA/MP alone, whereas 40 (42%) on AZA/MP-allopurinol co-therapy were successful; 21 (22%) anti-TNFα therapy, 5 (5%) another medical agent, 6 (6%) surgery. Interestingly, clinicians only identified 85/135 shunters (63%). Of the 50 unidentified, 15 had therapeutic 6TGN/6MMP levels despite 6MMP:6TGN ≥11, 7 no change in therapy & 2 surgery, leaving 26 truly unidentified.

Conclusions: Shunters are more common than previously documented (39%) and easily unidentified. The utility of TDM in shunters extends beyond AZA/MP resistance and ADR, identifying shunters in early stages of AZA/MP therapy and with dose escalation. AZA/MP±allopurinol achieved clinical remission/improvement in 61% of patients. This is the largest study to date to evaluate ≥12 month outcomes of TDM in shunters and supports its utility throughout the course of AZA/MP therapy.

P354
Analysis of outcomes after non-medical switching of anti-tumor necrosis factor agents

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Background: When multiple treatment options within a class are available, substitution with a less expensive or patient-preferred medicine may occur for cost-containment.[1] We examined medical outcomes and outpatient resource use associated with cost-based non-medical switching (NMS) of anti-TNF agents.

Methods: Electronic health record data (Humedica 2007 to 2013) were searched to identify patients (pts) ≥18 years old treated with an anti-TNF agent for an immune disorder (rheumatoid arthritis [RA], psoriasis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease [CD], or ulcerative colitis [UC]). A natural language processing algorithm[2] was used to categorize the reason for anti-TNF treatment adjustment (eg, switch, discontinuation) as related to cost or insurance, side effects, or lack of efficacy as indicated in physician chart notes. The NMS sample (N=158) included pts with stable disease in the 90-day baseline period (ie, no anti-TNF treatment change for side effects or lack of efficacy, no emergency room visit, and no hospitalization) who had a cost- or insurance-related switch to a different anti-TNF therapy. The NMS group was matched on key characteristics (including disease type, initial anti-TNF therapy, sex, and age) to controls who were stable and did not experience a medication change due to cost at baseline (N=4804). Outpatient resource utilization and rates of anti-TNF treatment adjustment for side effects and lack of efficacy were compared between the NMS group and controls in the 30 days, 90 days, and 1 year after the NMS date in unadjusted and adjusted analyses.

Results: Most pts had RA (65% for NMS and 76% for controls); 6% of the NMS group and 3% of controls had UC or CD. Experiencing a cost-based NMS was predictive of an increased likelihood of a subsequent anti-TNF treatment adjustment due to lack of efficacy or side effects during 1 year of follow-up (62% for NMS and 20% for controls, p<0.001) (**Figure**).

Conclusions: Non-medical switching of anti-TNF agents was associated with an increase in side effects and lack of efficacy that led to subsequent treatment change as well as increases in health care utilization. Cost-related switching of medications in otherwise stable pts may have unintended consequences and should be avoided.

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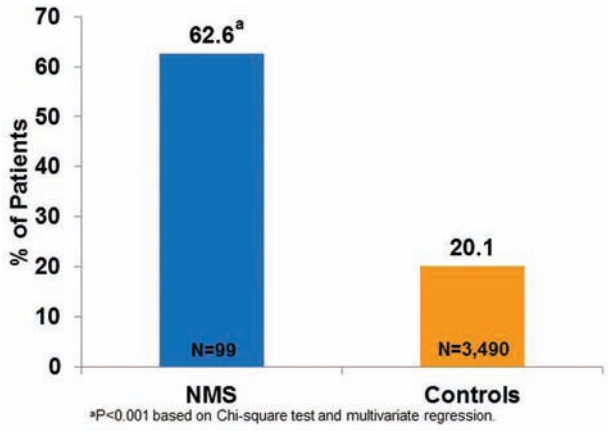

P355
What is treat-to-target of Crohn's Disease: the comparison of long-term outcome among patients with mucosal healing, deep remission and biological remission ?

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Background: Treat-to-target aiming to improve long-term outcomes of Crohn's disease (CD) is receiving increasing attention. However, great controversy existed in the treatment goals to be achieved. We aimed to examine whether a more strict treatment target predicts a better outcome in CD.

Methods: We conducted a retrospective, observational cohort study of patients with CD by using a prospectively maintained IBD database (October 1, 2001 through September 30, 2013).

The long-term outcomes of CD patients with complete MH were compared with those of patients with deep remission (DR,defined as the absence of mucosal ulceration and CD Activity Index scores less than 150) and biological remission(BR, defined as DR combined with negative surrogate markers of inflammation). The primary efficacy outcome was the proportions of CD-related intestinal surgery and hospitalization at the successive visits throughout follow-up.

Results: A total of 195 patients who had MH detected at the scheduled endoscopic follow-up evaluation to assess MH constituted the study population. These 195 patients were then divided into three homogeneous arms according to the normalization of simultaneous CDAI and/ or hs-CRP: the DR group (referred to DR patients with elevated hs-CRP, n=53), the BR group (referred to DR patients with normalized hs-CRP, n=106) and the MH only group (referred to patients with a CDAI >150 at the detection of endoscopic remission, n=36).

After a median follow-up period of 46.03 months (IQR, 28.15-67.93 months), 25 patients had CD-related bowel surgery, 44 patients had CD-related hospitalizationshospitalized, and 53 patients experienced CR. Of 151 patients performed at least one follow-up colonoscopy after the initial colonoscopy, 96 patients experienced an ER. Overall there were significant longer CD-related hospitalizations-free survival (133.5 ± 17.1 vs. 68.6 ± 5.1 vs.86.3 ± 8.6 months, P =0.004), ER-free survival (33.38 ± 3.7 vs. 20.3 ± 3.2 vs.33.7 ± 5.8 months, P =0.015), and CR-free survival (109.38 ± 12.1 vs. 50.52 ± 6.5 vs.50.6 ± 9.3 months, P =0.006) of patients in the BR group than both the DR and MH group. There was a trend, albeit not significant, for an increased proportion of patients remaining free of CD-related bowel surgery in the BR group (85.3 ± 7.3% vs. 67.8 ± 10.8% vs. 37.5 ± 19%, P=0.087). Patients with DR tented to had longer CFREM (P=0.03) but not less Crohn's related operations or hospitalizations or ER when compared with patients with MH only.

Conclusions: CD patients with appeared to have better long-term outcome than those with DR and MH. BR. A more strict treatment target predicts a better outcome in patients with CD.

P356
Durable Clinical Remission and Response in Adalimumab-Treated Patients with Ulcerative Colitis

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Background: Achievement of remission with adalimumab (ADA) treatment in patients (pts) with moderate to severe ulcerative colitis was demonstrated in ULTRA 1[1] and ULTRA 2.[2] Sustained efficacy was shown through week (wk) 52 in ULTRA 2 and up to 4 years in ULTRA 3.[2,3,4] Durable remission/response rates have not yet been reported for pts in ULTRA 2.

Methods: ULTRA 2 was a 52-wk double-blind (DB) trial in which pts were randomized to placebo or ADA [160/80 mg at wks 0/2, 40 mg every other wk (eow) from wk 4). Pts with inadequate response could move to open-label (OL) ADA (40 mg eow and then 40 mg wkly if necessary) from wk 12. In *post-hoc* analyses, durable remission (partial Mayo score [PMS] ≤2, no subscore >1), and durable response [PMS decrease ≥2 points and ≥30% from baseline, and rectal bleeding subscore (RBS) decrease ≥1 from baseline or RBS ≤1] were assessed in ADA wk 8 responders (by PMS, N=123) at multiple time points over 9 visits (wks 8, 12, 16, 20, 26, 32, 38, 44, 52): (1) at wks 32 and 52 and (2) at 100%, 89%, 78%, and 67% of all visits. Response and remission were also reported at each of the 9 visits. Missing data were handled using nonresponder imputation (NRI), whereby pts with missing data or those who received OL ADA were considered nonresponders, by modified NRI (mNRI) whereby only pts with missing data were considered nonresponders, and by last observation carried forward (LOCF).

Results: Remission was observed in 58% of ADA-treated wk 8 responders and was maintained through wk 52 (Figure). Response and remission were maintained at wks 32 and 52 in 44.7% and 32.5% (NRI) of wk 8 responders, respectively (mNRI: 51.2% and 36.6%, respectively) (Table). At 2/3 of all study visits, response and remission were maintained in 56.9% and 41.5% (NRI) of wk 8 responders, respectively (mNRI: 62.6% and 48.8%, respectively)

(Table). For all analyses, greater numerical rates of remission and response were observed in TNF-naïve v. anti-TNF-experienced pts (data not shown).

Conclusions: Maintenance ADA treatment in pts with response to ADA induction treatment led to durable remission and response through wk 52.

Reference:

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P357
Integrated care pathways for Inflammatory Bowel Disease Surgery: Design and first analysis.

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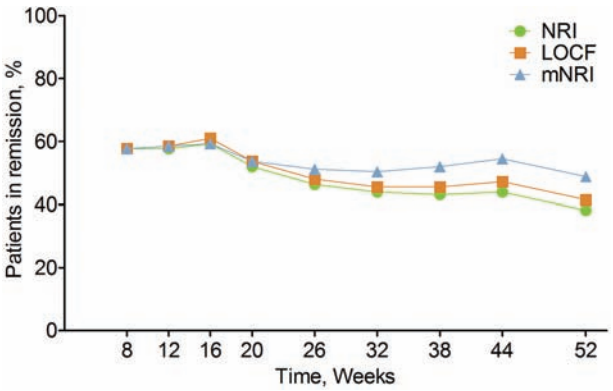
Background: Surgery has become an essential care component in Inflammatory Bowel Diseases (IBD) management. Although surgical and medical teams often work closely together, no integrated care pathways have been reported. In an existing IBD coordinated care program we aimed to fully integrate pre-operative, operative and post-operative IBD care.

Methods: The UCLA value-based care program for IBD consists of 9 highly coordinated medical care pathways. The surgical pathway was designed by a multidisciplinary team of specialists and nurses with patient input. Pre-operatively the indication for surgery was agreed upon during multidisciplinary case presentations. Coordination of pre-assessment, time of surgery, surgical quality indicators, and discharge was completed by the surgical IBD team. A 4-week post-surgery pathway included continuous tele-monitoring of pain, weight, temperature, nutrition, bowel function, pain medication, quality of life and productivity. In addition, tele-wound-monitoring was introduced. The surgical pathway was completed after a week 4 clinic visit and patients were assigned to their subsequent medical pathway. Included patients were compared to matched historic controls for initial performance analysis.

Results: Of the 1163 IBD patients enrolled in the IBD value-based care program, 46 patients undergoing major abdominal surgery entered the surgical care pathway and were compared to 41 controls. Characteristics: mean age 39 (20-70); 63%-CD, 35%-UC and 2%-IBD-U; surgery type: bowel resection (46%), stricturoplasty (33%), enteric fistula surgery (8%), lysis of adhesions (10%), and abscess drainage (4%). A 27% reduction in post-operative complications was observed; most common complications were ileus and infection. All patients completed the care pathway with a clinic follow up within 30 days after hospital discharge. In the controls 27% of patients had no GI clinic follow up and 49% had no surgical follow up after discharge. Emergency department (ED) visits (<30 days after surgery) were reduced by 7.5%; primary indications were abdominal pain, fever, and nausea/vomiting. On average, we observed 2-3 phone calls/patient and 10-15 eConsults/patient, as a result of which 9 ED visits/readmissions were likely prevented. Monitoring of post-surgery parameters and tele-wound monitoring was feasible and demonstrated meaningful provider decision support.

Conclusions: This integrated care pathway for IBD surgery was successfully implemented and strongly decreased post-surgical loss to follow up. In summary, this pathway showed clinically relevant Results with respect to enhancing patient value and controlling utilization-associated costs.



"Remission Rates Over Time in Week 8 Responders"

P358
Long term efficacy of granulocyte-monocyte-apheresis in ulcerative colitis elderly patients. The Italian Registry of Therapeutic Apheresis.

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Durable remission/response in ADA-treated patients who responded to therapy at week 8.

	Remission (% of patients)	Remission (% of patients)	Response (% of patients)	Response (% of patients)
	NRI	mNRI	NRI	mNRI
Weeks 32 and 52	32.5	36.6	44.7	51.2
% of visits (n/N)				
-- 100% (9/9)	18.7	N/A	37.4	N/A
-- 89% (8/9)	30.1	31.7	50.4	54.5
-- 78% (7/9)	36.6	39.8	52.0	58.5
-- 67% (6/9)	41.5	48.8	56.9	62.6

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Background: Granulocyte-monocyte-apheresis (GMA) is effective in the treatment of ulcerative colitis (UC). Thanks to its favorable safety profile, the use of this technique could be particularly suitable for elderly patients. However, information on the efficacy of GMA in this population is still scant. This observational study investigates the efficacy of GMA in elderly patients included in the Italian Registry of Therapeutic Apheresis.

Methods: Data of elderly (>65 years) patients with mild/moderate UC treated with a standard protocol of GMA (5 sessions in 5 weeks) were evaluated. Clinical evaluations were performed at 3, 12 and 24 months since the end of GMA session. The following parameters were assessed: incidence of clinical remission (CAI [Colits Active Index] <4); erythrocyte sedimentation rate (ESR); c-reactive protein (CRP); white cells blood count (WBC). Endoscopical evaluations were performed at a 3-month follow-up: the incidence of endoscopical remission (EAI [endoscopical activity index] 0/1) was assessed.

Results: Data for 74 patients (51 males, median age 68 years; CAI 7.12) were available; 62 patients were either steroid-resistant or steroid-dependent. The proportion of patients with remission of disease was 64% at 3 months, 62% at 12 months and 60% at 24 months. At 24 months, all other efficacy parameters had improved from baseline: CAI (7.12 vs 3.2), ESR (34.82 vs 12.8 mm/h), CRP (4.45 vs 0.80 mg/dl) and WBC (8.11 vs 6.12) (p<0.001 for all comparisons).

Endoscopic data were available for 32 patients. The incidence of mucosal healing was 44%; all patients with mucosal healing presented a clinical remission over the entire follow-up period.

No major adverse events were reported during GMA sessions.

Conclusions: Data collected on a sample of elderly patients included in the Italian Registry of therapeutic apheresis show that GMA is a safe and effective procedure over a long-term follow-up also in this population. Mucosal healing appears strongly associated with clinical remission.

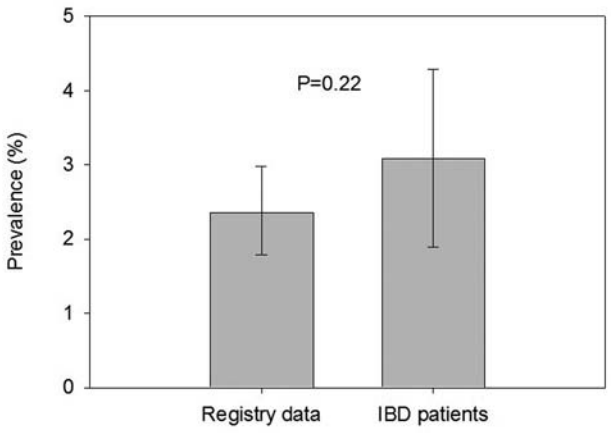

Figure 2: Comparison of proportions of congenital abnormalities in IBD pregnancies exposed to anti-TNF therapy from published studies with population-wide registries"

P359
Meta-analysis of the effects of anti- tumour necrosis factor alpha therapies on pregnancy outcomes in women with Inflammatory Bowel Disease

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Background: Inflammatory Bowel Disease (IBD) commonly affects women in the peak of their reproductive years, leading to patient and physician concerns about the risk of adverse pregnancy outcomes. The aim of this study was to perform a meta-analysis to quantify the risk of adverse pregnancy outcomes in IBD related to maternal exposure to anti-TNFα agents.

Methods: Published studies and abstracts were screened from databases (MEDLINE, SCOPUS, EMBASE and Cochrane Reviews) and international meeting abstracts. A meta-analysis using a random-effects model was used to pool estimates and report odd ratios for adverse outcomes, congenital abnormalities, preterm birth and low birth weight. A Chi-Squared analysis of independence was used to compare prevalence of congenital abnormalities pooled from 17 IBD studies compared with 5 pooled population-wide registries.

Results: In women exposed to anti-TNFα the pooled odds ratio (OR) for adverse pregnancy outcomes was: 1.14 (95% CI 0.73 to 1.78; p = 0.555; Figure 1). The pooled ORs for congenital abnormalities, preterm birth and low birth weight were respectively: 0.89 (0.37 to 2.13; p = 0.786), 1.21 (0.74 to 2.00; p = 0.45) and 1.36 (0.77 to 2.38; p = 0.28). The pooled rate of congenital abnormalities from studies in women receiving anti-TNFα treatments was not statistically different from rates of congenital abnormalities pooled from population-wide registries (χ^2=1.512, p=0.219; Figure 2). The publication bias and heterogeneity analyses indicated that the studies were comparable with no statistically significant evidence of publication bias.

Conclusions: Anti-TNFα therapy does not increase the risk of adverse pregnancy outcomes, congenital abnormalities, preterm birth or low birth weight compared with disease-matched controls or the general population. These findings may offer some reassurance for women and physicians regarding the safety profile of anti-TNFα during pregnancy in IBD.

P360
Adalimumab in perianal Crohn's disease treatment: Experience of a tertiary center

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Background: Perianal Crohn's disease (PACD) represents a phenotype with severe prognosis and significant morbidity. In literature few studies describe adalimumab (ADA) efficacy in PACD, especially in terms of time to achieve response and its durability.

Methods: Consecutive patients with PACD treated with ADA were prospectively monitored to assess ADA efficacy, using Perianal

Disease Activity Index (PDAI). Exam under anesthesia and/or magnetic resonance was performed in patients with complex perianal disease. Response was defined as a PDAI lower than 5 or a decrease in more than 5 points in PDAI. Remission was considered when PDA was lower than 3. Loss of response was defined by any increase in PDAI, by the recrudescence of draining fistulas, by the occurrence of any other perianal complication or the need for additional therapy
Results: Fifteen patients were treated, 9 of which were women (60%). The median age was 34 years-old (19-71). Seven were smokers (46,7%) and 4 were previous smokers (26,7%). Montreal classification was as follow: L1 in 5, L2 in 5 and L3 in 5. Two patients showed extra-intestinal manifestations (erythema nodosum). Six patients were previously treated with infliximab (40%: 4 intolerants and 2 loss response); 8 were taking azathioprine concomitantly (53%) and one methotrexate. Indications for treatment were perianal ulcer in 2 and penetrating disease in 13 (6 after abscess drainage; 7 perianal fistulas - 2 anovaginal fistulas and one anoscrotal). At baseline 2 patients had PDAI ≤ 5, 7 between 6-8 and 6 between 9-11. At Week 2, response was achieved in 80% (remission in 46, 7%). At week 14, 86,7% responded (80% were in remission). Four patients did not respond or lost their response: two recovered (PDAI ≤ 2) with adalimumab administrated weekly, one was proposed to infliximab and one developed an abscess. Three did not have a complete follow-up: one failed to attend the appointments, one suspended ADA due to intolerance and other was a non-responder. At week 52, 12 patients completed follow-up: 7 with PDAI 0, PDAI between 1-3 in 4 and one with PDAI 6.
Conclusions: Conclusion: ADA was effective in PACD, inducing fast response and healing, remission in 80% at week 14 and maintenance of remission in 73% patients at week 52.

P361
Effects of azathioprine on outcome of pregnancy in Inflammatory Bowel Disease patients: A prospective study

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Background: It is generally believed that Azathioprine (AZT) is harmless in pregnancy(P)of inflammatory Bowel
Disease patients(IBD) both for the pregnant women and fetus .Nevertheless studies are rare,frequently retrospective and concern generally small cohorts .
Methods: To assess in a prospective study influence of AZT on fetal prognosis and natural history of the
disease in IBD pregnant patients ,we have enrolled 261 consecutive IBD patients in a prospective long term follow-up study from 1/1/2005 to 31/12/2009 of whom 244 (Group I;GI) were pregnant during the study or have had pregnancies;37 had no P (Group II;GII). 37 patients (19 Ulcerative colitis :UC and 18 Crohn's disease :CD) received AZT (2,5 mg/kg/day),(GI:n=30;GII:n=7) during 29 to 36 months.Evaluation was based on characteristics of the last P with AZT and its outcome. Statistical analysis : Student Fisher's t test and Mann Withney's U test.
Results: Comparison of IBD GI patients who received AZT (IBD/GI/AZT+) and GI patients who did not received AZT
(IBD/GI/AZT-) did not show any significant statistical difference (SSD) as regards to demographic and anatomoclinical characteristics ,gestational statute and outcome of disease.The same Results were found when comparing UC/GI/AZT+ patients and UC/GI/AZT- patients. In return,CD/GI/AZT+ patients differ from CD/GI/AZT- patients by a greater number of anoperineal(27,7% vs 17,5%;p<0,4818) and proximal (11,1% Vs 0%;p=0,0109) locations.Caesareans (13,3% Vs 8,7%;p<0,629),stillbirths (3,3% Vs 1,5%;p=0,9613) and congenital abnormalities (3,3% Vs 0,5%;p=0,6318) were more frequent in IBD /GI /AZT+ than in IBD/GI/AZT- but didn't reach SSD whereas abortions (6,6% Vs 5,2%),premature births (6,6% Vs 5,2%) ,low weight birth (10% Vs 8,2%) where found at the same rates UC/GI/AZT+ patients didn't differ from UC/GI/AZT-patients as regards to gestational complications.Caesareans(21,4% Vs 10,2%;p=0,4366),low weight births
(14,2% Vs 8,2%;p=0,814) and congenital abnormalities (7,1% Vs 0%;p=0,26) were more frequent in CD/GI/AZT+ than in CD/GI/AZT- patients .Long term outcome of the disease ,was evaluated according to 4 heading: unchanged, improved,worsened, need for surgery.We found no SSD between IBD/GI/AZT+ and IBD/GI/AZT- patients and between IBD/GI/AZT+ and IBD/ GII/AZT+ patients.
Conclusions: Use of AZT in IBD pregnant women is associated with a slight increase in fetal risk mainly in CD.This
pejorative effect cannot be entirely imputable to AZT as this drug is prescribed in severe IBD;in this instance, fetal outcome may be due at least in part to the disease activity.

P362
Agalactosyl IgG predicts therapeutic effect of anti-TNF agents in patients with Crohn's Disease

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Background: Recent studies reported that clinical response to anti-TNF agents is associated with trough drug level and C-reactive protein (CRP) levels after treatment, however, biomarkers to predict therapeutic effect of anti-TNF agents before treatment are scarce. We previously reported that serum agalactosyl IgG level is an effective biomarker of disease activity in Crohn's disease (CD) (Shinzaki S, et al. Am J Gastroenterol 2008). In the present study, we investigated if agalactosyl IgG can predict long-term effect of anti-TNF agents.
Methods: Forty-six CD patients who met following criteria were enrolled; (1) scheduled maintenance treatment with anti-TNF agents (infliximab or adalimumab) was received, and (2) sera were collected within 1 month prior to administering initial treatment, and (3) followed-up more than 1 year after the initial treatment. Treatment change within 54 weeks was defined as follows; (1) increase in agents, or (2) shortening of treatment interval, or (3) switch to another anti-TNF agent, or (4) receiving surgery. Sustained clinical remission was defined as follows; (1) Crohn's disease activity index (CDAI) of < 150 at week 14, 38 and 54, and (2) no treatment change within 54weeks, and (3) CRP level of < 0.5 mg/dL at week 54. Serum IgG oligosaccharide structures were analyzed by high performance liquid chromatography and the ratio of agalactosyl peak and fully galactosyl peak in the fucosyl oligosaccharides (G0F/G2F) was calculated. G0F/G2F ratio of 1.4 was used as cut-off value to discriminate the G0F/G2F high and low group as previously reported. Endoscopic activity was assessed using modified Rutgeerts score.
Results: Before starting anti-TNF agents, 32 patients were in high G0F/G2F levels. Patients with high G0F/G2F tended to show higher CDAI

and endoscopic activity than those with low G0F/G2F before treatment (215.3 vs 156.3; p = 0.07, and 2.4 vs 2.1; p = 0.08, respectively). Patients with high G0F/G2F showed significantly higher CDAI and CRP levels at week 14 than those with low G0F/G2F (126.7 vs 83.1; p = 0.015, and 1.03 mg/dL vs 0.44 mg/dL; p = 0.029, respectively). CRP levels and endoscopic scores at week 54 were significantly higher in high G0F/G2F group than in low G0F/G2F group (1.60 mg/dL vs 0.57 mg/dL; p = 0.028, and 2.5 vs 1.1; p = 0.035). Treatment change rate was comparable in two groups (21.4% vs 25.0%; p = 0.65). Sustained clinical remission rate in high G0F/G2F group was significantly lower than that in low G0F/G2F group (18.8 % vs 50.0 %; p = 0.030).

Conclusions: Patients with high G0F/G2F showed higher disease activity and poor response to anti-TNF agents, suggesting that agalactosyl IgG (G0F/G2F) is a potential predictive biomarker of poor long-term response by anti-TNF agents.

P363
How did changes in medical protocols affect the length of resected ileum in Crohn's disease over the last decade?

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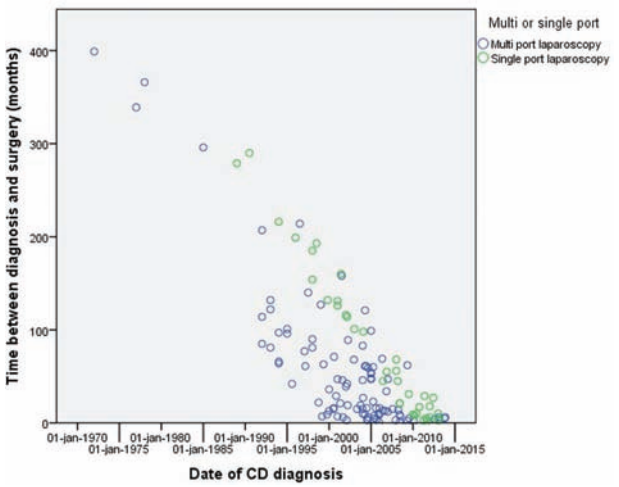
Background: During the last decade, treatment protocols have changed for patients with ileocolonic Crohn's disease (CD). Anti-TNF antibodies have become part of standard medical treatment and the step up approach has been formalized in clinical guidelines by the European Crohn's and Colitis Organisation (ECCO). We aimed to analyze if improved medical treatment has resulted in less extensive surgery and a longer delay between diagnosis and surgery.

Methods: In a retrospective cohort study, patients undergoing ileocolonic resection for CD at the AMC between January 1999 and October 2014 were identified from a prospectively maintained database. The length of the resection specimen was measured immediately postoperatively at the department of pathology according to a standard protocol.

Results: Of the 172 ileocolonic resections, 115 were performed laparoscopically (27 via single port). 55 patients were male (32.0%) and the median age at time of surgery was 28.0 years (IQR 23.0-39.8). Over the years, a significant reduction in time from diagnosis to operation was found (median of 27.0 months in 2004 versus 6.0 months in 2013; Spearman correlation coefficient -0.654, p <0.001)

No significant decrease in the length of the resected ileum was found during this time (median 20.0 cm iqr 12.0–30.0).0, Spearman correlation coefficient -0.137, p=0.145).

Conclusions: This study demonstrated a reduction in the time from diagnosis to operation in patients with ileocolonic CD. However, it could not be demonstrated that changes in medical protocols resulted in a decreased length of resected ileum.



"Time between diagnosis of CD and ileocolic resection (in months) with respect to date of diagnosis."

P364
Immunization status in IBD patients -a single centre study in Southern Italy

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Background: With the use of more potent immunosuppressive agents, the most recent ECCO guidelines have raised the need for a more accurate screening in IBD patients, not only to investigate former infectious disease but also to guide the choice for the therapeutic agent to use. The aim of the present study was to investigate the prevalence of hepatitis B and C, latent tuberculosis, and the immunization status for mononucleosis, varicella, and cytomegalovirus in a cohort of IBD outpatients.

Methods: We retrospectively revised the patient's charts from the past 5 years in our outpatient clinic; data on hepatitis B (HBsAg, anti-HBs, anti-HBc) and C (anti-HCV), tuberculosis (TBC; Mantoux skin test or Quantiferon Gold, and plain chest film), mononucleosis (anti-VCA IgG), varicella (anti-VZV IgG), and cytomegalovirus (anti-CMV IgG) were registered together with the following data: gender, disease, duration of disease, IBD therapy prior to testing. Moreover we evaluated potential risk factors for the presence of positive findings like age, disease, duration of

"Table 1 percentages of positive testing for former infections"

	Latent TBC (n = 171)	anti-HBs (n = 227)	HBsAg (n = 228)	anti-HBc (n = 207)	anti-HCV (n = 225)	anti-VZV (n = 83)	anti-VCA (n = 120)	anti-CMV (n = 113)
age ≤ 35 yrs % +ve	0%	2.0%	2.1%	2.3%	0%	81.1%	83.6%	38.8%
age > 35 yrs % +ve	7.5%	4.0%	1.5%	5.9%	3.9%	91.3%	93.9%	68.8%
p-value	**0.014**	0.98	0.761	0.21	**0.049**	0.172	0.073	**0.001**

disease, previous therapies in order to identify associated risk factors; vaccinated patients against hepatitis B were excluded from analysis.

Results: The charts from 968 IBD patients were reviewed. Data from 270 patients screened for biologic and/or thiopurine therapy were analysed (ulcerative colitis [UC] 119, Crohn's disease [CD] 151; mean age 41 years ± 15, males 152); median disease duration was 48 months (range: 0-360); data on screening positivity are given in table 1 by dividing patients in 2 age groups, less than or equal to 35 years and older than 35 years.

There was no difference between UC and CD patients; a significant positive correlation was found between age and anti-HCV positivity ($p<0.005$), anti-HBc ($p<0.03$), latent TBC ($p<0.004$), and anti-CMV positivity ($p<0.003$).

Conclusions: An age over 35 years significantly increases the probability to test positive for TBC, hepatitis C, and anti CMV; although not significant, an important percentage of younger patients was negative for Ebstein-Barr virus (16%) and for varicella (19%). The latter data may be important for vaccination issues.

P365
Direct rescue treatment is justified in moderate flares of Ulcerative Colitis worsening with oral corticosteroid therapy

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Background: : Intravenous corticosteroids (CS) are the treatment of choice for severe attack of ulcerative colitis (UC). Response to CS therapy can be assessed by simple clinical and biological parameters as soon as 3-5 day of initial treatment. The availability of predictive factors of response to steroid treatment allows the early introduction of rescue treatments. This fact can explain, at less in part, the fall in the colectomy incidence rate in this setting. Aims: To identify clinical and/or biological parameters at the moment to star CS therapy for a severe attack of UC associated with rescue treatment needed.

Methods: All UC patients admitted to three University hospitals between January 2005 and December 2011 were identified from electronic databases. Disease severity was defined according to the Montreal classification, and only patients with severe UC treated with intravenous CS were included. Demographic and epidemiological data were recorded, as well as clinical and biological parameters used to define severe attack (number of bowel movements, protein C reactive, hemoglobin, fever, tachycardia or hypotension).

Results: A total of 62 flares were included, 70% extensive disease, 82% not current smoking. 43% of flares required rescue treatment during hospital admission. 10 of the 14 flares (71%) who have been previously treated with oral CS for the index flare before starting intravenous CS required rescue treatment during hospital admission and 3 who didn't need rescue treatment become dependent to CS in the follow-up. In univariate analysis, not responding to oral CS in the index flare, not tobacco exposure, the absence of systemic symptoms or to have less of two severe criteria were associated to need of rescue treatment. In multivariate analysis only not response to oral CS for the index flare was an independent predictor of rescue treatment needed (HR XX, IC 95% xx-xx; P=0,018).

Conclusions: In sever attacks of UC, the only predictor factor associated to rescue treatment needed was the failure of oral CS for the index flare. This data suggest that patients with clinical worsening during oral CS therapy for a moderate flare of UC are candidate to direct rescue treatment with cyclosporine or infliximab without attempting the intravenous route of CS.

P366
Withdrawing or continuing maintenance treatment with thiopurines in patients with Crohn's Disease in sustained clinical remission: a lifetime risk-benefit analysis

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	35 year-old woman without extensive colitis	W	65 year-old woman without extensive colitis	W	35 year-old man with extensive colitis	W	65 year-old man with extensive colitis	W
	C		C		C		C	
Life expectancy, age at death (years)	79.86	79.84	82.98	83.03	73.96	73.87	79.38	79.28
Events for 1,000 patients-years								
Severe relapse	0.169	0.349	0.143	0.270	0.205	0.428	0.146	0.258
Lymphoma	0.347	0.302	0.579	0.337	0.564	0.484	0.905	0.509
Colorectal cancer	1.02	1.03	0.763	0.768	1.57	1.75	2.46	3.71
Relative risk compared to general population								
Lymphoma	1.31	1.14	3.18	1.85	1.34	1.15	3.13	1.76
Colorectal cancer	0.99	1.00	0.99	0.99	1.06	1.19	2.20	3.31

Paris, France, [4]THEN, Translational Health Economics Network, Paris, France

Background: Long-term treatment of Crohn's disease (CD) with thiopurines modifies the risk of various cancers, depending on gender and age for lymphomas, and presence of extensive colitis (EC) for colorectal cancer. We evaluated risks and benefits of withdrawing or continuing thiopurines in patients with CD in sustained clinical remission.

Methods: We developed a Markov model assessing risks and benefits of withdrawing or continuing thiopurines in a lifetime horizon. We simulated a cohort of CD patients in stable clinical remission for 5 years under thiopurines. The model was stratified by age, gender and presence of EC. Parameter estimates were taken from French hospital Diagnosis Related Groups (DRGs) databases, the French cancer and death national registries (FRANCIM), the CESAME cohort, the Saint-Antoine hospital database (MICISTA)), and from the literature. The primary outcome was life expectancy. Secondary outcomes included the probability of CD relapse, cancers, and causes-of-deaths. We conducted threshold analyses on age to assess potential age-related changes in best life expectancy according to the two strategies.

Results: The continuing strategy was globally associated with decreased lifetime risk of flares and increased risk of lymphoma. However, life-expectancy and risks associated with the two strategies differed markedly according to age at decision, gender and presence or absence of EC, as illustrated in Table 1. In terms of life expectancy, in patients without EC, withdrawal strategy was associated with increased life expextancy after the age of 41.7 years for men, and 47.0 years for women. In patients with EC, continuing thiopurines was associated with increased life expectancy, regardless of age.

Conclusions: Factors determining life expectancy associated with withdrawal or continuation of thiopurines in patients with CD and 5-year sustained clinical remission vary substantially according to gender, age and presence of EC. Individual decisions to continue or withdraw thiopurines in patients with CD in sustained remission should take into account age, gender, and presence of EC.

P367
Dietary fiber intake in children with Inflammatory Bowel Disease

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Background: High-fiber diet may play a potential anti-inflammatory role in inflammatory bowel disease (IBD), since it has been shown to maintain remission and reduce colonic damage. The aim of the study was to assess the quantity of dietary fiber intake in children with IBD.

Methods: The study group consisted of children who were in clinical remission or with mild ulcerative colitis (UC) or Crohn's disease (CD), assessed according to PUCAI (Pediatric Ulcerative Colitis Activity Index) or PCDAI (Pediatric Crohn Disease Activity Index), respectively. For the nutritional assessment, a 3-day dietary record method was used. Mean values of dietary fiber and its fractions were calculated based on literature data. Results were compared with adequate intake (AI) for age.

Results: 50 patients were evaluated: 27 with CD and 23 with UC. There were no statistically significant differences in age, weight and height between the CD and UC patients. The average intake of dietary fiber was 15.9 g per person/day, 8.7 g per 1000 kcal and 0.37g per kg of body weight. Insoluble fiber accounted for 66% (10.5 g/day) and soluble fiber 34% (5.4 g/day). There were statistically significant correlations between fiber intake and age (r=0.32) and between fiber and energy intake (r=0.51). CD patients had higher fiber intake values than UC patients but the differences were not statistically significant. 78% of patients didn't meet the AI recommendations.

Conclusions: Majority of IBD children with no or mild disease activity had low dietary fiber intake. The Results of the study indicate the need for the routine dietary assessment in these patients.

P368
Ustekinumab in super-refractory Crohn´s disease patients

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Background: Blockage of tumor necrosis factor(TNF) has been a major advancement in the therapy for Crohn's disease(CD). However up to 40% of patients do not achieve a response to induction with anti-TNF(primary non-responders) and of those who achieve a primary response, approximately 40% subsequently lose response. Medical therapy for active CD patient's who have lost response to currently approved medications is an unmet clinical need. Ustekinumab, a monoclonal antibody against the p40 subunit of interleukin-12/23 has demonstrated to be effective in inducing and maintaining remission in CD patients (Sandborn, NEJM2012). In Spain, its application is limited to compassionate use in refractory CD patients.

Methods: Patients with refractory CD previously treated at our institution with at least two anti-TNF agents and treated with Ustekinumab were enrolled. Data regarding activity of the disease prior and post induction therapy were analyzed. Induction dose was 3mg/kg subcutaneously followed by maintenance schedule of 90mg every 8 weeks (4 patients had an extra dose of 90 mg at week 4). Response to therapy was assessed at 8 weeks and at the end

Table 1 "MRI parameters collected for the study"

Total MaRIA total, mean±sd	45.5±18.3
Clermont score, mean±sd	23.6±9.4
Mean ADC, mean±sd	1.97±0.25
Minimal ADC, mean±sd	1.29±0.27
Active disease according to MaRIA, n(%)	
Non active	3 (7.7)
Active (≥ 7)	2 (5.1)
Severe (≥ 11)	34 (87.2)
Ileal activity according to Clermont score, n(%)	
Non active	6 (15.0)
Active (≥ 8.4)	1 (12.5)
Severe (≥ 12.5)	33 (82.5)
Colonic activity according to ADC, n(%)	
Non active	23 (57.5)
Active (any colonic segment ≤1.9mm²/s)	17 (42.5)
Ileal stenosis, n(%)	9 (22.5)
Pre-stenosis dilation, n(%)	8 (20.0)
Fistula, n(%)	9 (22.5)
Intra-abdominal abscess, n(%)	2 (5.0)
Sclerolipomatosis, n(%)	12 (30.0)
Enlarged mesenteric lymph nodes, n(%)	23 (57.5)

n : number; sd : standard deviation; MRI : magnetic resonance imaging ; ADC: apparent diffusion coefficient; MaRIA: Magnetic Resonance imaging Index of Activity

of follow-up and defined as a reduction >70 points from baseline CDAI, and clinical remission as CDAI<150 points.

Results: Eight patients received Ustekinumab for refractory CD. Six were female, half of them were non-smokers and median age was 39. Sixty-two percent of patients had ileocolonic involvement and behavior of CD was inflammatory in four, penetrating in three and stricturing in one patient (two patients had perianal involvement). All patients had previously received Infliximab and Adalimumab, and one patient had also received Certolizumab. All had failed Azathioprine and Methotrexate, and one patient also received Tacrolimus and two of them photoapheresis. Six patients had a primary non-response to the second or third antiTNF and two patients who had received IFX and ADA developed paradoxical psoriasis. Patients had a median CDAI score of 301[224-404] before treatment, 167[35-262] at week 8 after induction and 90[0-133] at the end of follow-up. Seven out of the eight patients had a clinical response to induction, and 3 of them(37,5%) were in clinical remission at week 8. Median follow-up on maintenance was 42 weeks and 6 patients are still receiving treatment and in clinical remission(75%). No serious adverse events were reported, the most common side affect was arthralgia referred by two patients.

Conclusions: Although our study included few patients, clinical Results suggest that Ustekinumab is an effective drug in maintaining remission in medium-term in CD patients super-refractory to immunomodulators and anti-TNF's. Efficacy of high induction doses must be confirmed in larger studies.

P369
Diffusion-Weighted magnetic resonance enterocolonography before treatment predicts remission after anti-TNF therapy in Crohn's disease

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Background: Almost one third of the Crohn's disease (CD) patients experienced primary failure to anti-TNF therapy. Owing to the cost and the potential side effects, determining predictors of anti-TNF efficacy remains a key point in clinical practice. Diffusion-weighted magnetic resonance entero-colonography (DW-MREC) without rectal distension and without bowel cleansing has shown good accuracy to detect and assess inflammatory activity in CD [1] [2].

We aimed to study DW-MREC parameters as predictors of clinical response (delta CDAI > or = 100), remission (defined as CDAI<150 AND CRP<5 mg/L) and surgery at week 12 after anti-TNF therapy.

Methods: Overall, 40 consecutive CD patients were prospectively and consecutively included. All the patients underwent a DW-MREC [1] [2] within 4 weeks before starting anti-TNF. Adalimumab was administered as 160mg at W0, 80mg at W2 and 40mg every other week. Infliximab was administered as 5mg/kg at W0, W2 and W6. The collected MRI parameters were reported in Table 1.

Results: MRI data and population characteristics are given in Table 1 and 2, respectively.

Overall, 25 patients (67.5%) achieved clinical response at week 12. High Clermont score value [1] [2] (27.2+/-8.4 vs 21.4+/-9.4, p=0.05) and active active segments defined as ADC<1.9[2] (47.8% vs 82.4%, p=0.03) were predictive of clinical response at week 12.

Overall, 20 patients (50.0%) experienced remission at week 12. Low mean ADC value (2.05+/-0.22 vs 1.89+/-0.25, p=0.03) and high total MaRIA (39.2+/-16.6 vs 51.7+/-18.2, p=0.03) were predictive of deep remission at week 12. Using a ROC curve, we determined a mean ADC of 1.96 as predictive cut-off of remission at week 12 (AUC=0.703 [0.535–0.872]) with sensitivity, specificity, positive predictive value and negative predictive value of 70.0%, 65.0%, 66.7% and 68.4% respectively.

No MRI factors were predictive of surgery at week 12.

Table 2 "Population characteristics (n=40)"

Disease duration, median [IQR]	34 [4 – 193]
Early Crohn, n (%)	10 (25.0)
Age at inclusion, mean±sd	36.8±15.0
IBD family history, n (%)	5 (12.5)
Active smoker, n (%)	17 (42.5)
Previous intestinal resection, n (%)	9 (22.5)
Anoperineal lesions, n(%)	14 (35.0)
Age at diagnosis, mean±sd	27.8±13.4
Montreal classification	
Age, n(%)	
A1	9 (22.5)
A2	26 (65.0)
A3	5 (12.5)
Location, n(%)	
L1	18 (45.0)
L2	5 (12.5)
L3	17 (42.5)
L4	5 (12.5)
Behaviour, n(%)	
B1	12 (30.0)
B2	17 (42.5)
B3	11 (27.5)
Anti-TNF, n(%)	
Infliximab	18 (45.0)
Adalimumab	22 (55.0)
Anti-TNF naive, n(%)	30 (75.0)
Concomittant therapies	
5-ASA, n(%)	2 (5.0)
Budesonide, n (%)	5 (12.5)
Corticosteroids, n (%)	4 (10.0)
Thiopurines, n (%)	16 (40.0)
Methotrexate, n (%)	3 (7.5)
CDAI at inclusion, median [IQR]	225 [170-393]
CRP at inclusion (g/L), median [IQR]	20.0 [1.0-293]

N : number ; IQR : interquartile range ; sd : standard deviation.

Conclusions: ADC value and Clermont score retrieved from DW-MREC, reflecting the inflammatory activity, predict response and remission after anti-TNF therapy in CD. DW-MREC is useful in detecting and assessing inflammatory activity in CD but also in predicting efficacy of anti-TNF induction therapy.

References:

[1] Buisson A et al., (2013), Diffusion-weighted magnetic resonance imaging for detecting and assessing ileal inflammation in Crohn's disease, Aliment Pharmacol Ther

[2] Hordonneau C et al., (2014), Diffusion-Weighted Magnetic Resonance Imaging in Ileocolonic Crohn ' s Disease: Validation of Quantitative Index of Activity, Am J Gastroenterol

P370
IBD-Control Questionnaire: validation and evaluation in clinical practice

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Background: The use of patient-reported outcome measures in clinical practice is increasingly advocated as a mean of supporting patient-centered care, informing decisions and driving service quality. IBD-Control Questionnaire has been recently developed and it is intended to measure overall disease control from the patient's perspective in the last 2 weeks1. We aimed to validate IBD-Control questionnaire in our clinical practice, namely its subscores IBD-Control-8 and IBD-Control-VAS.

1 - Bodger K et al. Gut 2013;0:1-11

Methods: A single-center, blinded, prospective study evaluating consecutive patients in an outpatient basis during September to November 2014. IBD-Control questionnaire was completed by each patient prior to medical evaluation. Then, two trained physicians blinded to the questionnaires, recorded activity indices (Harvey-Bradshaw index - HBI, Simple Clinical Colitis Activity index - SCCAI, Montreal Classification), Global Physician assessment and protein C-reactive (PCR) value. Inactive disease was defined by disease activity indices within reported remission ranges (HBI< 5, Montreal classification S0). For IBD-Control-8, a cut-off of >=13 points and for IBD-Control-VAS a cut-off of >=85 points were used to identified patients with quiescent IBD.

Statistical tests: spearman test,X2.

Results: 77 consecutive IBD-patients were evaluated, from which 53 with Crohn's disease and 24 with Ulcerative Colitis. Mean age: 43.3 years (±14.4); Female gender: 53.2%. Mean scores: IBD-Control-8 (range 0-16) 13.2 (±3.7), and IBD-Control-VAS (range 0-100): 81.2 (±17.8).

Strong correlation between IBD-Control-8 and IBD-Control-VAS (r=0.71, p<0,001). Moderate-to-strong correlations between IBD-Control-8 and: HB index (r= -0.58), SCCAI (r= -0.60), Montreal classification (r= -0,66) and Global Physician assessment (r= -0.70). IBD-Control-VAS achieved similar Results (HBI: r=-0.57; SCCAI: r=-0.42; Montreal classification: r=-0.50; Global physician assessment: r= 0.65; p< 0.001 for all Results). Weak correlation between IBD-Control-8 and IBD-Control-VAS with PCR value (r= -0.16 and r= -0,23, respectively).

IBD-Control-8, with a cut-off of >=13 points and IBD-Control-VAS with a cut-off of >=85 points were both significatively associated with inactive IBD (p<0.001, for each score).

Conclusions: IBD-Control-questionnaire revealed a moderate-to-strong correlation with Harvey-Bradshaw index, Simple Clinical Colitis Activity index, Montreal classification and Global Physician assessment, and a poor correlation with PCR value. IBD-Control questionnaire may be valuable in clinical practice, mainly for an accurate non-onsite evaluation of IBD-patients.

P371
Are biologics a safe option for elderly patients with inflammatory bowel disease?

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Background: A significant proportion of patients with inflammatory bowel disease (IBD) are elderly. In general, the management of elderly patients is similar to that of young patients, although there is a paucity of data on the use of biologics in this age group. The main concerns relate to toxicities such as infections which may be higher in this age group (Cottone M, et al. Clin Gastro Hepatol 2011;9:30-5, Lichtenstein G, et al. Clin Gastro Hepatol 2006;4:621-30).We therefore aimed to review our IBD database to examine the outcomes for patients over the age of 60 years who have received anti-TNF agents.

Methods: Barnet and Chase Farm Hospitals are sister district hospitals in Hertfordshire serving a population of 500,000. Data were extracted from the hospital electronic patient record for all patients with Crohn's disease (CD) or ulcerative colitis (UC) who had received anti-TNF drugs (Infliximab [IFX] or Adalimumab [ADA]) over the age of 60. Demographic data, disease distribution, previous treatments, and outcomes were obtained.

Results: Our database had 155 patients in all age groups currently on or previously on anti-TNF drugs. Twenty patients (13% of total) were identified for this study (mean age, 70 years; range 22-84; CD=16; UC= 4). Median age at IBD diagnosis was 60 yrs (CD; range 22-84) and 57 yrs (UC; range 52 -60). Median age starting biologics was 64 yrs (CD; range 59-85) and 62 yrs (UC; range 58-77). CD patients received IFX (n=9) and ADA (n=7), compared with UC patients (IFX=3, ADA=1). Drugs previously trialled included 5-ASA drugs (CD-75%; UC-50%), thiopurines (CD-56%; UC-100%), corticosteroids (CD-100%; UC-100%), tacrolimus (n=1) and some patients had switched biologics (CD-43% of ADA users; UC-1 ADA user). Patients were on biologics for a median 1.75 yrs (CD) and 1.88 yrs (UC). Steroid-free clinical remission was achieved in 50% of patients (CD and UC). Primary non-response was seen in 2 patients (CD-1, UC-1). Minor adverse events (all CD patients) included flu-like illness and weight gain (n=1), eczematous rash (n=1) and drug-induced lupus (n=1, drug discontinued).

Conclusions: We have administered anti-TNF agents to 20 patients over the age of 60 including 7 patients over the age of 70 yrs. The clinical remission rates were comparable with our younger cohort of patients with a 50% steroid-free remission rate. Only one patient had to discontinue the drug due to a lupus-like syndrome, and no patient experienced any infection related toxicities. All the patients satisfied published guidelines for starting biologics and although

caution is necessary in terms of excluding high risk patients, we feel that age alone should not be a contra-indication to starting this class of drugs.

P372
Efficacy and safety of endoscopic balloon dilatation in the Inflammatory Bowel Disease: Results of the ENEIDA database.

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Background: Background: Endoscopic balloon dilation (EBD) is the endoscopic treatment of choice for short stenosis in Crohn's diseases (CD). Several uncontrolled observational studies have shown that EBD in selected patients is a safe and an effective alternative to surgery. Previously published series have limitations due to the heterogeneity of technique and different endpoints which makes comparisons difficult, and generally with small series of patients.

Aim: To evaluate the efficacy and safety of EBD in clinical practice environment in Spanish hospitals adhered to the ENEIDA project.

Methods: Methods: We identified all the patients undergoing EBD from the ENEIDA database. Additional information not included in the database was requested to the participating centres (14 hospitals): patient's clinical information; stenosis data; and information about the effectiveness and complications of the EBD. Technical success was defined when the endoscope got pass through the stricture after the procedure and therapeutic success when it was not necessary another endoscopic or surgical treatment after 1 year or until the end of the follow-up. A logistic regression analysis was performed to assess the factors associated with therapeutic success.

Results: Results: A total of 306 dilations were performed in 154 patients (140 CD, 12 ulcerative colitis and 2 indeterminate colitis) with a mean of 1.98 dilation per patient. In 41% of the cases the strictures were in the anastomotic site. The therapeutic and technical success was achieved in 47.4% and 65.2% of the EBD respectively with a median follow-up of 24 months (1-88). In multivariate analysis, the length of stenosis (≤ 4 cm) with an OR of 3.38 (95% CI:1.38-8.26;p=0.008) and the technical success with an OR of 2.57 (95% CI:1.23-5.40;p=0.012) were associated with therapeutic success; whereas the balloon diameter (≤ 12 mm) with an OR of 0.4 (95% CI:0.16-0.93;p=0.034) and the need of anti-TNF therapy with an OR of 0.26 (95% CI:0.13-0.50;p<0.005) were inversely associated with therapeutic success. The rate of major complications was 5.4%.

Conclusions: Conclusions: In a clinical practice environment, the EBD has a similar efficacy and safety than has been reported in tertiary care centres. The length of the stenosis (≤ 4 cm), the technical success, the balloon diameter (>12 mm) and not needing anti-TNF for disease control were the only factors associated with the therapeutic success. Randomized prospective studies are required to set what other factors are related to the response to EBD.

P373
Meta-analysis: Does folate supplementation reduce colorectal cancer risk in patients with inflammatory bowel disease?

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Background: Colorectal cancer is a serious complication of inflammatory bowel disease (IBD). Folate has been shown to be a potentially chemopreventative agent in sporadic colorectal cancer (CRC). Patients with IBD are at risk of folate deficiency though intestinal malabsorption and also competitive inhibition by concurrent sulfasalazine use. To date there have been several studies reporting folate supplementation in patients with IBD and CRC but no consistent effect has been shown.

Methods: We followed a pre-specified and peer-reviewed protocol; the PRISMA statement, a 27 item checklist deemed essential for reporting systematic reviews and meta-analyses of randomized controlled trials and observational studies. We searched electronic databases for studies reporting folate use and CRC incidence in patients with IBD. There were no date or language restrictions. We produced a pooled effect size (ES) with 95% confidence intervals (CI) using a fixed effects model. Heterogeneity amongst studies was calculated using Cochran's Q statistic and I2. We tested for the effect of different study variables on the overall result using meta-regression and subgroup analyses.

Results: Ten studies, published since 1987, were included in the meta-analysis and reported on a total of 622 cases of IBD associated CRC. We found an overall protective effect of folate supplementation on the development of CRC, pooled ES 0.57 (95% CI, 0.36 - 0.78). Only 3 studies reported matched or adjusted Results. There was low to moderate heterogeneity amongst studies, Cochranes Q= 12.87(p=0.169), I2 30%. Sensitivity analysis suggested that folate use was protective in studies that included dysplasia as an outcome, hospital based studies, high quality studies, studies from North America and those that had matched or adjusted Results.

Conclusions: Chemoprevention remains an attractive option for patients with IBD to prevent dysplasia, reduce the burden of surveillance colonoscopy and also reduce the need for proctocolectomy in patients with ulcerative colitis. The ideal chemopreventative agent would be safe, well tolerated, inexpensive and have a role in suppressing inflammation and malignant transformation 55. Any further reduction to the risk of CRC in IBD is to be welcomed and folate supplementation, as a safe intervention, may be attractive options if further focused population based studies on this topic confirm the findings of this meta-analysis.

P374
The clinical usefulness of the web based message system between patients with Crohn's disease and their physicians

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Background: Crohn' s disease(CD) is a chronic relapsing disorder of unknown etiology and many CD patients encounter unpredictable events not catched at one single outpatients visit. For not to miss these events associated with clinical activity, we previously developed a novel, web-based, self-reporting CD symptom diary (CDSD) using website. There was also a message system below the score box for helping the many unpredictable events or questions of the patients. The aims of the present study was to assess the clinical usefulness of the system by analyzing the message lists during no visiting period.

Methods: We opened the communication system using message between patients and their doctors at the same web page already made for symptom diary (www.cdsd.or.kr). Patients can send a message easily whenever they need and the doctor can read it and send the answers immediately using their phone or computer. For the real time comunication, we used an alarm when the message was sent. We retrospectively reviewed all the 686 message lists from 152 patients and the medical records of the patients from July 2012 to July 2014. The patients baseline characteristics and clinical feature of the disease were also assessed. The messages were classified into several categories and each catetories were subdivided again into several categories.

Results: The mean age of the 152 CD patients was 29.7 ± 10.7 years and male to female ratio was 99:53. Mean message number per patients was 4.5. The most common problem list was about symptom (381 cases, 55.5%) and questions about their treatment were in 71 cases(10.3%). In cases of symptoms, abdominal pain was most common problem in 145 cases(21.1%) and hematochazia in 36 cases (5.2%). Symptoms other than abdomen were also noted in 73 cases(11.1%). Problems about medication were the most frequent messages associated with treatment in 65 cases (91.5%). Patients under 40 years sent more variable messages, however, patients above 40years, showed the tendency to focus on symptoms and treatment (p=0.025).However, it was not significantly different according to the disease extent and behavior. The answer rate by their doctors was 56.3% and early visiting by their physician's answer was needed in 28 cases(7.3%).

Conclusions: Patients could get the advice or answers by their physicians in charge directly about their unpredictable problem without visiting clinics or internet searching . In addition, cases needed early visit could be also achieved in 7.3% using the system. Although we need a long term follow up, our Results showed that the message sending system on the websites (www.cdsd.or.kr) could be a useful communication tool for the patients and physicians during non-visinting period.

P375
Efficacy of Exclusive Enteral Nutrition (EEN) in Active Crohn's Disease with Complications or Failure of Medical Treatment

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Background: Complicated active Crohn's disease (CD) patients may not need emergent surgery or not be suitable for surgery due to malnutrition. They may also not be appropriate for corticosteroids or biologics due to stricture, intestinal fistula and/or abdominal abscess. Some patients had poor response to medical therapy. We aim to investigate the efficacy of EEN in induction of remission in active CD patients with complications or poor response to drugs.

Methods: Active CD patients who had been diagnosed as complicated disease with stricture, intestinal fistula, abdominal abscess and/or no response to drugs, were recruited since July 2013 to November 2014. Patients were offered EEN. Nutritional markers and high sensitivity C-reactive protein (hs-CRP) were evaluated at baseline, week 4, and week 8, respectively. Disease activity was assessed by the Harvey-Bradshaw index.

Results: 20 patients (7 female and 13 male, mean ages 26.1 ± 12.97) were involved. 5 patients were no response to drugs; 13 patients accompanied with complications and 2 patients exhibited both of these two characteristics. 3 patients were further excluded because of intolerance to EEN. Of the remaining 17 patients, 2 patients had no improvement and 1 of them stopped EEN 4 weeks later; the other 15 achieved clinical remission in 4 weeks (CDAI before EEN 6.2 ± 2.0 vs. EEN by 4weeks 2.9 ± 1.2, P=0.001). After 8 weeks, 14 were kept in remission (CDAI before EEN 6.2 ± 2.0 vs. EEN by 8 weeks 2.5 ± 1.2, P=0.000) while 2 patients were transferred to surgery due to progressive bowel obstruction. After EEN, BMI of these patients increased significantly (before EEN16.3 ± 1.89 vs. EEN by 8 weeks 17.8 ± 1.85, P=0.031). By 4 weeks, hs-CRP was significantly decreased compared to baseline (12.1 ± 4.45 vs. 6.1 ± 4.64, P=0.001). 6 patients who complicated with intestinal fistula or abdominal abscess performed colonoscopy and Magnetic Resonance Elastography (MRE) after EEN treatment for 8 weeks. The Simple Endoscopic Score for Crohn's Disease (SES-CD) was decreased significantly (before EEN7 ± 1.67 vs. EEN by 8 weeks 2.8 ± 1.60, P=0.001);

three patients (50%) reached mucosal healing and the abscess/fistula disappeared in 2 of the 6 patients.
Conclusions: EEN is effective for inducing early clinical remission to active CD patients with complications and/or poor response to drugs. Large prospective study needed to further confirm this conclusion.

P376
Mucosal healing in IBD: Therapy maintenance or de-escalation therapeutic approach in patients achieving mucosal healing

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Background: Mucosal Healing (MH) has become an important therapeutic goal in Crohn's Disease (CD) and Ulcerative Colitis (UC), but only few data concerning therapeutic management of patients after achievement of MH are available.
Aim: to evaluate differences in clinical relapse after achieving MH in patients who continued therapy with immunosuppressors (IMM) such as Thiopurines-Methotrexate and/or biologics (BIO) administered before achieving this goal and in patients who stopped/reduced therapy with IMM/BIO (de-escalation therapy). Moreover, we analyzed for potential predictive biomarkers of clinical relapse.
Methods: 80 pts with inflammatory bowel diseases (IBD) with endoscopically confirmed MH were retrospectively analyzed (49 UC and 31 CD; 40 male). We assessed therapies before and after MH, smoking status and the following blood tests at baseline and at 6, 12 and 18 months: erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), Hemoglobin (Hb), white blood cells (WBC) and neutrophil count (NBC). Data are mean values ± SD. Analysis was performed with the Wilcoxon test and logistic regression.
Results: mean age was 42.3 ± 15.8 yrs. Median follow-up time was 29 months (range 3-120). The Results showed that neither de-escalation therapy (p=n.s.) nor smoking status (p=n.s.) influenced clinical relapse (26,6 ± 19.5 months) in the whole cohort. We found same Results in both subgroups, UC and CD. Significant variations of the examined variables were registered for CRP (p=.019) and ESR (p=.001) from baseline to month 18 in CD patients. In UC patients ESR (p= .013), WBC (p= .039), NBC (p= .048) but not CRP (p=n.s.) variations from baseline to month 18 were significant as clinical relapse predictors.
Conclusions: In patients achieving MH de-escalation of immunosuppressant/biologic therapy does not influence time to clinical relapse in patients with IBD. But this approach may reduce potential side effects and is cost-effective.

P377
Assessment of safety and efficacy of ferric carboxymaltose (Ferinject ®) in the management of iron deficiency with anaemia (IDA) or without anaemia in children and adolescents with inflammatory bowel disease (IBD)

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Background: Iron deficiency is common in children with IBD with a prevalence of 6-74%. The aetiology is multi-factorial with reduced dietary intake, low iron intestinal bioavailability, decreased internal iron turn-over and blood loss. IDA leads to impaired quality of life with increased financial burden and disruption of school attendance. Oral iron supplementation can take up to 6 months to replenish stores with an increased side effect profile. Ferric carboxymaltose (FC) offers the advantage of using higher single doses and less hospital attendances. Very few studies exist in the use of FC in Paediatrics. The aim of this study was to assess the safety and efficacy of FC in treating iron deficiency with or without anaemia in children with IBD.
Methods: We retrospectively reviewed our electronic database (disease phenotype, gender, age) on paediatric IBD patients with IDA treated with FC over a 2 year period. IDA was confirmed by combining haemoglobin, haematocrit, MCV, Ferritin and iron levels as well as clinical symptom of tiredness and lethargy. Patients were given a 15-30 minute FC infusion; bloods were repeated after 4-6 weeks. Safety was assessed by identified adverse events, efficacy by improvement of symptoms and laboratory Results.
Results: 102 children/adolescents with IBD were identified who had received FC, 59 male, 43 female; however due to the lack of complete data only 56 patients were included in the study, 34 male, 22 female, age range 7-19 years, median 16 years. The disease phenotypes were Crohn's disease (n=46) and Ulcerative colitis (n=10). Complete data were available in 40 patients. Commonest presenting complain was tiredness and lethargy (n=12/40). Each patient received one dose of FC. Haemoglobin (Hb) pre FC, range 69-118 g/L, median 104, Hb post FC 83-136, median 123; Haematocrit (HCT) pre FC, range 0.233-0.36 L/L, median 0.329, HCT post FC 0.28-0.41, median 0.375; Mean corpuscular volume (MCV) pre FC, range 58.2-79 fL, median 73.6, MCV post FC, range 60.3-85.4, median 81.1; Iron Pre FC, range 1.7-7.5 mcg/L, median 4.5, iron post FC, range 3.1-22.6, median 13; Ferritin Pre FC, range 6-475 mg/L, median 58, ferritin post FC, range 12-2658, median 175. Significant improvements of blood indices were seen, Hb rise of 19 g/L, HCT rise of 0.04 L/L, MCV rise of 7.5 fL, iron rise of 8.5 mcg/L and ferritin rise of 117mg/L. 2/40 patients (5%) developed an allergic reaction with fever, shivering and vomiting, no other allergic reactions were seen. Clinical symptoms improved in 11/12 (92%) patients reporting tiredness.
Conclusions: Paediatric patients with IBD seem to benefit from receiving intravenous ferric carboxymaltose(Ferinject ®) with improvement of their subjective symptoms and their blood indices.

P378
Early hs-CRP normalization and mucosal healing are effective predictors for 1-year mucosal healing

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Background: High sensitive C reactive protein (hs-CRP) and mucosal healing are effective predictors for Crohn`s disease(CD).

We evaluated the predictive validity of hs-CRP and mucosal healing after induction for one-year mucosal healing.

Methods: Consecutive CD patients who initiating a sheiduled infliximab therapy(5 mg/kg at week 0, 2, 6 and every 8 weeks thereafter) were enrolled. Hs-CRP was tested before each infliximab injection. Simple endoscopic scores for Crohn's disease (SES-CD) at 14wk and 52wk were evaluated by 2 experienced endoscopists. Mucosal healing was defined as SES-CD 0-2.

Results: 39 patients with an average age of 26.23±5.27yrs were prospectively enrolled in this study. Hs-CRP at 0,2,6,14wk were 9.44±5.13, 3.87±4.67, 3.02±3.91, 5.64±5.48mg/l, respectively. hs-CRP at week 6was related with mucosal healing at one year, while there were no obvious relationship between hs-CRP at 0,2,14wk. ROC curve indicated that for a hs-CRP cut-off of 1.65mg/l, the sensitivity for predicting one-year mucosal healing was 83% and the specificity was 62% (area under curve [AUC], 0.76; P<0.01). 21 patients achieved mucosal healing at week14. 86% (18/21) of them maintained a sustaining mucosal healing at 52wk. Logistic regression analysis showed positive relationship between mucosal healing at 14wk and at 52wk (P=0.01).

Conclusions: Early hs-CRP normalization and mucosal healing are effective predictors for one-year mucosal healing in CD patients undergoing infliximab therapy.

P379
Prolonged and repeated steroid exposure in inflammatory bowel disease: National population based study

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Background: The use of oral steroids in the management of inflammatory bowel disease should be reserved for active disease and has no role in maintenance. Prolonged or repeated exposure to steroids is indicative of steroid dependent disease and also correlates with quality of care.Our aim was to determine steroid exposure patterns using a nationally representative database.

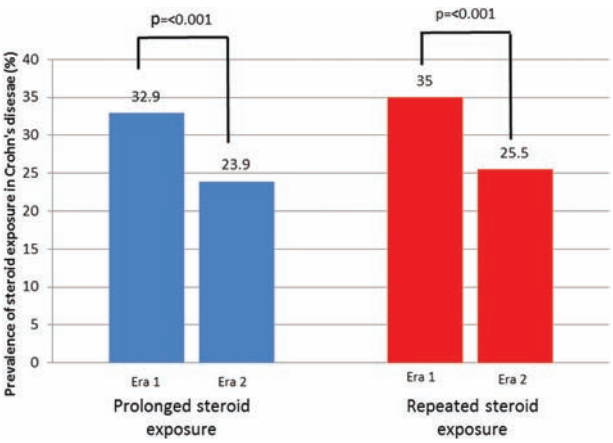

Figure 1. "Prevalence of prolonged steroid exposure and repeated steroid exposure between era 1 (1990–1993) and era 2 (2005-2005) for Crohn's disease. 2 group proportion test used to compare outcomes between groups"

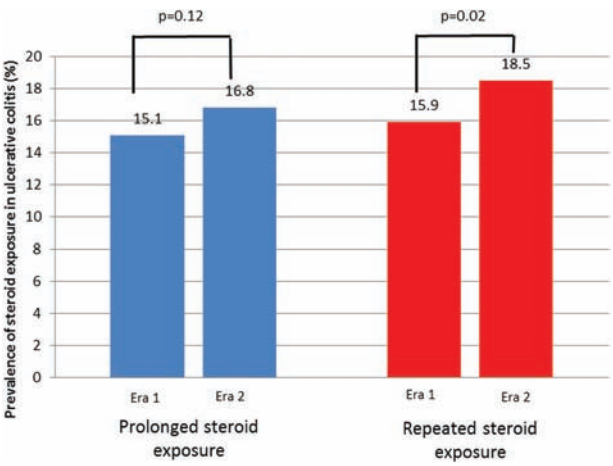

Figure 2: "Prevalence of prolonged steroid exposure and repeated steroid exposure between era 1 (1990–1993) and era 2 (2005-2005) for ulcerative colitis. 2 group proportion test used to compare outcomes between groups"

Methods: We constructed an incident cohort of patients with Crohn's disease (CD) and ulcerative colitis (UC) diagnosed between 1990 and 2009 using the Clinical Practice Research Datalink (CRPD), a validated research database representing an 8% sample of the UK population. We defined "prolonged steroid exposure" as continuous use for greater than 3 months duration and also defined "repeated steroid exposure" as restarting steroids within 3 months of cessation of a previous course of steroids. Patients were categorised if they had prolonged or repeated steroid exposure within 5 years of diagnosis which are markers of steroid dependence. We divided our cohort to compare patterns between era 1, 1990-1993 and era 2, 2002-2005 and compared the prevalence (number of users/total number within the era) of steroid exposure between these time periods using the 2-group proportion test.

Results: In CD, there were 474 and 2096 incident cases diagnosed in era 1 and era 2 respectively. The prevalence of patients requiring prolonged steroid exposure in CD, decreased by 27% (p<0.001) from 32.9% to 23.9% between era 1 and era 2 respectively. There was also a 27% (p<0.001) decrease in repeated steroid exposure, from 35% to 25.5% between era 1 and era 2 respectively (figure 1).

In UC, there were 1598 and 4626 incident cases diagnosed in era 1 and era 2 respectively. However, the prevalence of patients requiring prolonged steroid exposure remained stable at 15.1% and 16.8% (p=0.12) between era 1 and era 2. Repeated steroid exposure increased by 16% (p=0.02) from 15.9% to 18.5% between era 1 and era 2 (figure 2).

Conclusions: In CD, prolonged steroid exposure and repeated steroid exposure has decreased from era 1, 1990-1993 to era 2, 2002-2005. In UC, prolonged steroid exposure has remained stable but repeated steroid exposure has increased. Falls in steroid exposure in CD are most likely explained by concurrent increases in immumomodulator and anti-TNF use. These changes have not been demonstrated in UC.

P380
Risk Factors for Drug-induced Lupus secondary to Anti-tumor Necrosis Factor Agents used in Inflammatory Bowel Disease: A Multicenter Case-control Study in Madrid

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Background: Drug-induced lupus (DIL) is a rare adverse event in patients treated with anti-tumor necrosis factor (antiTNF) agents. We aimed to determine the prevalence, clinical characteristics, laboratory features and risk factors for DIL in inflammatory bowel disease (IBD) patients treated with this biologic therapy.

Methods: IBD patients from 5 university hospitals in Madrid diagnosed with anti-TNF induced lupus who met DIL criteria were

revised. Demographic and IBD characteristics were studied. A case/control 1:2 design was performed to identify risk factors for DIL. Controls with IBD were matched to cases by: type of IBD (Crohn disease or ulcerative colitis), antiTNF drug (infliximab or adalimumab) and exposure time to drug. A DIL case was considered in patients with the next criteria: 1) temporary relationship between clinical manifestations and the antiTNF agent 2) at least one serologic criteria: positive antinuclear antibodies (ANA) or positive anti-double-stranded-DNA antibodies (antiDNA) and 3) at least one no serologic criteria: arthritis/arthralgia, malar rash, serositis, fever or asthenia, oral ulcers, renal or hematologic disorder.

Results: A total of 661 patients were exposed to an antiTNF drug. We observed DIL in 15 patients 2.27% (IC95%:1.06-3.48). Mean age was 43 ± 13.6years, 55.6% were female; thirty-nine patients (86.7%) had Crohn disease. Thirty-three patients (73.3%) originally were treated with infliximab and 12 (26.7%) were treated with adalimumab. DIL occurred after a mean treatment duration of 17 months (range: 1-50 months). Features of lupus included presence of ANAs (100% cases), arthritis/arthralgia (93.3%), other symptoms (46.6%), antiDNA (13.3%) and dermatologic manifestations (13.3%). All the cases studied and four of the controls had positive ANA titers. This difference was statiscally significant (p<0.001)

Risk factors evaluated were age, gender, tobacco, autoimmune conditions, concomitant immunosuppressive treatment and antiTNF drug dosage. Only tobacco was statistically significant, OR=4.9 (IC95%:1.3 - 18.7)

All the cases studied improved DIL after ending antiTNF therapy and ANA returned to normal values (63.6%). One patient continued with the same treatment and suffered a DIL clinical worsening. Three patients switched to another antiTNF drug and only one DIL relapsed.

Conclusions: DIL prevalence in our IBD patients treated with antiTNF is similar to other retrospective reports. ANAs were detected in all patients. The predominant clinical manifestation was joint disorders and we found tobacco was a risk factor for DIL. AntiTNF withdrawal is almost always needed to improve symptoms and switching the antiTNF could be an option when this treatment is required.

P381
Feasibility and value of stool anti-TNF measurement in IBD patient in loose of response: a preliminary study

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Background: In a preliminary study including 11 patients with severe UC on IFX induction treatment, the authors found an association between faecal IFX levels, a drop in circulating IFX trough levels (TLI) and treatment non-response. To our knowledge, no studies have been carried out on faecal anti-TNF levels (IFX and ADA) in cases of loss of therapeutic response in UC and CD patients. The aim of this preliminary study was to assess the feasibility of this test in determining faecal anti-TNF levels (IFX and ADA) in the two types of IBD and to investigate whether this correlates with clinical or endoscopic activity.

Methods: Retrospective study were including from a clinical database and from biological collection data, the first 36 IBD patients with faecal calprotectin levels above of 1800µg/g stools. Faecal anti-TNF assays were conducted on all of these patients and compared with the results of 6 IBD patients with a faecal calprotectin level below 500µg/g (below 500µg/g in 3 cases and below 100µg/g in the other 3 cases). At the same time, we analysed trough levels of anti -TNF and antibodies. All measurements were obtained just before infusion or injection of anti TNF drugs. Exclusion criteria were severe acute colitis and patients under anti TNF therapy under induction regimen.

Results: 42 samples were analysed (20 CD, 22 cases on IFX treatment). The 36 patients with faecal calprotectin levels > 1800 µg/g exhibited clinical activity. An anti-TNF (> 0.2µg/ml of stools) was reported in 7 cases. In 5 cases, the patient was treated with IFX (22.7%) and in two cases with ADA (10%) (p: NS). Anti-TNF was found to be present in stools in 5 cases of UC (22.7%) and in two cases of colonic Crohn's disease (10%) (p: NS). A positive anti-TNF threshold of stools was only isolated in cases where calprotectin was over 1800µg/g (19.4%). No correlation to clinical activity or response to optimisation was reported among patients with or without faecal anti-TNF. Circulating anti-TNF levels at the time of the measurement were higher for IFX and ADA in the presence of feacal anti-TNF. In the 7 cases showing faecal anti-TNF, an endoscopy detected ulcers in the colonic mucosa (100%) as compared with 5 /29 colonic diseases showing ulcers in the absence of faecal anti-TNF (14%, p<0 .05).

Conclusions: Excluding severe colitis and induction regimen, feacal anti-TNF can be detected in cases of CD as well as UC, irrespective of the anti-TNF used. The presence of colonic ulcers appears to be a pre-condition of intestinal leaks which inversely have no effect in these cases on circulating anti-TNF levels. Large-scale prospective studies would better determine the potential value of this new parameter in IBD patients.

P382
Prevalence of impaired muscle strength in an IBD outpatient cohort.

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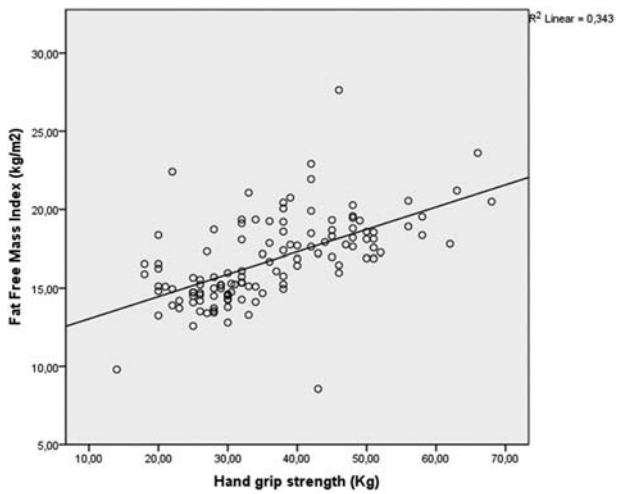
Background: Patients with inflammatory bowel disease (IBD), with active or quiescent disease, often have an impaired nutritional status, due to decreased food intake, nutrient malabsorption, and/or hyper metabolic state. This can cause depletion of fat stores, loss of muscle mass and thereby decreased physical performance. We aimed to evaluate physical performance by muscle strength in an IBD outpatient cohort from daily clinical practice.

Methods: We included consecutive IBD outpatients as part of a large prospective study on nutritional status. Muscle strength, as indicator for physical performance, was assessed by handgrip strength (HGS). A hydraulic hand dynamometer was used in sitting position with elbow flexed 90 degrees in free position and neutral position of the forearm and wrist, recording the highest value of a triplicate assessment of the non-dominant hand. A cut off below the 10th percentile of the HGS was defined as impaired [1] . Fat and fat free mass were assessed by air displacement plethysmography. The fat free mass index (FFMI) includes a correction for height and was used as indicator for muscle mass. Spearman's rank correlation was used for assessing the correlation between FFMI and HGS. Moreover



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multivariate logistic regression analysis was performed to identify independent risk factors for impaired HGS.

Results: In total 115 consecutive IBD outpatients were included, comprising 84 CD and 31 UC. Of these patients, 57% was female, mean age was 46,8 (SD 15) years, mean disease duration of 150 (SD 121) months, and mean body mass index was 25,4 (SD 4,0) kg/m^2 . Of all patients, 31% had a HGS below the 10th percentile, being 29.8% of CD and 35.5% of UC patients.

The Spearman's rank correlation coefficient showed a significant correlation between HGS and the FFMI (R = 0,586; p<0,01).

Using multivariate logistic regression analysis, disease phenotype (UC or CD), active disease, and history of surgery did not affect the presence of reduced HGS in the total group of IBD or in CD patients only. In the latter group, also no effect of disease location was found.

Conclusions: About one third of IBD patients from daily clinical practise were found to have an impaired HGS, which correlated with a diminished FFMI. This was not affected by disease phenotype, disease activity, and surgical history in the total group, nor by disease location in CD patients. It would be of relevance to check dietary intake, and to study whether dietary advice and/or physical exercise may improve muscle strength.

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P383
Overweight impairs short-term outcomes of laparoscopic IBD surgery. A comparative analysis of 639 consecutive patients.

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Background: This study aimed to assess the impact of body Mass Index (BMI) on inflammatory bowel disease (IBD) laparoscopic surgery outcome.

Methods: From 1998 to 2013, all patients who underwent a laparoscopic colorectal resection performed for IBD were prospectively included. This cohort was split in 3 groups, according to the body mas index (BMI) of the patients: under-weighted patients (BMI ≤ 18.5), normally weighted patients (18.5 < BMI < 25), and over-weighted patients (BMI ≥ 25).

Results: 639 consecutive laparoscopic colorectal resections for IBD were analyzed, including 324 ileocolonic resections (51%), 130 subtotal colectomies (20%), 147 ileal pouch-anal anastomoses (IPAA) (23%), 21 segmental colectomies (3%), and 17 abdominoperineal resections (3%).

Compared to normally weighted patients, over-weighted patients showed a significantly increased intra-abdominal septic complication (IASC) rate (16 vs. 10%, p=0.038) but similar length of hospital stay, conversion rate, overall postoperative morbidity rate, severe (Clavien-Dindo ≥ 3) postoperative morbidity rate, and reintervention rate. Conversely, outcomes of under-weighted patients showed no difference, compared to those of normally weighted patients.

Per-procedure analysis showed similar outcomes between the 3 groups for ileocolic resection and subtotal colectomy. For IPAA, over-weighted patients had significantly increased severe postoperative morbidity (34 vs. 14%, p=0.008) and IASC (34 vs. 13%, p=0.004) rates, compared to normally weighted patients, whereas under-weighted and normally weighted patients had similar outcomes.

Conclusions: Overweight significantly impairs short-term outcomes of laparoscopic IBD surgery, especially after IPAA.

P384
Golimumab maintenance treatment and fecal calprotectin predict continuous clinical response in ulcerative colitis.

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Background: In PURSUIT-Maintenance (M), patients with moderate to severe ulcerative colitis who had clinical response to golimumab induction treatment at week (wk) 6 were more likely to achieve continuous clinical response (CCR) through wk 54 if they received maintenance treatment with golimumab 50 or 100 mg (47.0% and 49.7% of patients, respectively) than if they had withdrawal of golimumab (31.2%). Subjects were assessed for UC disease activity using the Mayo score at wks 30 and 54 and by partial

Table. Multivariable Model Predicting Continuous Clinical Response.

Predictor	Odds Ratio	95% Confidence Interval	*P*-value
Calprotectin wk 6 (log)	0.55	0.394–0.775	.0006
Calprotectin change from wk 0–6 (log)	1.34	0.989–1.810	.0587
Treatment (golimumab maintenance vs withdrawal)	1.91	1.234–2.957	.0037

Mayo every 4 wk (loss of response was confirmed by endoscopy); patients who maintained response through wk 54 were considered to be in CCR.[1] Our current analysis sought to identify early predictors of CCR.

Methods: This post hoc analysis included 456 patients from PURSUIT who were responders at wk 6 after golimumab induction and entered maintenance treatment.[2] Potential predictors evaluated were age; gender; disease duration (≤5y vs >5y); disease extent (extensive vs limited); Mayo score at induction wk 0 (<9 vs ≥9); Mayo score at induction wk 6; stool frequency and rectal bleeding (Mayo) at induction wk 6; CRP, calprotectin, and lactoferrin at induction wk 6 and change from induction wk 0-6; Mayo change from induction wk 0-6; CRP normalization at induction wk 6; mucosal healing (Mayo endoscopy score 0 or 1) at induction wk 6; and golimumab maintenance vs withdrawal. Potential interactions between factors were evaluated. Final stepwise selection of terms was used with significance levels for entry and retention of 0.50 and 0.15, respectively.

Results: In univariate analysis, factors significantly associated with CCR were treatment group, wk-6 fecal calprotectin, and wk-6 lactoferrin. Wk-6 calprotectin and lactoferrin were correlated (r=0.78; P<.0001). results of the final multivariable model are shown in Table.

Conclusions: In this post hoc analysis of PURSUIT, maintenance treatment with golimumab and wk-6 calprotectin levels were significant predictors of CCR in moderate to severe UC patients who responded to golimumab induction at wk 6.

Sponsorship: Financial support for this study was provided by Janssen Research & Development, LLC., Spring House, PA, USA.

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P385
Azathioprine and 6-Mercaptopurine use in the Swiss IBD cohort: adverse effects, causes of discontinuation and risk of "flares" according to 6-TG levels

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Background: To characterize and analyze in the Swiss IBD Cohort : a) reported Azathioprine (AZA) and 6-Mercaptopurine (6-MP) adverse effects (AE), b) causes of discontinuation and c) response to therapy according to gastroenterologists' clinical judgment, d) whether level of 6-TGN < 235pmol/8 x10^8 red blood cells (RBC) is associated with a higher risk of "flare" occurrence.

Methods: Retrospective statistical description, Cox model and Kaplan-Meier survival estimation.

Results: 1499 patients with Crohn's Disease (CD) and 1066 with Ulcerative colitis (UC).

a) Of 1670 patients ever treated with AZA/6-MP, there were 611 reported AE: 149 intolerances are observed (24.4%), 81 pancreatitis (13.2%), 61 hepatitis (10.0%), 33 hematologic side effects (5.4%), 20 hypersensitivities (3.2%), 17 infections (2.8%), 13 cases of fatigue (2.1%), 7 malignancies (1.2%) and 207 not further specified AE (33.9%).

b) Of 566 reported causes of discontinuation according to gastroenterologists' clinical judgment, 209 "treatment no long needed" (36.9%), 196 "breakthrough/loss of response (34.6%), 92 "patient wish" (16.3%), 45 "primary non-response" (7.9%) and 21 "Conception/Pregnancy or wish of it" (3.7%) were described.

c) Of 1187 gastroenterologists' clinical judgment of AZA/6-MP responses, 417 (35%) were judged as "successful", 639 (54%) as "failure", 131 (11%) "unknown".

d) Of 364 CD patients under AZA/6-MP, 199 (54.7%) developed a "flare" during the observation period (median 13.3 mo, IQR 11.9-23.4, range 5.8-59.0). Of 204 patients with UC under AZA/6-MP, 106 (52.0%) developed a "flare" during the observation period (median 14.0 mo, IQR 12.2-24.9, range 7.3-48.2). 6-TGN levels ≥ 235 pmol/8 x 108 RBC showed a not statistically significant tendency to improve "flare"-free survival time in CD and UC (HR=1.157, 95CI: 0.680-1.971, p=0.590).

Conclusions: In the SIBDC, AZA/6-MP are frequently used, AE and failure are frequently reported, 6-TGN levels ≥ 235 showed a tendency to improve "flare"-free survival.

P386
Durability of the anti-HBs titers after vaccination against Hepatitis B virus (HBV) in patients with Inflammatory Bowel Disease (IBD)

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Background: Among immunocompromised patients who respond to the HBV vaccine, clinically significant HBV infection has been documented in those who do not maintain anti-HBs concentrations > 10 IU/l.

Aims: 1) To understand the kinetics of the anti-HBs titers over time in IBD patients who have initially responded to the vaccination. 2) To identify predictive factors of negativization of anti-HBs titers over time.

Methods: This multicenter study included IBD patients vaccinated in the COMVI-B trial (EUDRA CT number: 2010-023947-14), where patients with negative HBV serology and without previous vaccination against HBV were randomized 1:1 to receive Fendrix ® or double doses of Engerix® at months 0, 1, 2 and 6. Patients with anti-HBs > 10 IU/l 2 months after the 4th dose were followed-up. Anti-HBs titers were then measured at 6 and 12 months. When anti-HBs titers were < 10 IU/l during the follow-up, they were considered negatives. Long-term maintenance of positive anti-HBs titers was estimated using Kaplan-Meier curves. Cox-regression analysis was performed to identify potential predictive factors for losing anti-HBs protective titers during follow-up.

Results: 132 patients were included (median age 48 years, 55% males, 49% Crohn's disease and 51% ulcerative colitis). Thirty-one percent of patients were on immunomodulators, and 32% on anti-TNF drugs. Fifty percent of patients received each of the vaccines (Engerix® or Fendrix®). The cumulative incidence of negativization of the anti-HBs titers was 15% after 6 months and 21% after 12 months of follow-up. The incidence rate of negativization of the anti-HBs titers was 23% per patient-years of follow-up. In the multivariate analysis (adjusted by the patient's age and the treatment with thiopurines or anti-TNF drugs), to have had anti-HBs ≥ 100 IU/l (vs. < 100 UI/l) after the vaccination was the only factor that was associated with a lower probability of negativization of anti-HBs titers during the follow-up (HR=0.08, 95%CI=0.02-0.3, p<0.0001). The type of vaccine administered was not associated with a different risk of negativization of anti-HBs titers.

Conclusions: A high proportion of IBD patients with protective anti-HBs titers after vaccination lose them over time (approximately, 25% of patients per year of follow-up). The risk of losing protective anti-HBs titers is dramatically increased in patients achieving anti-HBs below 100 IU/l after the vaccination. Thus, anti-HBs > 100 IU/l should be the threshold to consider HBV vaccination success in IBD patients.

P387
Disease course and colectomy rate in ulcerative colitis: a follow-up cohort study of a tertiary referral center in Tuscany

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Background: The disease course and colectomy rate of ulcerative colitis (UC) varies largely in population-based and referral center cohorts. In addition, the impact of changing treatment paradigms with the increasing use of immunomodulators (IM) and biologics may greatly vary among community and referral centers. We retrospectively evaluated our cohort of patients with a confirmed diagnosis UC from the 1960 to 2012, in order to determine the disease course and colectomy rate, and to identify risk factors that predict the need for surgery, including the influence of medical management.

Methods: Our study identified a cohort of 1,772 UC patients (1,011 males, mean age 45 ± 17yrs) which were followed up for a mean of 11 ± 9 yrs (range 1 - 49 yrs) at the AOU Careggi University Hospital, a referral center for Tuscany.

Results: Disease extension was E1, E2, and E3 at diagnosis in 20%, 54% and 26% of patients, respectively. At final follow-up, disease extension increased in 20% of cases, and in more than half of patients with E1. Extraintestinal manifestations (EIMs) were reported by 11% of patients, while the use of systemic corticosteroids (CS), IM or anti-TNF agents was reported in 68.6%, 19.9%, and 6.4% of cases, respectively. The number of patients treated with IM or anti-TNF increased significantly in last two decades, compared to the period 1960-1990 (26.1% vs 10.4%; p<0.008). The overall colectomy rate was 5.9% (104 pts), with a Kaplan-Meyer estimation of 1.4% at one year, 7.7% at 10 years and up to 13% at 30 years of follow-up. At univariate analysis, duration of disease, EIMs and more extensive disease (E3 vs E2+E1) were more frequently associated with surgery (p=0.008). The 1-, 5- and 10-yrs colectomy rate was not significantly reduced in the last two decades. More importantly, patients treated with IM, anti-TNF or both within 3 yrs from diagnosis didn't show a different colectomy free survival compared to patients treated after 3 yrs (9 vs 10 yrs, p=0.08; 7 vs 7 yrs, p= 0.13; 10 vs 10 yrs, p=0.91, respectively [median values]). Similar results were observed also when only patients diagnosed after 2001 were included in the analysis.

Conclusions: The overall colectomy rate in our referral center cohort is rather low, and did not changed significantly in last two decades, despite a wider use of IM and/or anti-TNF. Duration of disease, disease extension and presence of EIM emerged as predictors of colectomy. In contrast, the early introduction of IM/anti-TNF therapy, within 3 yrs from diagnosis, did not influence significantly the colectomy rate.

P388
Fistula Healing in Perianal Crohn's Disease - With or Without Anti-TNF Therapy?

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Background: Anti-tumor necrosis factor (TNF) therapies are used to treat fistulising perianal Crohn's disease (CD). We evaluated the clinical and radiological outcomes of patients with perianal Crohn's fistulas in the pre-anti-TNF and in the post-anti-TNF era.

Methods: A local database of 270 consecutive patients with CD treated at our institution between 2000 and 2014 was established.

Results: Ninety patients were in the non-anti-TNF group and 180 were treated with anti-TNF therapy (Infliximab or

Adalimumab). Clinical response rates were significantly higher in the anti-TNF group (74% vs 62%, p=0.04). Similarly, radiological response rates were higher in the anti-TNF group (56% vs 28%, p<0.01).

Cox Regression analysis demonstrated fistula duration (p=0.01) and biologic therapy (p=<0.01) to be significant at the univariate level. At the multivariate level, patients on anti-TNF therapy had a faster radiological response over a 6-year follow-up period (OR=2.25, CI= 1.14-4.46, p=0.02). A short duration of CD (less than 5 years) contributes to a faster time to clinical response (OR=1.77, CI=1.03-3.05, p=0.04).

Treatment with anti-TNF therapy is an independent predictor of radiological response (OR 3.55, CI 1.59-7.91, p<0.01). Patients with L1 luminal disease are 3 times more likely not to go into clinical remission on both univaraite and multivariate analyses (OR=3.08, CI=1.47-6.46, p=0.01). The duration of CD is also a poor predictor of clinical response to therapy (p<0.01).

Conclusions: Patients on anti-TNF therapy have improved clinical and radiological response rates compared with patients without. Anti-TNF therapy is a positive predictor of radiological response to therapy.

P389

A double-blind clinical trial on *Trichuris suis* ova (TSO) in active Crohn's disease resulted in a significant placebo effect both in patients and investigators without objective evidence of reduced inflammation

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Background: A randomized, double blind, placebo controlled phase II study with an planned interim analysis and using 3 doses of TSO in mildly to moderately active ileo-/colonic, uncomplicated Crohn's disease failed to show evidence of a therapeutic benefit regarding remission or response according to the CDAI as compared to placebo, but resulted in an unexpectedly high placebo remission rate of 43% [1]. The goal of this analysis was to explore tentative reasons for this high placebo response.

Methods: Primary endpoint was the rate of clinical remission (CDAI<150) at week 12 (LOCF; ITT analysis). Exploratory analyses of baseline data, change of biochemical parameters and components of the CDAI as well as physician global assessment were performed and in particular results of the primary endpoint of the two stages of the study were calculated (see Table 1 for stage definition).

Results: There was no effect of any of the baseline parameters analyzed (duration of disease, BMI, sex, age, CDAI) on the remission rate. CRP and calprotectin were initially somewhat more elevated in patients who did not achieve remission, but overall no clinically relevant change from baseline was seen in any of the groups. No significant difference in change of single CDAI components was found between treatment groups. In a small subpopulation of 37 patients mucosal healing was studied and occurred in 2 patients each with 250 TSO and placebo and 1 each in the other two groups. Physicians' global assessment showed success of treatment in 25.4% and benefit in 57.1% of all patients without any difference between groups. Interestingly, the observed clinical remission rates were not consistent between the 2 stages of the study (Table 1).

Conclusions: The high clinical remission rate (42.9%) in the placebo group according to CDAI was not accompanied by any relevant change of initially elevated biochemical parameters of inflammation or mucosal healing at endoscopy. This finding casts further doubt on the suitability of the CDAI as sole primary endpoint in Crohn's disease, as it is susceptible to record subjective symptom improvement which is not reflected by biochemical markers and/or endoscopic sign of inflammation. Physicians' global assessment was as well rather positive in all groups. The different remission rates in the two stages might be explained by the low group size in each stage as well as by a potential selection bias in favour of 'believers' in alternative medicine.

*on behalf of the International TSU-2 Study Group (TRUST-2)

References:

[1] Schölmerich J, et al., (2014), Efficacy and safety of Trichuris suis ova fo rtreatment o fmildly-to-moderately active Crohn's disease: A randomised, double-blind, placebo-controlled, phase II study, UEG Journal, 2(1S):A123 (OP392)

Number (%) of patients with clinical remission (CDA<150) at wk 12 (LOCF). Stage I/II contain patients enrolled before/after the recommendation of the interim analysis, respectively

	TSO 250	TSO 2.500	TSO 7.500	Placebo	Total
Stage I	15/39 (38.5%)	10/39 (25.6%)	20/39 (51.3%)	14/39 (35.9%)	59/156 (37.8%)
Stage II	---	15/32 (46.9%)	14/33 (42.4%)	16/31 (51.6%)	45/96 (46.9%)
Overall	15/39 (38.5%)	25/71 (35.2%)	34/72 (47.2%)	30/70 (42.9%)	104/252 (41.3%)

P390
Thiopurines are more effective in Crohn's Disease than in Ulcerative Colitis, despite a global high rate of treatment failure: A single centre experience in the use of thiopurines in the era of biologics

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Background: Thiopurines are widely used in inflammatory bowel disease(IBD) since they have shown efficacy in both ulcerative colitis(UC) and Crohn's disease(CD); whether or not thiopurines have different efficacy depending in the kind of IBD is still to be clarified. Treatment fails in a proportion of patients either due to adverse events or lack of efficacy. Biologics may have varied the clinical use of thiopurines as a primary treatment for IBD. We aimed to evaluate the current use of thiopurines in the era of biologics.

Methods: Retrospectively analyzed clinical records of all IBD patients treated with thiopurines at our centre, remain with an stable follow up. Dates of diagnosis and starting thiopurines were collected. We considered thiopurines failure(TF) if biologics had to be added to thiopurines or thiopurines had to be stopped due to lack of efficacy or adverse event(AE).

Results: 575 patients included; 52,5% males, mean age 31yrs (range 17-84); 459CD, 116UC.

Overall, 304 patients (53%) experienced TF; a majority of them (67%) moved to or added biologics.

Median cumulative survival time of thiopurines (no TF) in CD was 86(95%IC 68-104) months and in UC was 23(95%IC 11-35) months (p<0.001). The cumulative proportion of CD patients that remained with no TF was 60%, 45%, 33% and 21%, and of UC patients was 35%, 25%, 12% and 8% at 50, 100, 150 and 200 months of treatment respectively (p<0.001). UC patients were twice as likely to experience thiopurines failure than CD patients (HR 2.2; 95%IC 1.7-2.8; p<0.001)

147 patients (25,5%) stopped thiopurines due to AE (8% digestive intolerance, 5% acute pancreatitis, 5% myelotoxicity, 4% hepatotoxicity). No differences between UC(31 %) and CD(24%) in probability of suffering AE forcing thiopurine withdrawal.

Most of those AE occurred in the early period of treatment: 67% of cases of digestive intolerance in the first year, 58% of cases of hepatotoxicity in the first 6 months and 80% of cases of acute pancreatitis in the first month. Myelotoxicity causing TF occurred along the follow up (mean 40 months, range 1-204).

157 patients had TF due to lack of efficacy. UC patients were twice as likely to experience thiopurines lack of efficacy than CD patients (HR 2.3; 95%IC 1.6-3.3; p<0.001)

Conclusions: In our experience, thiopurines were more effective in CD than in UC patients, although more than 50% of IBD patients experienced some kind of thiopurine treatment failure.

Current clinical usefulness of thiopurines as primary treatment for IBD seems to be modest in the long term favoring the use of biologics.

P391
Effect of Adalimumab on Clinical Laboratory Parameters in Paediatric Crohn's Disease Patients from IMAgINE 1

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Background: Adalimumab (ADA) was shown to be effective for inducing and maintaining clinical remission in children with moderately to severely active Crohn's disease (CD) in IMAgINE 1.[1] Changes in laboratory values indicative of systemic inflammation were evaluated.

Methods: Patients (pts), 6-17 years-old, with baseline (BL) Paediatric CD Activity Index >30 received open-label induction ADA at weeks (wks) 0/2 by body weight (<40 kg, 80/40 mg; ≥40 kg, 160/80 mg). At wk 4, pts were randomized to double-blind (DB) higher-dose (HD) ADA (<40 kg, 20 mg every other wk [eow]; ≥40 kg, 40 mg eow) or lower-dose (LD) ADA (< 40 kg, 10 mg eow; ≥40 kg, 20 mg eow) for 48 wks. The proportion of pts with abnormal values at BL, who later achieved normal values at wk 52 were evaluated. Albumin levels of >3.4 g/dL, platelet counts of <500x10^9 platelets/L, and CRP levels of <1 mg/dL were considered normal. Mean change in hemoglobin from BL to wk 52 was also assessed. Last observation carried forward (LOCF) was used for missing data.

Results: Overall, HD ADA-treated pts with abnormal laboratory values at BL achieved normal albumin levels (75%), platelet counts (53%), and CRP levels (64%) at wk 52 (Table). HD ADA also improved mean hemoglobin levels at wk 52 (mean change from BL LD -0.96 v. HD 3.43 g/L, p<0.001).

Normalization of laboratory values in pts with abnormal values at BL (LOCF)

	Wk 52	Wk 52	Wk 52
n/N (%)	LD	HD	Overall
Albumin (N=36)	6/24 (25.0)	9/12 (75.0)**	15/36 (41.7)
Platelet count (N=75)	11/30 (36.7)	24/45 (53.3)	25/75 (46.7)
CRP (N=103)	28/53 (52.8)	32/50 (64.0)	60/103 (58.3)

**p<0.01 for HD v. LD by Pearson's chi-square test and Fisher's exact test

Conclusions: ADA led to normalization of laboratory values in clinically meaningful proportions of pts who had abnormal albumin levels, platelet counts, and CRP levels at BL in IMAGINE 1. Improvements in hemoglobin levels were also observed at wk 52.

Reference:

1. Hyams et al Gastroenterol 2012;143:365

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P392
Low uptake of cervical screening in immunosuppressed patients with Inflammatory Bowel Disease at a district general hospital

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Background: ECCO guidelines strongly recommend regular cervical screening for women with inflammatory bowel disease (IBD), especially if treated with immunomodulators. We wanted to investigate if our immunosuppressed female IBD patients were being screened in

accordance with the NHS Cervical Screening Programme (CSP) and identify if they were at increased risk of cytological abnormalities.
Methods: We searched our database for patients commenced on azathioprine, mercaptopurine, methotrexate, infliximab or adalimumab from June 2005 to October 2013. We excluded patients who were on these drugs for less than one year, were not of cervical screening age (25-64) or had had a hysterectomy. Information provided from general practitioners, local cytology department and Open Exeter (CSP database) were used to identify women participating in CSP and if they showed any abnormalities.
Results: 153 patients met the criteria to participate in the CSP. 115 (75%) were up-to-date compared to a national participation rate of 78.3%. 25 (16%) had participated in the CSP but were not up-to-date at the time of report. 9 (6%) had not participated in the CSP and 4 (3%) actively declined participation. Date from the 2013 National CSP demonstrates that 5.3% of those screened displayed low grade abnormalities and 1.2% had high grade abnormalities. Of our 153 patients 13 (8.5%) had cytological abnormalities. 5 (3%) patients had abnormalities before immunosuppressive therapy with 1 (0.7%) patient showing high grade abnormality (moderate dyskaryosis with CIN1 confirmed) which subsequently remained negative whilst on immunosuppression. Our results identified 7 (4.6%) patients with low grade abnormal cytology results after commencing immunomodulators (3; borderline nuclear changes in squamous cells, 2; mild dyskaryosis, 2; low grade dyskaryosis and high risk HPV detected). Only 1 (0.7%) patient had high grade dyskaryosis during immunosuppression but their follow up cytology was negative.
Conclusions: IBD patients are at increased risk of cytology abnormalities which is concerning since our CSP participation is below the national average. However data from our unit suggests that commencing immunosuppression therapy did not increase that risk any further. This data underlines that IBD specialists need to educate and encourage patients to participate in the CSP programme.

P393
Measles, Mumps and Rubella Seronegativity Rates in IBD Patients Commencing Biologic Therapy

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Background: Serological testing to confirm immunity to varicella zoster and hepatitis B is established practice in Inflammatory Bowel Disease (IBD) patients where the use of immunomodulators or biological therapy is anticipated. Data, however, are few on the seronegativity rates for measles, mumps and rubella in IBD patient populations. The measles, mumps, rubella (MMR) vaccine is live and therefore cannot be administered to immunosupressed patients. Currently, there is uncertainty as to whether immunity to these viruses should be routinely tested prior to the initiation of immunomodulators or biologic therapy, particularly where individuals have been previously vaccinated.
Methods: We identified 98 IBD outpatients due to commence biologic therapy with available measles, mumps and rubella serology from an institutional database. A national immunization programme for measles, mumps and rubella was instituted in 1988. Subjects born subsequent to the year 1981 were considered to have participated in MMR immunization programme. Enzyme-linked immunosorbent assays were used to determine seronegativity to measles, mumps, rubella and varicella zoster.
Results: The study cohort comprised n=60 Crohn's Disease and n=38 Ulcerative Colitis patients [median age 42.7 years (18 - 76.9); female gender n=52 (53%)]. N=72 (73%) subjects were born prior to 1981 and therefore were not considered to have received MMR vaccination. The proportion of the study cohort seronegative for measles, mumps, rubella and varicella zoster were: 1%, 6%, 9% and 0%, respectively. Seronegativity rates for measles, mumps and rubella in the pre-MMR (n=72) versus post-MMR (n=26) cohorts were: 0% vs. 4%; 1% vs. 19%; and 8% vs. 12% respectively.
Conclusions: A significant proportion of IBD patients are seronegative for mumps and rubella viruses even where previous MMR immunization has occured. Confirmation of immunity to these viruses should be routinely performed in all IBD patients, irrespective of immunization status, prior to the initiation of immunomodulator or biologic therapies.

P394
Prevalence of malnutrition in patients with Inflammatory Bowel Disease - a Romanian National Register based study

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Background: Malnutrition may be associated in patients with inflammatory bowel diseases (IBD). It is multifactorial (inadequate intake, inflammation, malabsorption, therapy related) and may worsen disease prognosis. The aim of this study was to assess the prevalence of malnutrition in IBD patients.
Methods: We analyzed available data from 614 patients registered in the IBDProspect multicenter national registry in the last 5 years. We defined malnutrition as involuntary weight loss during the previous 3 months, mild when less than < 5% and moderate-severe when more >=5% of initial weight.
Results: Malnutrition was found in 30.1% of patients (10% mild and 20% moderate-severe), with a mean age of 40±17.9 years. There were no differences between age, gender or smoking status groups. Prevalence of malnutrition increased with disease activity. For Crohn's disease (CD), malnutrition was associated with the presence of intraabdominal fistulas, abscesses or intestinal bleeding (p=0.036) and was marginally statistically significant more frequent in patients with ileo-colonic extension (p=0.053). In ulcerative colitis (UC) patients, prevalence of malnutrition was significantly lower in proctitis than more extensive disease (p=0.004). Association of anemia was significantly higher in malnourished CD (p<0.0001) and UC (p<0.002) patients. Malnutrition was significantly more frequent in patients treated with steroids (p<0.0001), independent of disease phenotype or extension; but there was no difference in patients treated with aminosalicylates, immunosuppressants or anti- TNF.
Conclusions: Nutritional assessment should be performed in all IBD patients as its prevalence is higher in active, more extensive or steroid treated disease.

P395
Therapeutic adherence in patients with inflammatory bowel disease.

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Background: Ulcerative Colitis (UC) and Crohn's disease (CD) are subtypes of inflammatory bowel diseases (IBD). Medical treatment is for life to maintain long-term remission in patients with IBD. Previous studies in patients with IBD have shown poor Therapeutic Adherence (TA) with a rate between 30 and 45%. However, there are no studies performed in countries from Latin America that have eval-uated TA in IBD patients. The aim of this study is to evaluate the frequency of adherence in patients with IBD a Third Level Hospital Care and to determine factors associated to TA as well as to identify the most useful survey for evaluating TA in our population.
Methods: A cross-sectional study was performed in patients with IBD (UC 82% and CD 19%) between the period March and June 2014. Four questionnaires were applied (Morisky-Green, Haynes-Sackett, Morisky Medication Adherence Scale MMAS-8 and Soria Zaira and Nava UNAM). Descriptive statistics were performed, X2 test, Student's t test and Cohen's Kappa. SPSS version 17 was used.
Results: A total of 130 subjects were evaluated and 28 patients were excluded due to incomplete infor-mation in the questionnaires. In patients with UC, 60% were in clinical remission, endoscopic remission in 13% and 7% in histological remission. In CD 75% were in clinical remission and 55% had ileo-colonic localization. In the Morisky Green's survey identified patients with good TA (47%) have basic education. Hayness-Sackett showed that patients with good adherence were older than 40 years old and had more than 10 years of disease evolution (P=0.05). The MMAS-8 scale showed good adhesion to 19.4%, medium 24.1% and 56.5% low. The factor associated to good adherence was home occupation (P<0.05). The survey Soria-Zaira (UNAM) identified patients that had adherence to medical-behavioral activity in 62% 71% in diet and 74% in exercise. We observed that the evaluation of Morisky-Green and Morissky Medication Adherence Scale (MMAS-8) provided a more objective diagnosis of adherence to treatment and had high concordance between them (kap-pa= 0.74; P <0.05). When the adherence was assessed by Zaira Soria-Nava survey, we found a sig-nificant agreement with the classification of MMAS-8 (P <0.05).
Conclusions: The good TA was 47% by Morisky-Green, 86% by Haynes-Sackett, 44% by validated scale for EII (MMAS-8) and 88% by Soria-Zaira UNAM. The factors associated to better adherence treatment were basic education, age in the fourth decade of life, more than 10 years of disease evolution and activities at home.

P396
Adalimumab induction therapy achieves clinical remission and response in chinese patients with Crohn's Disease

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Background: Adalimumab (ADA) has demonstrated efficacy for induction and maintenance of remission in patients (pts) with Crohn's disease (CD) in Western and Japanese studies. The 8 week (wk) efficacy and safety of ADA is reported in Chinese pts with moderately to severely active CD and elevated high-sensitivity (hs)-CRP in ongoing Study M14-232 (NCT02015793).
Methods: In this Phase 2 study, adult Chinese pts with CD [CD Activity Index (CDAI), 220-450; hs-CRP, ≥3 mg/L] were enrolled. Pts (N=30 total), were randomized 1:1 and stratified by CD severity (CDAI ≤300 or >300) to receive 1 of 2 ADA induction dosing regimens for the 8 wk double-blind (DB) period: 160/80 mg at wks 0/2, 40 mg at wks 4 and 6 OR 80 mg at wk 0, 40 mg at wks 2, 4, and 6. At wk 8, all patients were able to enroll in an 18 wk open-label (OL) phase to receive 40 mg ADA every other wk. Efficacy outcomes assessed included: remission (CDAI <150), response [decrease in CDAI ≥70 points from baseline (BL)], and reductions from BL in hs-CRP and fecal calprotectin (FC) levels over time. Nonresponder imputation (NRI) was used for missing categorical data and last observation carried forward (LOCF) was used for missing hs-CRP and FC. No formal hypothesis testing was performed.
Results: Enrolled pts had mean age 34.5 years (yrs), mean CD duration 2.6 yrs, and mean CDAI 315 at BL. Median BL hs-CRP levels in the 80/40 and the 160/80 groups were 30.6 and 31.9 mg/L respectively; corresponding values for FC were 802 and 945 mcg/g. BL use of immunomodulators and corticosteroids was similar between groups (overall 70% and 27% of patients, respectively). Clinical and biological response was observed at wk 2 in most pts in both groups (Table), and was maintained from wks 4 to 8. Remission rates increased over time and were numerically greater in the 160/80 group at each visit v. the 80/40 group. Greater median reductions from BL in hs-CRP levels at each visit and greater median reductions in FC at wks 4 and 8 were observed at each visit in the 160/80 group v. the 80/40 group. Adverse event rates were similar in the 80/40 (40%) and 160/80 (46.7%) groups.
Conclusions: Treatment of Chinese pts with moderately to severely active CD with 160/80 ADA induction resulted in achievement of remission in 2/3 of pts at wk 4. The safety profile of ADA was consistent with previous trials. High response and remission rates may reflect a short duration of disease.

Efficacy outcomes in ADA-treated patients

	Week 2	Week 2	Week 4	Week 4	Week 6	Week 6	Week 8	Week 8
	80/40 (N=15)	160/80 (N=15)	80/40 (N=15)	160/80 (N=15)	80/40 (N=15)	160/80 (N=15)	80/40 (N=15)	160/80 (N=15)
Response	66.7	80.0	93.3	93.3	93.3	86.7	93.3	86.7
Remission	26.7	46.7	40.0	66.7	60.0	73.3	60.0	66.7
Median reduction from BL in hs-CRP, mg/L	-14.1	-25.4	-12.1	-21.1	-12.7	-21.6	-11.9	-21.6
Median reduction from BL in FC, mcg/g	ND	ND	-135	-207	ND	ND	93	-274

P397
Analysis of Mucosal TNFSF15/TL1A Expression in Korean IBD Patients

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Background: It has been well known that genetic mutations and the epidemiology of inflammatory bowel disease (IBD) differ between Asia and the West. However, TNF superfamily member 15 (TNFSF15) gene has been identified as a common susceptibility gene in Asian and Western IBD patients, suggesting that TNFSF15 may play an important role in the pathogenesis of IBD. TNFSF15/TNF-like cytokine 1A (TL1A) is a proinflammatory cytokine and a member of the TNF α superfamily, mainly expressed on activated T cells. We investigated mucosal TL1A expression by immunohistochemistry (IHC) in Korean IBD patients.
Methods: TL1A expression was investigated in resected ileal specimens from 8 Crohn's disease (CD) patients and 8 non-IBD controls by IHC using an affinity-purified mAb against TL1A. TL1A expression was also studied in endoscopically biopsied colonic specimens from 8 ulcerative colitis patients and 8 non-IBD controls. In addition, the mucosal expressions of CD3, CD4, and CD8, T cell markers, were examined in ileal and colonic specimens of IBD patients and non-IBD controls.
Results: The expression of TL1A at the protein level was absent or minimal in ileal and colonic tissues from controls. On the contrary, intense expression of TL1A was identified in ileal and colonic specimens from IBD patients, especially in CD patients. Staining for TL1A was significantly increased in inflammed area of ileal tissues compared to non-inflammed area from CD patients. CD3, CD4, and CD8 expressions were also significantly increased in ileal and colonic specimens from IBD patients compared to those from controls.
Conclusions: Mucosal TL1A is upregulated in IBD patients, suggesting an important role of TL1A in the pathogenesis of IBD. Further functional studies of TL1A will provide a better understanding of the pathogenesis of IBD.

P398
An Open-label, Pilot Study to Assess Feasibility and Safety of Fecal Microbiota Transplantation in Patients with Mild-Moderate Ulcerative Colitis: preliminary results.

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Background: Fecal microbiota therapy (FMT) has been successful in treating Clostridium difficile (CDI) colitis, while its possible application in the management of inflammatory bowel disease (IBD) remain unclear. We report preliminary results of an open label feasibility trial on fecal microbiota transplantation in mild to moderate ulcerative colitis.
Methods: Outpatients affected by active ulcerative colitis (UC) (partial Mayo score major or equal to 4 with an endoscopic Mayo score major or equal to 1 with no upper limit on Mayo score), negative for C. difficile toxin were enrolled. Concomitant medications were admitted if stable 2 weeks before and thought the trial. Enrolled patients underwent to colonoscopy and received three administration of FMT using 200 cc of fecal slurry from an healthy donor proposed by the patient, negative for active infections. Primary outcome was feasibility and safety of FMT in UC. Secondary end points were: clinical remission defined as partial Mayo score minor or equal to 2 with no subscore major or equal to 1 and clinical response, defined as reduction of Mayo score of at least 2 points at week 2, 6, 12; endoscopic remission defined as Mayo score = 0 at week 6. Consecutive patients with similar clinical features, candidates to anti-TNF-a or immunosuppressant, acted as a "real life" controls (standard therapy, ST).
Results: we enrolled 8 patients for FMT group and 7 patients for ST. Baseline characteristics were similar between FMT (6M, 2 F; mean age 37 ± 7 yo) and ST group (5M, 2 F, mean age 37 ± 10 yo): Pancolitis in 47%, left-side colitis in 33%; 80% were on steroids and 5-ASA, 40% on immunemodulators. In FMT group we observed: 1 SAE (kidney stone) and 2 drop out for disease worsening, while in ST group: 1 SAE (cerebral arterial thrombosis), 2 drop out for disease worsening, 1 infusion reaction. Clinical remission and clinical response for FMT and ST group were respectively: 37.5%/50% and 28.6%/28.6% at week 12, 25%/25% and 14.3%/57.1% at week 2, 25%/50% and 42.8%/42.8% at week 6. Endoscopic remission was observed in 33.3% of FMT group of patients while it was not evaluated in ST group.
Conclusions: The proposed protocol for FMT seems to be safe and well-accepted by UC patients. This FMT protocol have a good potential in inducing clinical response in real life mild-moderate UC patients. Further studies are mandatory.

P399
Short- and long-term outcomes of infliximab treatment for refractory ulcerative colitis and associated prognostic factors: a Japanese single-center study

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Background: In Japan, infliximab (IFX) has been established as a useful treatment option for patients diagnosed with refractory ulcerative colitis (UC). However, the details of IFX treatment in Japanese patients with refractory UC remain unclear. The aim of this study was to analyze the short- and long-term outcomes of IFX treatment in patients with refractory UC and related prognostic factors.
Methods: Retrospective data were collected for 111 patients with refractory UC who received IFX treatment at the IBD Center, Sapporo Kosei General Hospital from July 2005 to November 2013. The Lichtiger clinical activity index (CAI) score of these subjects was >= 5. Remission was defined as a CAI score of <= 4. These scores were calculated at baseline as well as at 2 and 6 weeks and 1 year following IFX administration, and the cumulative colectomy rate following IFX administration was estimated using the Kaplan-Meier method. The prognostic factors that influenced remission rate and cumulative colectomy rate were evaluated using multivariate logistic regression analysis and multivariate Cox regression analysis, respectively.
Results: Of the 111 subjects (mean age, 37.4 years), 47 were female. The mean duration of disease was 5.2 years and the mean CAI score at baseline was 9.4. 70 had total colitis, 39 had left-sided colitis and 2

had proctitis-type colitis. Concomitant treatment with immunomodulator (IM) was administered to 77% subjects. Previous treatment included calcineurin inhibitor treatment in 42 subjects. Steroid resistance was observed in 51 subjects, whereas 60 demonstrated steroid dependence. Remission rates at 2 and 6 weeks and 1 year were 46%, 58% and 48%, respectively. Previous treatment with calcineurin inhibitors was a significant prognostic factor for the lower remission rate at 6 weeks and 1 year, whereas concomitant IM was a significant prognostic factor for the higher remission rate at 6 weeks, as analyzed by multivariate logistic regression analysis. Sex (female) was also a significant prognostic factor only for the higher remission rate at 1 year. The 1-, 3-, and 5-year cumulative non-colectomy rates were 80%, 78% and 75%, respectively. Previous treatment with calcineurin inhibitors and total colitis type were poor prognostic factors that significantly decreased the cumulative non-operation rate. In contrast, sex (female) was a prognostic factor for the lower non-operation rate.
Conclusions: This retrospective study revealed good short- and long-term outcomes of IFX treatment in Japanese patients with refractory UC. Previous treatment with calcineurin inhibitors and total colitis type were prognostic factors for the poor outcomes of IFX treatment, whereas concomitant IM and sex (female) were prognostic factors for the good outcomes.

P400
Setting standards for multi-disciplinary team driven care in inflammatory bowel disease service provision - an expert consensus on key specialists to be involved

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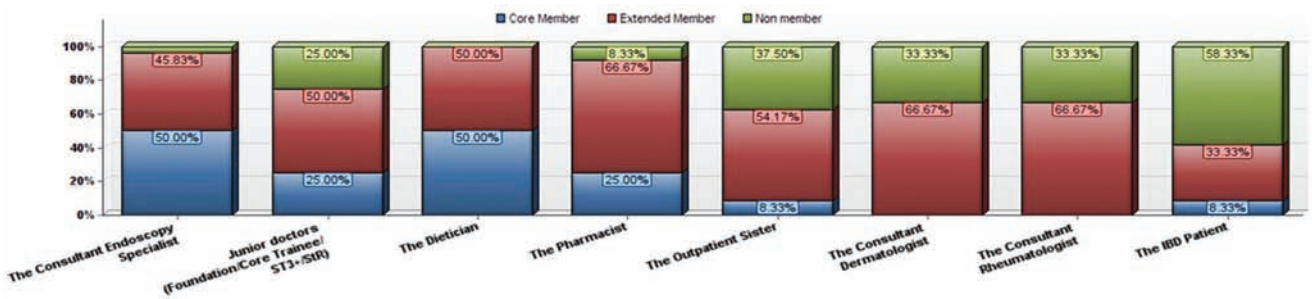
Background: Multidisciplinary Team (MDT) driven care is arising intuitively within the Inflammatory Bowel Disease (IBD) setting. There are no clear evidence-based definitions of which specialties should be key IBD MDT members. Providing a standardised framework, with a clear definition of key members, may enhance its capacity to establish effective quality improvement. This study aims to obtain a definition the key specialties that should be members of the IBD MDT, through expert-based consensus.
Methods: This was a prospective, qualitative study using an online survey. An eligibility criterion was established to ensure panel members had recognised expertise in the field of IBD. Consensus was defined by an agreement of greater than 70% across panelists. The definition of a 'core member' was a regular attendee with contractual IBD MDT responsibilities and an 'extended member' was an attendee invited only by a core member without contractual IBD MDT responsibilities. Dichotomous responses were represented in proportions.
Results: In total, 24 participants were recruited into the expert panel. Consensus for being a core member was demonstrated for radiologists [24/24], gastroenterologists [24/24], colorectal surgeons [24/24], IBD nurse specialists [24/24], histopathologists [21/24] and the MDT co-ordinator [21/24]. Consensus for being an extended member was demonstrated for paediatricians [17/24], research fellows [17/24] and psychologists [22/24].
Heterogeneity (<70% agreement) in opinion was present on the role of the consultant endoscopy specialist, junior doctors, the dietician, the pharmacist, the outpatient nurse, the consultant dermatologist, the consultant rheumatologist and the IBD patient.
Conclusions: The core members of the IBD MDT, with contractual recognition of IBD MDT responsibilities, should be radiologists, gastroenterologists, colorectal surgeons, IBD nurse specialists, histopathologists and the MDT co-ordinator. The extended members should be paediatricians, research fellows and psychologists. Defining key specialists as IBD MDT members is necessary to reduce variation in care standards. An evidence-based recognition through expert consensus can aid contractual definition of IBD MDT responsibilities for core members. Further validation and specialist role definition are required prior to implementation into standards.

"Figure 1 - Bar chart demonstrating consensus (> 70% agreement) for core members and extended members of the IBD MDT."



"Figure 2 - Bar chart representing heterogeneity in opinion (< 70% agreement) for specialists in the IBD MDT"

P401
Adalimumab as first-line anti-TNF treatment in ulcerative colitis. A "real-life" observational study

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Background: Recently, randomized controlled trials have demonstrated that Adalimumab (ADA) is effective in the induction and maintenance treatment of moderate to severe ulcerative colitis (UC) that did not present sufficient response to conventional therapy, including corticosteroids and immunosuppressants. However, the absolute benefit in terms of clinical practice requires new evidence when used as the first anti-TNF treatment. Our goal is to obtain data on efficacy and safety of ADA in treating patients with active ulcerative colitis who had not previously received another anti-TNF.
Methods: Retrospective review of 17 patients older than 18 years diagnosed with UC refractory to conventional treatment, ADA-treated for 1 year, according to product label in real-life situations. Response and clinical remission at 6 months and 1 year was assessed according to partial Mayo index.
Results: Seventeen patients (10 men) with a mean age of 49.7 years. Duration of disease 6 years. Montreal classification of UC: Extent - E2 6 patients (35.3%), E3 11 patients (64.7%). Severity - S1 2 patients (11.8%), S2 10 patients (58.8%), S3 5 patients (29.4%). Receiving concomitant immunosuppressive treatment 16 patients, 15 with azathioprine / 6MP (88.2%) and 1 with methotrexate (5.9%). All were treated with induction with ADA at doses of 160/80 mg and maintenance with ADA 40 mg every 2 weeks. Response and remission in 16 (94.1%) and 12 (70.6%) at 6 months and 15 (88.2%) and 14 (82.4%) at 12 months was observed. Eight patients (46.1%) required intensification of treatment. Colonoscopy was performed in 11 patients at 12 months; 7 (63.6%) had mucosal healing. Treatment was suspended in 4 patients (23.5%), 1 of them for loss of efficacy. In 2 patients malignancies were diagnosed, 1 of them showed recurrence of low-grade bladder urothelial carcinoma and another was diagnosed with lung cancer (ex-smoker). Four patients had mild infectious complications. One patient (5.9%) required colectomy due to sustained activity refractory to second anti-TNF treatment with infliximab.
Conclusions: ADA has shown efficacy in the treatment of UC as first line anti-TNF in real clinical practice, in adult patients. Response and remission real clinical data with ADA as first line anti-TNF in UC are higher than randomized controlled trials efficacy data of ADA versus placebo. It is important to monitor the development of new neoplasias, mainly if there are risk factors or history of neoplasia.

P402
Anal neoplasia in inflammatory bowel disease is associated with HPV and perianal disease

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Background: Patients with inflammatory bowel disease (IBD) may develop anal squamous cell carcinoma. Little is known about predisposing factors.
Methods: We retrospectively reviewed the records of IBD patients diagnosed with anal neoplastic lesions presenting at our Center between March 1st 1994 and September 9th 2014. Histological specimens were reviewed to classify anal neoplastic lesions. Presence of HPV was assessed using immunohistochemical staining in combination with global and type-specific molecular PCR for HPV16 and 18. Lesions with p16 block-positive staining (p16+) and negative PCR for HPV underwent additional immunostaining for p53.
Results: We identified 17 IBD patients with anal neoplastic lesions (8M/9F, 9 ulcerative colitis/7 Crohn's disease/1 indeterminate colitis). Invasive squamous cell carcinomas (SCCs), high grade anal intraepithelial neoplasms (ASIN-H) and low grade anal intraepithelial neoplasm (ASIN-L) were identified respectively in 6, 8 and 3 patients. In the SCC group, 5/6 patients had Crohn's disease with perianal involvement compared to 2/8 and 0/3 in the ASIN-H and ASIN-L group, respectively. Information regarding medical therapy at the time of anal cancer diagnosis was available in 10 patients, of which 5, 2 and 2 were on thiopurine, steroids and biological therapy, respectively. In patients with SCC, 3/6 and 1/6 were HPV 16+ and 18+ respectively. The patient who was HPV18+ had more than a 10 year history of UC and underwent proctocolectomy with ileo-anal pouch anastomosis 11 years before development of anal cancer. Eight out of 8 patients with ASIN-H lesions were HPV16 but not 18 positive. One out of 3 patients with ASIN-L was HPV16+.
Conclusions: In our experience, anal neoplasia in IBD is associated with HPV infection and perianal Crohn's disease. Prospective studies are needed to confirm these results.

P403
Colectomy is not a cure for ulcerative colitis: A systematic review

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Background: Colectomy for ulcerative colitis (UC) is associated with short- and long-term complications. Estimates of the frequency of such complications are highly variable. Understanding the true burden of surgical complications is important to clinicians in assessing the risks and benefits of colectomy versus continued medical therapy. A systematic review was therefore conducted to ascertain the frequency or incidence of surgical complications occurring in patients undergoing selected colorectal procedures for UC.
Methods: Embase, MEDLINE and The Cochrane Library were searched for studies published from 2002-2014 reporting the incidence of any of the following surgical complications of colorectal procedures in adults with UC: ileo-anal anastomosis or ileal pouch-anal anastomosis, ileo-anal pouch procedure, restorative proctocolectomy, subtotal colectomy or total colectomy. Included studies were randomised controlled trials (RCTs) and prospective or retrospective non-RCTs. Conference proceedings from January

2011-January 2014 were also searched manually. Quality assessment for risk of bias was conducted for each individual study.
Results: A total of 99 studies (98 non-RCTs and one RCT) enrolling 184,157 patients and reporting outcomes from surgical procedures conducted between 1976 and 2014 were identified. Early complications (occurring ≤ 30 days postoperatively) were reported in 11-44% of patients (32 studies). Late complications (occurring >30 days postoperatively) were reported in 19-55% of patients across studies. The most frequently occurring short-term complications (≤ 30 days) were infectious complications (16%) and general pouch-related complications (8%). The most frequent long-term complications (>30 days) were pouchitis (30% of patients), Crohn's disease of the pouch (25% of patients) and infertility (50% of patients).
Conclusions: Approximately one third of patients undergoing surgery for UC are anticipated to experience long-term or later occurring postoperative complications. Colectomy is not a cure for UC, although it remains an appropriate therapeutic strategy for specific groups of patients.

P404
Calcineurin inhibitors are safe and effective for induction of remission in patients commencing vedolizumab for IBD

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Background: Vedolizumab, a monoclonal antibody to alpha-4 beta-7 integrins recently approved for inflammatory bowel disease, has demonstrated efficacy in randomized clinical trials. However in these trials patients were not eligible to receive concomitant calcineurin inhibitors during induction. Therefore the success and safety of using calcineurin inhibitors as induction agents in combination with vedolizumab is unknown.
Methods: University of Chicago patients with CD and UC who received vedolizumab and who were followed for at least 12 weeks were fully characterized and included in an IRB-approved post-marketing study. Response and remission rates in those with concomitant exposure to tacrolimus or cyclosporine were specifically analyzed. Clinical activity was assessed using the Harvey Bradshaw Index (HBI) or Simple Clinical Colitis Activity Index (SCCAI) at baseline and at pre-defined times of follow-up. Clinical response was defined as a reduction of 3 or more in HBI or SCCAI and clinical remission was defined as HBI less than or equal to 4 or SCCAI less than or equal to 2.
Results: Between May 2014 and November 2014, 130 patients had initiated vedolizumab therapy. 69 patients (31 male, median age 35, CD 63.8%) had returned for post-induction follow-up at the time of this abstract. 7 of these patients (1 CD, 6 UC, 10.1%) received tacrolimus or cyclosporine during the induction phase of vedolizumab; 4 had active disease at baseline and 3 who were in clinical remission but calcineurin inhibitor-dependent. All 7 of these patients achieved or maintained clinical remission by week 14 of vedolizumab treatment and 5 (71.4%) were off all calcineurin inhibitors at this follow-up. Patients on concomitant calcineurin inhibitors v those on no calcineurin inhibitors achieved higher rates of clinical remission (100.0% v 34.2%) and response (80.0% v 51.2%). Apart from one episode of sinus congestion, no adverse events were reported with duel therapy with calcineurin inhibitors and vedolizumab.
Conclusions: Using a combination of cyclosporine or tacrolimus with vedolizumab to induce remission in inflammatory bowel disease is effective and safe. This induction strategy should be studied further in select patients.

P405
Pediatric Crohn's disease with iron deficiency anemia: A follow-up study of intravenous iron treatment

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Background: Iron deficiency anemia(IDA) is largely recognized as a treatable cause of anemia,in Cronh's Disease(CD)(ault and pediatric patients)Increasing evidence demonstrates the efficacy and safety of several IViron formulas,compared with oral iron.However,in pediatricIBD patients withIDA, this evidence is yet insufficient. As far as we know, no previous prospective studies have reported the use of IViron in pediatric CD.The present study aim's to evaluate the safety,tolerance and short and long term efficacy of these formulas in this patients.
Methods: Pediatric patients with CD-IDA(outpatient setting), were prospectively recruited, during a 40-month period(May2011-October2014).Disease activity (PCDAI) determined before and after treatment. Anemia defined according to OMS criteria. Treatment with IV iron (iron sucrose-age<14years or ferric carboxymaltose-age ≥ 14years).Total dose determined according to Ganzoni formula. Hemoglobin(Hb),serum ferritin and transferrin saturation,determined before treatment and, 4weeks after treatment.
Results: Twenty patients (14 female; mean age:17,2 years[25-7,3]) included. Mean disease duration:5,1years(12,3-0,3); mean age at diagnosis:12,1years(17,4-05).Before IV iron treatment, 11 patients were in remission and 9 had mild active disease(mean 12,7 [25-7,5]). Previously to IV iron treatment, mean Hb:10,5 g/dl(11,9-7,9), mean ferritin 20,1 ug/L(90-0,7) and mean transferrin saturation:6%(14-2). Mean Hb in patients < 12 years:11g/dl(11,5-10,3),females ≥ 12years:9,9 g/dl(11,9-7,9) and males ≥ 12 years:11,1g/dl (11,9-10). Considering disease activity,patients in remission: mean Hb of 10,5 g/dl (11,9-7,4)and mean ferritin:6,8ug/dl(18,7-0,7);mild disease patients, mean Hb:10,6 g/dl (11,9-9,6);mean ferritin:43,3ug/dl [133,9-4,9]. Nine patients treated with iron sucrose (mean dose 672,6 mg dl [850-450]) and 11 with ferric carboxymaltose (mean dose 828,6 mg dl [1000-650]). No major adverse reactions were documented.Response to treatment: mean Hb (whole sample) 12,7g/dl(14,5-11,4),mean Hb in patients<12 years:12g/dl(12,6-11,4);females ≥ 12 years: 12,6g/dl (13,6-12,3);males ≥ 12 years: 13,3g/dl(14,5-10). Mean Hb in iron sucrose group: 12,3g/dl (13,2-11,4) and ferric carboxymaltose group: 13,1g/dl (14,5-11,4).Within a mean follow-up period after treatment of 18months(40-1,2), 6 patients needed re-treatment[after a mean period of 15,5 months (25-2)].
Conclusions: Our prospective study, with a significant follow-up period, further demonstrates the efficacy and safety of both IV iron formulas. Although only a small number of patients needed re-treatment in this study, it reinforces the importance of long term follow-up of the iron status in pediatric CD patients, especially in those in remission and/or mild disease activity.

P406
Adipose derived regenerative cells injection as a novel method of enterovesical fistula treatment in Crohn's Disease: A case report

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Background: Up to date, the mesenchymal stromal cells (MSC) have been adapted in the treatment of fistulising Crohn`s disease with promising results. However, in most of the trials the MSC were obtained from healthy donors or needed long cultivation in laboratory environment.

Methods: A 52-year-old female, suffering from Crohn`s Disease for 12 years, did not achieve remission since the time of diagnosis, despite numerous treatments such as anti-TNFs and other non-standard therapies (i.e. tacrolimus or mycofenolate mofetil). The fistulising and penetrating subtype of the disease led to numerous laparotomies and several repositions of the ileostomy due to the formation of enterocutaneous fistula and lack of healing.

Patient was hospitalized with suspicion of urosepsis and symptoms suggestive of faecaluria. At the time two fistulas were present - enterocutaneous and perianal. The urine culture revealed severe polibacterial infection susceptible only to imipenem, however the targeted therapy did not lead to alleviation of the symptoms. The cystoscopy performed after oral application of methylene-blue colorant showed the presence of enterovesical fistula, approximately 3x1cm, with active suppuration of the intestinal content. As the patient was in critical state with signs of cachexia and had undergone numerous laparotomies, the standard surgical intervention was not considered.

After the acceptance of the Ethic Commitee, the injection of adipose derived regenerative cells (ADRC) into the enterovesical fistula was performed. Under general anaesthesia, a manual liposuction was carried out. 260 ml of lipoaspirate was immediately transferred into the CellCelution 800 system. After 2 hours, 5ml of ADRC suspended in Ringer solution was obtained.

During cystoscopy 4,5 ml solution containing 2,43*10^7 ADRC was injected through the needle routinely used for the botulin injections, in 0,5 mL portions around the fistula into the detrusor muscle. All procedure took 20 minutes. Obtained ADRC expressed in 99,5 ± 0.4% CD73, CD90 , CD105 and 9.0 ± 0,5% cells CD34, CD19, CD11b and HLA-DR surface markers.

Results: During the first 24 hours after the treatment patient suffered from temporal mild hypertension. No other AE were observed. Control cystoscopies after 2 and 3 weeks revealed complete healing of the fistula. During 5-month follow-up, the symptoms suggestive of enterovesical fistula did not recur.

Conclusions: In our study for the very first time we managed to close the enterovesical fistula in critically-ill CD patient resistant to standard treatment, as traditional surgical approach was no longer appropriate. Further studies are needed to assess the safety and efficacy of the estabilished method.

P407
Prevalence of methotrexate intolerance in pediatric inflammatory bowel disease

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Background: Methotrexate (MTX) intolerance is defined as gastrointestinal and behavioural symptoms occurring before (anticipatory/associative) or after MTX administration that could lead to treatment discontinuation. Although a common complication of the drug, its prevalence is difficult to assess probably due to the subjective nature of the symptoms. A Methotrexate Intolerance Severity Score (MISS) questionnaire developed in rheumatology has shown a prevalence of MTX intolerance of 50.5% for children with juvenile idiopathic arthritis. In children with inflammatory bowel disease (IBD), the exact prevalence of MTX intolerance has never been evaluated. The aim of this study was to determine the prevalence of MTX intolerance in paediatric IBD using the MISS questionnaire.

Methods: From July to November 2014, patients with paediatric IBD followed in the IBD clinic of Sainte Justine hospital who had received at least 2 months of MTX along with their parents were contacted by telephone and invited to complete the MISS questionnaire. A cut-off score of >=6 points with >=1 points for anticipatory and/or associative and/or behavioural items was used to define MTX intolerance.

Results: Sixty-four patients and 44 parents completed the MISS questionnaire. Two patients refused to participate. MTX treatment had been initiated between 2004 and 2009 for 23 patients and between 2010 and 2014 for 41. Thirty-eight patients (59%) were males and mean age (±SD) at initiation of MTX was 13.4 ± 3.7 years. Thirty-two (50%) and 27 (42%) were deemed intolerant to MTX based on the responses of the child and parents, respectively. The mean (±SD) MISS score was 6.2 ± 5.8 for children and 6.8 ± 6.9 according to parents. There was a good correlation between parents' and children's answers: r=0.77.

Seventy percent of patients had gastrointestinal symptoms after taking MTX, 52% had symptoms when thinking of MTX (associative), 52% had symptoms prior to taking MTX (anticipatory) and 50% had behavioural symptoms. Prevalence of gastrointestinal symptoms was: 38% abdominal pain, 72% nausea, and 25% vomiting. The other symptoms noted were headaches (n=4), fatigue (n=2), alopecia (n=1) and negative conditioning to ondansetron (n=1).

Conclusions: MTX intolerance is frequent in paediatric IBD. The MISS questionnaire was feasible and could be implemented to identify early those patients who are most likely to develop MTX intolerance, precluding the need to discontinue treatment after initiation. Further studies seeking to identify clinical and socio-demographic factors predisposing to MTX intolerance are currently being pursued.

References:

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Differences in biologic efficacy and dose-escalation among anti-TNF agents in Crohn´s disease and ulcerative colitis

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Background: Secondary loss of response is a frequent event occurring during anti-TNF therapy that usually requires dose intensification. The aim of this study was to evaluate differences in the prevalence of dose-escalation among Crohn´s disease (CD) and ulcerative colitis (UC) patients treated with infliximab (IFX) or adalimumab (ADA) in clinical practice.

Methods: We performed a retrospective observational study of patients with IBD receiving IFX/ADA treatment from January 2011 until April 2014 at our Unit. Patients losing response after 2 months or more of anti-TNF maintenance therapy and in whom treatment was intensified were included. Differences in the rates of dose intensification and intensification time, between CD patients on IFX/ADA treatment were compared. We also evaluated differences in the risk for intensification between CD/UC patients on IFX treatment.

Results: Of 83 patients (CD=62, UC=21) receiving anti-TNF treatment (IFX=44, ADA=39), 34 patients (CD=19, UC=15) received dose intensification (IFX=23, ADA=11). Clinical remission was achieved in 76.9% of CD patients treated with ADA and 69.6% of CD patients on IFX treatment. We observed clinical remission in 81% of UC patients treated with IFX. No statistically significant difference was found between any of the groups.

Intensification was observed in 20% and 25% of CD patients treated with ADA and IFX respectively. Loss of response occurred in the first year of IFX/ADA treatment in 88% and 64% of cases respectively. Although the percentage of earlier loss of response was higher in the IFX group, no statistically significant differences were found. The rate of intensification per CD patient-month during the first year of IFX/ADA therapy was 2.8 and 1.5 respectively.

Significantly more UC patients on IFX treatment experienced dose intensification compared with CD patients (72% vs 25%; p=0.0366). The relative risk to experience loss of response to IFX in UC patients was 2.05 (95% CI 1.10-3.82) significativily higher than the risk of intensification in CD patients. The rate of intensification per patient-month during the first year of IFX therapy was 2.8 for CD and 3.9 for UC (p<0.005). De-escalation was higher in UC than CD patients although no significative statistical differences were found.

Conclusions: In our large cohort of IBD patients receiving anti-TNF treatment dose intensification is often required.

In nearly 25% of CD patients on anti-TNF treatment, dose escalation was required especially in the first year of treatment independently of which anti-TNF was being used.

UC patients on IFX treatment showed a higher risk for loss of response compared with CD patients, although deintensification was possible in a higher percentage of UC patients

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Smoking is associated with extra-intestinal manifestations in inflammatory bowel disease

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Background: Smoking influences the disease activity in inflammatory bowel disease (IBD). We aimed to study the association between smoking and extra- intestinal manifestations (EIMs) in IBD.

Methods: The association between smoking and EIMs such as joint complaints, chronic skin disorders and eye complaints was investigated in three cohorts. The COIN- study is a large prospective cohort study with data collected by questionnaires about demographics, disease course and associated cost items. In the Groningen cohort, questionnaires on cigarette smoke exposure and disease behaviour in IBD patients were collected. The JOINT- study is a prospective longitudinal study focused on IBD patients with and without back pain and peripheral joint complaints. A putative dose-response relationship between smoking and EIMs, and the association between smoking and specific phenotypes of arthropathies was explored.

Results: In the COIN study, 3,030 patients (1,558 Crohn's disease (CD), 1,054 ulcerative colitis (UC) and 418 IBD-unspecified) were enrolled; 16.0% were current smokers. In the Groningen cohort, 780 IBD patients (420 CD, 298 UC, 62 IBD-unspecified) were included; 23.6% were current smokers. In the JOINT study, 255 patients (186 CD, 69 UC) were enrolled; 23.5% were current smokers. EIMs were significantly more prevalent in the smoking IBD population (COIN: 39.1% vs. 29.8%, p <0.001 and Groningen: 42.8% vs. 31.2%, p <0.001). This association was more pronounced in CD than in UC. Joint complaints were the most prevalent EIM in both CD and UC. Of all EIMs, smoking appeared to have the most significant association with joint complaints (COIN: CD 30.7% vs. 22.1%, p <0.001, UC 25.3% vs. 18.5%, p =0.11 and Groningen: CD 46.4% vs. 40.4%, p =0.26, UC 31.0% vs. 23.0%, p =0.34). Likewise, in the JOINT study, smoking was more prevalent in IBD patients with artropathies (30.3% s. 13%, p =0.001). A dose-response relationship is suggested by the fact that EIMs were more prevalent in heavy smoking patients compared to low exposure smokers (56.0% vs. 37.1%, p =0.10). Smoking was not associated with a specific phenotype of spondylarthropathy.

Conclusions: The results of three cohort studies confirm a positive association between smoking and extra-intestinal manifestations in IBD. This association appears to be subject to a dose-response effect.

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Anti-TNF improves iron availability in Inflammatory Bowel Diseases, modulating Pro-hepcidin in an Erythroferrone-independent fashion

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Background: Anaemia is a common feature of Inflammatory Bowel Disease (IBD), resulting from a combination of iron deficiency and of anaemia of chronic disease (ACD). ACD is characterized by macrophage iron retention induced by inflammatory conditions. Hepcidin, an acute phase protein, is the master inducer of iron accumulation during ACD. Hepcidin is potently induced by pro-inflammatory cytokines, such as IL-6 and inhibited by Erythroferrone, a newly discovered hormone, which is produced by erythroblasts in response to erythropoietin (EPO) stimulation (Kautz L, Nat Genet 2014; Kautz L, Blood 2014). Remarkably, TNF downregulates EPO, thus it reduces Erythroferrone production. Aim of the study was to evaluate whether anti-TNF therapy, while downregulating several pro-inflammatory mediators, modulates hepcidin and Erythroferrone production, leading to a restoration of normal iron homeostasis in IBD.

Methods: Sera were collected from 21 IBD patients undergoing Infliximab or Adalimumab therapy, before each anti-TNF administration, for the first 6 weeks of therapy. Pro-hepcidin, a dosable hepcidin precursor, EPO, Erythroferrone, C reactive protein (CRP), iron markers and haemoglobin levels were measured by means of immunoassays and clinical activity indexes evaluated.

Results: Serum pro-hepcidin was significantly decreased between baseline and week 6 (139.42 ± 18.96 vs. 94.14 ± 9.19 ng/ml, p=0.0048); consistently, circulating levels of other acute phase proteins, such as ferritin and CRP were reduced (68.19 ± 18.23 vs. 37.48 ± 13.22 ng/ml, p=0.0223 and 1.80 ± 0.42 vs. 0.53 ± 0.11 mg/dl, p=0.0036, respectively); we also detected an increase in serum iron (37.71 ± 2.77 vs.

45.14 ± 3.78 µg/dl, p=0.0501) and total transferrin (201.5 ± 8.12 vs. 241.2 ± 10.99 mg/dl, p=0.0048), which is consistent with the reduction of systemic inflammatory activation. Remarkably, at week 6, haemoglobin was significantly increased (11.44 ± 0.33 vs. 12.14 ± 0.29 g/dl, p=0.0137). No changes in EPO nor in Erythroferrone levels were detected.

Conclusions: Anti-TNF therapy improves iron metabolism and, subsequently, anaemia in IBD. This effect appears to be related to a relevant decrease of hepcidin, a master regulator of ACD. The downregulation of hepcidin production is likely to be induced by the modulation of the cytokine network, rather than to modifications of the newly identified EPO-Erythroferrone axis.

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Five year outcomes of Crohn's anastamotic strictures treated with balloon dilatation

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Background: Clinically relevant stricture is usually defined as a luminal narrowing with pre-stenotic dilatation and obstructive symptoms. Ileal resection is a good treatment for symptomatic Crohn's related strictures, but disease recurrence after 15 years is more than 50%, with the need for a second resection. Long-term outcome of endoscopic balloon dilatation is unclear as most cohorts have a follow-up time of less than 3 years.

Methods: All endoscopic balloon dilatations performed in Crohn's disease (CD) patients treated at St Mark's Hospital, Wolfson Unit, between 2007 and 2009 were retrospectively reviewed with the aim of collecting long-term (>5 year) data. Pre-endoscopic imaging was obtained for all patients with information collected on length of stricture, signs of activity of Crohn's disease and upstream dilatation. Clinical data on symptoms before and after each dilatation were obtained. Endoscopic data including level of activity, size of balloon and therapeutic success was collected.

Results: A total of 37 patients were identified from hospital records with a median age of 46 years (39-55) with 16/37 (43%) male and a median follow-up period of 6.48 years (5.81-7.89). The median duration of disease was 24 years (17-30). From cross-sectional imaging (CT/MRI), length of stricture was described in 31/37 cases with a median of 20 mm (15-40) and features of active inflammation (mucosal enhancement) at anastomosis in 22/30 (73%) with upstream dilatation in 14/30 (48%). At the time of endoscopy, active disease was described in 24/27 (88.9%) of reports with a median balloon dilatation size of 15mmHg which achieved therapeutic success (passable) in 33/37 (89%). 6/37 (16%) have had surgical resection.

The median number of dilatations was 2 (range 1-6) with a median time to repeat dilatation of 23 months (7.2-56.9). 60% of patients required repeat dilatations. It was not necessary to perform repeat dilatations in 9/37 (24%) patients. Active disease at time of endoscopy was the only factor that predicted for repeat dilatations (p=0.006). (Table 1)

Multivariate analysis of factors predicting repeat dilatation

Underlying demographics	Age	0.29
	Duration of disease	0.432
Cross-sectional imaging	Mucosal enhancement	0.107
	Upstream dilatation	0.271
Endoscopy	Active disease (i2-i4)	0.006
	Size of balloon diameter	0.094

Conclusions: At long term follow-up, 16% of patients required surgical resection. 24% of patients were well with no further endoscopic intervention required. 60% required intercurrent endoscopic dilatations. This is the longest follow-up period in the literature and demonstrates that the effects can be durable and avoidance of surgery possible in a group of patients with anastamotic strictures.

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Fecal calprotectin as predictor of relapse in asymptomatic Ulcerative Colitis

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Background: To assess the predictive ability of relapse of fecal calprotectin (CF) in asymptomatic ulcerative colitis (UC) patients.

Methods: Retrospective analysis of UC patients with a FC assay done being asymptomatic. Patients with clinical activity within the 6 months prior to the FC assay were not included, as well as those who needed a treatment change in the previous three months.

Variables collected included demographic characteristics, tobacco use, phenotype UC according to Montreal's classification and the levels of FC (mcg/gr). We perform an analysis of the clinical course of the disease after a 12 months clinical follow-up period, considering a significant clinical relapse in those who required treatment changes to control the new onset symptoms.

Results: We included 101 patients (56 men, 45 women). Mean age at diagnosis was 33,03 ± 15,73 years (2-78y); 15 (14,9%) were smokers. Extensive colitis was found in 62,4% of patients, 34,7% had left colitis and 3% proctitis. Mean value of FC was 182,4 ± 237,47 mcg/g (1,3 - 1135).

During the next 12 months following the FC assay, 28 patients (27,7%) suffer a relapse of the disease; 14 of those requiring only a dose increase of salicylates, 4 treated with steroids and 10 needing both jointly.

FC value was higher in patients who required treatment modification (314,45 ± 283,37 vs 131,79 ± 197,05; p 0,001); 80,8% of those patients with FC less than 200 mcg/g maintained asymptomatic in the next year of follow-up, whereas when FC was higher than this threshold only the 50% kept asymptomatic in that same period of time (p 0,002). A FC level lower than 200 mcg/gr appears as a protective factor against clinical relapse during the next year follow up (odds ratio 0,384(IC-95% 0,211-0,698)).

No significant differences were found in the mean FC level regarding the type of treatment modification needed, being 278,10 ± 309,09 mcg/g for patients requiring only dose increase of salicylates and 399,65 ± 288,09 mcg/g for those treated with steroids (p 0,792). No relation was found between sex, tobacco use and UC characteristics and the risk of clinical relapse.

Conclusions: FC values lower than 200 mcg/g in asymptomatic UC patients predict a good course of the disease within the next year

follow-up, whereas higher levels imply a 50% incidence of relapse. Probably histologically active disease without endoscopic or clinical impact may explain the low positive predictive value of higher FC levels.

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Healthcare expenditures for inflammatory bowel disease peak in patients with a short disease duration

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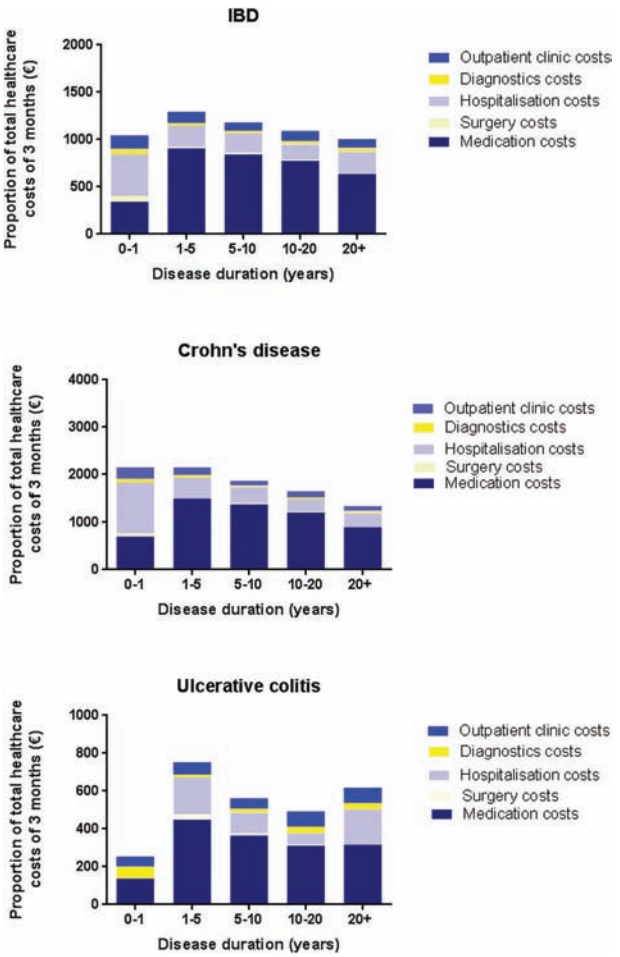
Background: We aimed to study whether disease duration influences the healthcare costs in inflammatory bowel disease (IBD) patients in a large cohort.

Methods: A large number of IBD patients from academic and non-academic hospitals were prospectively followed for two years (the COIN- study). At baseline, the disease duration of all patients was calculated. Used healthcare resources, disease activity and quality of life were assessed using three-monthly questionnaires. Healthcare resources were multiplied by their unit prices to obtain costs. These parameters were cross-sectionally compared between patients with a short (0-1 yr), median (1-5 yrs), long (5-10 years) and extended (10-20 yrs and >20 years) disease duration at baseline.

Results: A total of 3,030 patients (1,558 Crohn's disease (CD), 1,054 ulcerative colitis (UC) and 418 IBD-unspecified) were enrolled in the study. Fifty-six patients had a disease duration of 0-1 years, 502 of 1-5 years, 569 of 5-10 years, 899 of 10-20 years and 998 of over 20 years.



"Distribution of total healthcare costs during disease duration"

The proportion of patients with active disease gradually decreased over time, being 30.4% in IBD patients with a short disease duration, and 13.2% in those with an extended disease duration (CD: from 36.0% to11.8%; UC: from 21.1% to 16.5%). The total IBD healthcare costs peaked at 1-5 years of disease duration, which was mainly due to a high number of TNFalpha inhibitor users (CD: 30.7% vs. 17.7% after 20 years; UC: 5.7% vs. 3.4% after 20 years).

In patients with a longer disease duration, total healthcare costs were lower than in the first years after diagnosis. In CD, healthcare costs after the first year following the diagnosis shifted from hospitalisations to medication costs (TNFalpha- inhibitors). Hereafter, medication costs remained the major driver of total healthcare costs. In UC, total healthcare costs decreased over time, but increased again in patients with a disease duration of 20yrs or more, due to an increase of hospitalisations. The quality of life was lowest in patient shortly after diagnosis of IBD and increased gradually in both CD and UC patients with a longer disease duration (median IBD- questionnaire: CD from 175 to 179; UC from 179 to 190).

Conclusions: The healthcare costs of IBD peak in patients with a short disease duration. The quality of life is higher in patients with a longer disease duration.

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Cannabidiol for symptomatic treatment of ulcerative colitis: Results from a randomised, double-blind, placebo-controlled, parallel group, multi-centred pilot study

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Background: There is accumulating evidence that cannabidiol (CBD) has anti-inflammatory properties that could be exploited for the symptomatic relief of IBD. This proof-of-concept double blind, randomised, placebo controlled trial assessed the efficacy, safety and tolerability of CBD botanical drug substance (BDS) in patients with mild to moderate UC.

Methods: Patients with left-sided or extensive UC aged ≥18 years, with a Mayo score 4-10 (endoscopy score ≥1) and on a stable dose of 5-ASA (or previously used 5-ASA), were randomised 1:1 to receive either CBD BDS (GWP42003) (29 patients) or placebo (31 patients). The IMP was presented as hard gelatin capsules containing 50 mg GWP42003 (purified from a proprietary *Cannabis sativa* L. chemotype containing predominantly CBD and 4% Δ^9-tetrahydrocannabinol [THC]); or excipients alone for the placebo. Patients titrated to their maximal tolerated dose over two-weeks, aiming to achieve 500 mg daily (250 mg b.d.) and maintained this dose for 10 weeks. The primary endpoint was the number of patients in remission (Mayo total score ≤2; no sub-score >1) at week 10. Statistical tests were two-sided at the 10% significance level.

Results: Patients in the active group found the IMP more difficult to tolerate than placebo patients, taking on average one-third fewer capsules during the maintenance period, and having a higher number of compliance-related major protocol deviations than placebo (12 vs. 4); principally insufficient exposure. With only 59% protocol-compliance in the GWP42003 group, the more relevant per-protocol (PP) analysis set was used to assess many efficacy measures. Remission was observed in both treatment groups at the end of treatment; whilst proportionally in favour of GWP42003 (28% vs. 26%), the difference was not significant (p=0.753; Intention to treat analysis set). PP analysis of the Mayo total and partial Mayo scores revealed significant treatment differences in favour of GWP42003 (p=0.068 and p=0.038, respectively). PP analysis of Physician's Global Assessment of Illness Severity, Subject Global Impression of Change and patient-reported quality of life outcomes also significantly favoured GWP42003 (p=0.069, p=0.003 and p=0.065, respectively). All 60 patients were included in the safety analysis; the majority of AEs were mild to moderate in severity and many in the GWP42003 group were likely attributed to the THC. A higher proportion of GI-related AEs, indicative of a worsening in underlying UC, were seen in placebo patients.

Conclusions: Whilst this exploratory trial did not reach its primary endpoint, several signals suggest that GWP42003 may be beneficial for the symptomatic treatment of UC; larger trials are warranted.

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Fecal calprotectin and serum C-reactive protein predict outcome of infliximab induction therapy in inflammatory bowel disease.

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Background: The neutrophil granulocyte-derived protein calprotectin is an inflammatory marker in Crohn's disease (CD) and ulcerative colitis (UC). We assessed the importance of the numerical decrease of FC with infliximab induction therapy with C-reactive protein (CRP) and clinical activity evaluated by Harvey-Bradshaw index (HBi) and partial Mayo score (pMS).

Methods: Out of 180 patients with IBD, 144 with CD and 36 with UC were treated with infliximab. Indices, FC and CRP were evaluated at two occasions: at baseline before infliximab introduction and after 12 weeks. Responders were followed 24 weeks further to assess the FC values with incident outcome. Values are presented as median and interquartile range (IQR). Spearman nonparametric correlation test served for correlation analyses. Sensitivity, specificity and likelihood ratio were analyzed using the ROC (receiver operating characteristic) curve. Survival curves were analyzed with Kaplan-Meier analysis and log-rank test. P<0.05 was considered significant.

Results: After induction, 151 patients (83%) responded to therapy and 116 (65%) attained clinical remission. At baseline, HBi was 11 (6.5-17.5), pMS 8.5 (7.5-9), FC 2060 (1495-5507) µg/g and CRP 13 (6.5-35.5) mg/L. Following induction therapy, indices, FC and CRP declined from baseline levels (all p<0.01). Among responders, FC decreased to 210 (70-358) µg/g compared with non-responders 1425 (304-2171) µg/g. The corresponding CRP levels were 2 (1-4) mg/L and 5.5 (3.5-27.5) mg/L. In those reaching remission, FC and CRP decreased to 207 (75-354) µg/g and 2 (1-3.5) mg/L, respectively. Clinical responders were followed 24 weeks to predict incidents (dosage increase, shortening of infusion interval, surgery) based on FC levels. The ROC optimal cut-off point was 221 µg/g (sens 90%, spec 71%, likelihood ratio 3.15). Area under the curve was 0.88. Using FC 221 µg/g as cut-off, FC exceeding 221 µg/g after induction therapy was studied in conjunction with an incident within 24 weeks. In those with FC < 221 µg/g, two out of 75 patients (3%) had an incident within 24 weeks of induction therapy, among those with FC >221 µg/g that number was 25 out of 41 (61%) within the same period. Clinical activity correlated with FC (Spearman r=0.62, p<0.001) as well as with CRP (Spearman r=0.60, p<0.001).

Conclusions: Clinical indices (HBi, pMS) correlate well with FC and CRP levels during infliximab induction therapy. The indices, FC

and CRP levels decreased significantly from baseline levels among patients responding to infliximab treatment. However, a FC level >221 µg/g after induction therapy is associated with a disease incident within the following 24 weeks in half of the cohort.

P416
Is faecal calprotectin (FC) a reliable marker of isolated small bowel Crohn's disease (CD) activity?

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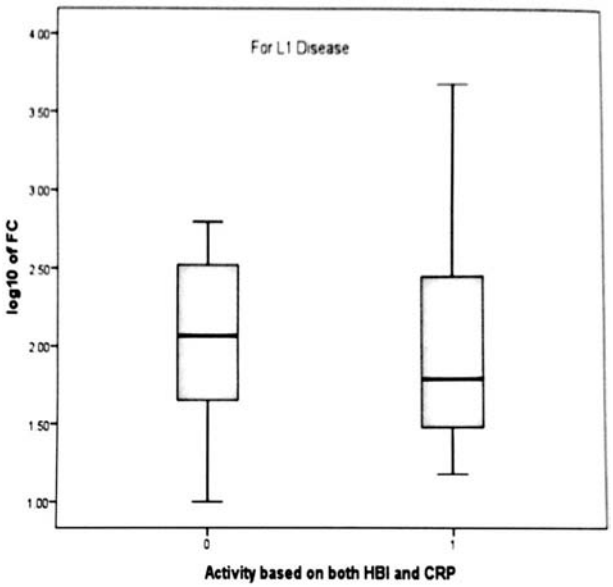
Background: FC is considered a useful diagnostic tool in both the diagnosis and assessment of activity in CD. However,accuracy in small bowel disease(Montreal classification L1) compared to colonic(L2) and ileocolonic(L3) remains undetermined. We aimed to establish whether FC can be used to assess disease activity in L1 disease with the same degree of confidence as other disease locations.



"Fig1"

Table: Demonstrating significance of the relationship between the mean FC of patients at specific disease locations according to disease activity based on HBI, CRP or both.

	Active disease by HBI or CRP	Active disease by HBI alone	Active disease by CRP alone
L1	P=0.95 (Fig1)	P=0.78	P=0.67
L2	P=0.05 (Fig2)	P=0.78	P<0.01
L3	P<0.01 (Fig2)	P<0.01	P<0.01

Methods: Prospective evaluation of 197 consecutive patients receiving treatment with infliximab or adalimumab. All patients had FC measured (all FC in units of IU/ml)
at the same time as C-Reactive Protein(CRP) and Harvey Bradshaw Index(HBI). Active disease was defined as HBI ≥ 5 and/or CRP >5. FC for comparisons were Log10 transformed. Significances between means were obtained using independent 2 sample t-test and the oneway ANOVA test.
Results: Patients were divided according to Montreal classification; L1(n=28),L2(n=59) and L3(n=108). Mean FC for the 3 groups were 344(median=100),379(median=80) and 288(median=71) respectively(P=0.728). There was a significant difference in FC between those with active disease and remission (543 versus 216 P< 0.015). The association between FC and disease activity were made between the 3 disease locations are shown in table.
Conclusions: FC was associated with disease activity in colonic and ileocolonic disease. FC could not discriminate between active disease and remission for isolated small bowel disease. Assessment of patients with isolated disease should include other modalities(cross-sectional imaging and endoscopy).

P417
Ileal pouch-anal anastomosis for dysplasia or cancer complicating inflammatory bowel disease: should a total mesorectal excision always be performed? An analysis of 39 consecutive patients.

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Background: Updated S-ECCO guidelines in patients undergoing a restorative coloproctectomy with ileal pouch-anal anastomosis (IPAA)

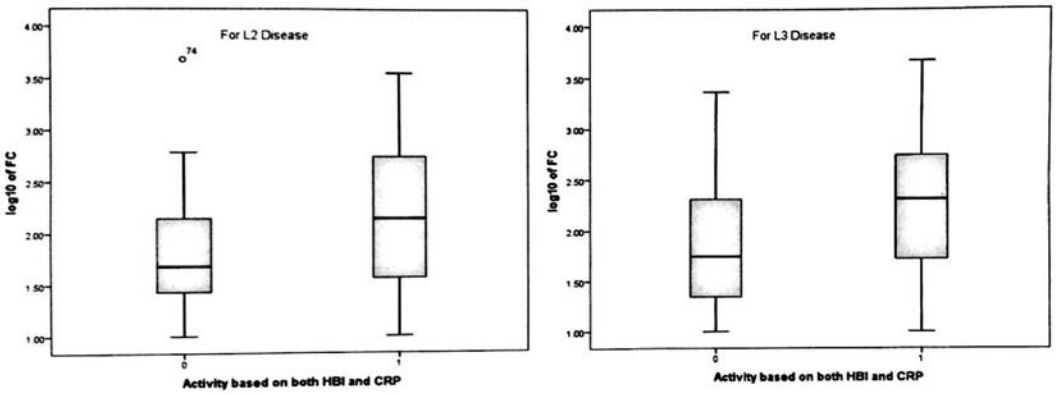

Fig2"

for colorectal dysplasia or cancer complicating inflammatory bowel disease (IBD) state that an extensive lymph node dissection, including a total mesorectal excision (TME), should always be performed, even in the absence of preoperatively known rectal cancer and despite the risk of postoperative sexual disorders. This study aimed to compare the oncological outcomes of patients who underwent IPAA for colorectal neoplasm complicating IBD with or without TME.

Methods: From 1998 to 2014, all patients who underwent an IPAA for neoplasm complicating an IBD were included. This population was split in 2 groups: IPAA with TME and IPAA without TME.

Results: 39 consecutive patients were enrolled (10 women, 29 men, with a mean age of 51 [27-77] years), including 24 (62%) restorative coloproctectomies and 15 (38%) completion proctectomies performed after previous subtotal colectomy. Surgical dissection included a proctectomy with TME in 14 (36%) patients and without TME in 25 (64%) patients.

In the TME group, indication for surgery included colonic dysplasia (n=1, 7%), rectal dysplasia (n=6, 43%), colonic cancer (n=1, 7%), and rectal cancer (n=6, 43%). In the no TME group, indications included colonic dysplasia (n=14, 56%), rectal dysplasia (n=9, 35%), unlocated dysplasia (n=1, 4%), and colonic cancer (n=1, 4%). Among the 8 patients from the TME group without preoperatively know rectal cancer, pathologic examination of the specimen showed rectal dysplasia in 3 patients and pT1 rectal cancer in 3 patients (pTisN0R0, pT1sm2N0R0, and pT1sm3N0R0). In the 25 patients from the no-TME group, pathologic examination of the specimen showed rectal dysplasia in 6 patients and rectal cancer in 2 patients: 1 with high grade dysplasia but associated with a cystic lesion in the muscular layer (genuine pT2N0 (0/10)? Or proctitis cystica profunda?) and 1 pT2N0 (0/37) R0.

After a mean follow-up of 53 months [2-124], cancer recurrence was observed in 4 patients from the TME group and in no patient from the no-TME group.

Conclusions: These results do not support systematic TME during IPAA surgery for colorectal dysplasia or colonic cancer complicating IBD. Considering its demonstrated association with postoperative sexual disorders, TME should be discussed on a case-by-case basis during multidisciplinary team meetings.

P418
Looking beyond the mucosa: transmural healing after one-year anti-TNFα therapy in Crohn's disease

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Background: Crohn's disease (CD) may show full-thickness involvement of the bowel wall,frequently with extramural complications.Although the capability of anti-TNFα agents to induce and maintain clinical and endoscopical remission has repeatedly been described,their role in the treatment of transmural inflammation is still unclear.

Aim of this study was to analyze transmural healing (TH) in consecutive CD patients after a one-year treatment with anti-TNFα and to correlate TH with mucosal healing (MH),biological markers(CRP and fecal calprotectin) and clinical activity(CDAI)

Methods: 11 patients with moderate to severe ileocolic CD were enrolled. All underwent ileocolonoscopy and MRI-enterography before and after one-year treatment with anti-TNFα; clinical remission was defined as CDAI< 150,response as a 70-point reduction from baseline. CRP and fecal calprotectin(FC) (positivity cut-off respectively >0,50 mg/dl and >150 µg/gr) were also measured.Endoscopic activity was assessed by SES-CD,range 0-40,with remission defined as score<3 and response as a 50% decrease from baseline at one year.MRI activity was measured by MRI-enterography global score (MEGS),range 0-296,a score which takes into account transmural and extramural features of disease,with active disease defined as a score ≥1,and response as above.

	Baseline	After 1 year	Statistical Analysis
SES-CD	11 ± 4	7 ± 4	p=0.001
MEGS	30 ± 13	19 ± 10	p=0.001
Transmural subscore	22 ± 12	14 ± 8	p=0.002
Extramural subscore	90%	75%	p=ns
CDAI	243 ± 85	169 ± 103	p=0.03
CRP	3,2 ± 3	2,5 ± 4	p=0.03
FC	290 ± 180	169 ± 163	p=0.02

Results: We enrolled 6 males and 5 females,mean age 38 ± 14 ys,mean disease duration 7 ± 5 ys.According to the Montreal classification the phenotype was L1 in 27%,L2 in 9% and L3 in 64%;the behavior was B1 in 9%,B2 in 64%,and B3 in 27%; resectional surgery related to CD was observed in 9%.Signs of mesenteric inflammation were only lymph node enlargement or comb-sign.3 patients were treated with IFX,8 with ADA.Mean SES-CD,MEGS,CDAI,CRP and FC values significantly decreased at one year(table);56% of patients had clinical remission and 9% response,biological remission was achieved in 54% and 72% according to FC and CRP respectively;endoscopic improvement was 64%,18% achieved MH.Mean MEGS score was unrelated to MH (p=0.8);18% had transmural improvement but none had complete normalization of MRI finding.Elevated CRP at one year was correlated with presence of extramural involvement only(p=0.04) and mean CRP level were higher (4,3 ± 5 ng/ml) in the presence of comb-sign(p=0.04).

Conclusions: Biologic therapy is effective in inducing clinical,biochemical and endoscopical remission of CD while extramural inflammation may persist longer than one year,as indicated by persistently elevated CRP levels.Transmural healing probably needs longer therapy to be achieved.

P419
Rapid Changes in Laboratory Parameters and Early Response to Adalimumab: Pooled Analysis from ULTRA 1 and ULTRA 2

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Background: The efficacy and safety of adalimumab (ADA) for induction and maintenance of clinical remission in patients with

Mean changes from baseline in laboratory parameters

	Baseline Mean	Baseline Mean	Week 4	Week 4	Week 8	Week 8
	PBO (N=468)	160/80 ADA (N=470)	PBO	160/80 ADA	PBO	160/80 ADA
Albumin (g/L)	41.6	41.9	-0.1 (N=457)	0.7*** (N=455)	0.4 (N=422)	1.2*** (N=434)
hs-CRP (mg/L)	12.8 (N=461)	12.7 (N=464)	-2.5 (N=448)	-4.7* (N=443)	-0.4 (N=412)	-5.0*** (N=425)
Total protein (g/L)	69.6	69.9	-0.1 (N=456)	0.2 (N=454)	0.4 (N=423)	1.1** (N=434)
Hematocrit (fraction)	0.403	0.400	-0.002 (N=451)	0.005** (N=449)	0.002 (N=423)	0.012*** (N=433)
Hemoglobin (g/L)	130.3	129.6	-1.5 (N=454)	0.9*** (N=451)	-0.4 (N=424)	3.0*** (N=433)
Red blood cell count ($x10^{12}$/L)	4.42	4.39	-0.02 (N=450)	0.04** (N=449)	0.04 (N=423)	0.14*** (N=433)

moderately to severely active ulcerative colitis (UC) was demonstrated in ULTRA 1[1] and ULTRA 2.[2] Early changes in laboratory parameters, Mayo subscores and health-related quality of life (QoL) were assessed in a pooled analysis of patients from both studies.

Methods: ULTRA 1 patients were randomized to placebo (PBO) or ADA [80/40 or 160/80 mg at weeks (wks) 0/2, 40 mg every other wk (eow) from wk 4] in the 8 to 12 wk double-blind (DB) phase. ULTRA 2 was a 52-wk DB trial in which patients were randomized to PBO or ADA (160/80 mg at wks 0/2, 40 mg eow from wk 4). Pooled data from patients who received 160/80 mg ADA or PBO in both studies were evaluated in *post-hoc* analyses. Mean changes from baseline (BL) at wks 4 and 8 in albumin, high-sensitivity (hs)-CRP, total protein, hematocrit, hemoglobin, and red blood cell count (RBC) were evaluated. Mean changes from BL at wks 2, 4, 6, and 8 in Mayo subscores [rectal bleeding subscores (RBS) and stool frequency subscores (SFS)] were evaluated, and QoL (Inflammatory Bowel Disease Questionnaire, IBDQ scores) were evaluated at wks 4 and 8. results were compared for ADA- v. PBO-treated patients using the ANCOVA model. Last observation carried forward (LOCF) was used for missing data.

Results: ADA treatment significantly improved albumin, hematocrit, hemoglobin, and RBC compared to PBO at wks 4 and 8 (Table), and greater reductions in hs-CRP were observed in ADA-treated patients v. PBO at wks 4 and 8. Significant reductions in mean RBS (-0.6 v. -0.3) and mean SFS (-0.5 v. -0.2) were observed in ADA- v. PBO-treated patients, respectively, as early as wk 2 (all $p<0.001$), and were sustained up to wks 4, 6, and 8. Mean IBDQ scores were significantly improved in ADA- v. PBO-treated patients at wk 4 (29.2 v. 19.4) and wk 8 (31.4 v. 22.8), respectively (all $p<0.001$).

Conclusions: ADA treatment resulted in early, rapid improvements in laboratory values, including reductions in hs-CRP levels, in patients with moderately to severely active UC. Clinically meaningful early reductions in RBS and SFS, and early improvements in IBDQ scores were also observed following ADA treatment.

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P420
Thiopurine metabolite testing to guide management in inflammatory bowel disease (IBD) yields clinical benefit at 12 months: A retrospective observational study.

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Background: Azathioprine & 6-mercaptopurine (AZA/MP) metabolites, 6-thioguanine nucleotides (6TGN) & 6-methyl-mercaptopurine (6MMP), are commonly measured. Cross-sectional observational data have led to a proposed "therapeutic range". Short-term studies support the use of therapeutic drug monitoring (TDM) to guide AZA/MP dosing and to identify "shunters" (preferential 6MMP producers). However, few data have evaluated TDM-led management in the longer-term. We therefore evaluated patient outcomes ≥12 months after AZA/MP TDM-led management in a large adult IBD cohort.

Methods: A multi-centre cross-sectional retrospective study was performed in 3 Australian IBD Services. Data were collected from clinical records of IBD adults, on AZA/MP for ≥4 weeks at index TDM. Patient demographics, disease characteristics, physician global assessment, IBD therapy at index TDM, and again ≥12 months after TDM-led management were collected. Indications for TDM were categorized. Therapeutic 6TGN was defined as 235-450pmol/$8x10^8$RBC. Shunters were defined as a 6MMP:6TGN ratio ≥11. Statistical analyses were performed using SAS 9.3.

Results: 343 patients were included for analysis. 247 (72%) had Crohn's disease (CD), 177 (52%) male, mean age 41 years, 218 (64%) had active disease at baseline. TDM was most commonly performed for proactive dose assessment (48%), flare (23%), ongoing active disease (21%) & adverse drug reactions (7%). Prior to TDM, 52% of patients would have had blind dose escalation, cessation of AZA/MP or escalation to another therapy. Overall, TDM led to continuation of AZA/MP (±dose adjustment ±allopurinol) in 290 (85%). At 12 months, 248/343 (72%) were in clinical remission, 19 (6%) improved disease activity, 67 (19%) active disease and 9 (3%) unknown activity status. Of the 267 with 12-month clinical remission/improvement, 157 (60%) achieved this with AZA/MP alone (±allopurinol). In comparison, this was achieved with anti-TNFα therapy, another medical agent, surgery in 61 (23%), 13 (4%) and 25 (9%) respectively. Univariate logistic regression analysis found only baseline remission to be a predictor of 12-month clinical remission/improvement on thiopurine therapy (OR 2.87, CI 1.20-6.89, p=0.02).

Conclusions: AZA/MP TDM-led management allows many patients apparently "failing" therapy to continue the agent and also identifies "shunters". TDM facilitates appropriate adjustment of therapy. TDM also promptly identifying those who require escalation to another agent or surgery, leading to an overall remission rate of 72% compared to 36% at baseline. AZA/MP±allopurinol alone achieved clinical remission in 60% of patients. This is the largest study to pragmatically evaluate longer-term outcomes of AZA/MP TDM and supports its clinical value.

P421
Transitional care in Inflammatory Bowel Disease - a single center experience

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Background: Inflammatory bowel disease (IBD) is a chronic disease with a natural history of relapse and remission. Approximately 25% of IBD patients are diagnosed before the age of 16 years. The approach to investigation and treatment, service provision and ideology of care differe between children and adults . This calls for an organized and planned transition process. Yet, transition clinics are still scarce. A transition adolescent-young adult IBD clinic was established in a tertiary referral center in 2013. Patients are seen conjointly by pediatric and an adult gastroenterologists, an IBD nurse, dietitian and a psychologist. The aim of this study is to quantitavely describe the importance of the trnasitional care in IBD.
Methods: We conducted retrospective review of all patient files visiting the transitional clinic. A self-efficacy questionnaire (the "IBD-yourself") was used to assess patients' skills for self-management of chronic conditions, their self-advocacy, and their healthcare utilization before and after joining our clinic. In general, each question obtained a 4 point score (1 - Yes, definitely and 4 - No,definitely not). We have also compared their self-efficacy according to disease extent, disease duration and therapeutic strategy.
Results: Twenty one patients visited the clinic in january/2013-November/2014. The vast majority (20/21) had Crohn's disease, the average age was 19.4±2.1 (range 17-27) years, and average disease duration 4.9±3 (range 0.67-10) years. Ten patients (48%) were treated with immunomodualtors, 6 patients (29%) with 5ASA, 4 patients (19%) with anti TNF mediactions and 1 patient was not treated at all. The transitional process, completed by 15 (11 males). included an average of 3-4 meetings over an average of 7±4.1 months. Significantly higher self efficacy score after completing the transition compared to before starting it was noticedin the following domains: knowledge of IBD (P=0.01), of diagnostic tests (P=0.0004), of medication use (P=0.003), self manegment in an outpatient clinic (P=0.016), understanding the transition process (P=0.0001) and self readiness for transition (P=0.013). A positive correlation between number of meeting and coping with IBD (r=0.56, p=0.029) was noticed as well. No correlation was found between disease extent, disease duration, therapeutic strategy and change of readiness during the transition.
Conclusions: An organized adolescent-young adult IBD transition clinic significantly contributes to higher cores in self manegment of IBD. The transition process is a major part o a successful transfer to the adult gastroenterologist and should be implemented in IBD Centers.

Table 1: Respondent Demographics

Demographics n=33	Patient n = 11	IBD Nurse specialist n= 10	Gastroen-terologist n= 12
Gender Female (%)	4 (36%)	10 (100%)	1 (8%)
Median Age (Range)	46 (25–73)	37 (30–61)	51 (39–58)
Diagnosis Crohn's (%)	4 (36%)	n/a	n/a
Median years diagnosed (Range)	12 (2–30)	n/a	n/a
Travel in past 5 years Yes (%)	10/11 (91%)	n/a	n/a
Problems with IBD when travel Yes (%)	5/11 (45%)	n/a	n/a
Median years in Post (Range)	n/a	6 (3–18)	10 (3–18)

Table 2: Website quality evaluation parameters

	All n=33	Patient n = 11	IBD Nurse specialist n= 10	Gastroen-terologist n= 12
Global Quality Score Median (Range)	4.5 / 5 (3–5)	5 (3–5)	4.5 (4–5)	4.5 (4–5)
Quality parameters (Strongly agree %)				
Accurate source of information	20 (60%)	9 (82%)	7 (70%)	4 (33%)
Appropriate citations used as evidence	22 (67%)	7 (64%)	9 (90%)	6 (50%)
Balanced and unbiased	23 (70%)	8 (73%)	9 (90%)	6 (50%)
Easy to navi-gate	23 (70%)	8 (73%)	8 (80%)	7 (58%)
Adequate information to prepare for travel	18 (55%)	5 (45%)	7 (70%)	6 (50%)
Improved IBD-related travel knowledge	26 (79%)	9 (82%)	9 (90%)	8 (67%)
Would recommend to friends/ colleagues	33 (100%)	11 (100%)	10 (100%)	12 (100%)

P422
'IBDPassport': Evaluating the quality of an internet-based travel resource for Inflammatory Bowel Disease

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Background: Travellers' with Inflammatory bowel disease (IBD) are at greater risk of travel-related morbidity with European guidelines recommending expert consultation prior to travel, particularly for those on immunosuppression.[1] Previous research into travel and IBD found travel consultations and patient travel preparation and knowledge to be deficient.[2,3] As a result we developed a dedicated, evidence-based non-profit IBD travel advice website(www.

ibdpassport.com)to enhance informed, safe travel.Here we present formal evaluation of this website.

Methods: A link to the website, along with a structured web-based survey was sent to a sample of 15 UK IBD patients,IBD nurse specialists and gastroenterologists respectively.The survey contained demographic questions and asked respondents to rate the content, functionality and credibility of the website using a series of parameters including a 5-point Global Quality Score and Integrity Score [5]. Readability statistics were graded on a 100 word sample of text from each page on the website using the Flesch Reading Ease and Flesch-Kincaid Grade level scores.

Results: A total of 33 individuals responded (73% response rate; 11, 33% Patient; 10, 30% Nurse; 12, 36% Gastroenterologist (Table 1). The mean Global Quality score for all respondents was 4.5 out of a possible 5 (Range 3-5). The Flesch-Kincaid Grade level score was US school grade 10.9 (range 7.2-17.1)and median Flesch Reading Ease score 50.5 out of a possible 100(Range 22.4-65.1).The integrity score was 4.0 out of 6.The majority of respondents strongly agreed that the website was an accurate source of travel information for IBD (60%),used appropriate citations (67%), and was easy to navigate(70%).26/33(79%)felt the website improved their knowledge of travel-related issues in IBD(Table 2).All respondents would recommend the site to friends or colleagues.

Conclusions: IBD Passport is the first internet-based travel resource created for both IBD patients and professionals to provide IBD-specific travel information. Our findings demonstrate that patients and healthcare professionals consider IBD Passport to be an excellent quality, evidence-based resource. The readability statistics are favorable when compared to results from other studies examining website quality.

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P423
Evaluation and long-term benefit of mucosal healing in Crohn's disease patients treated with infliximab

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Background: For decades, the main therapeutic goal in Crohn's disease (CD) was clinical remission. Since the introduction of infliximab (IFX), mucosal healing (MH) was suggested as a new therapeutic goal in CD patients, but its long-term benefit on the natural history of CD is still debated. The aim of this study was to assess MH and to evaluate its effect on disease long-term outcome in CD patients treated with IFX.

Methods: In a single center observational retrospective study, we evaluated consecutive CD patients receiving IFX as maintenance therapy between 2007 and 2010 and presenting objective signs of intestinal inflammation before therapy. MH was evaluated on the report of the first endoscopy performed after IFX introduction and was defined as the absence of any ulceration. Clinical remission, defined by the referring physician assessment, was evaluated 3 to 6 months after IFX introduction. Hospitalizations, major abdominal surgeries and treatment modifications during the follow-up after IFX introduction were collected.

Results: In our center, 153 CD patients received IFX between 2007 and 2010 with a median time between diagnosis and IFX introduction of 62 months (Q1-Q3: 18-152). The mean follow-up duration after IFX introduction was 42 ± 22 months. Seventy-four patients (48%) had a colonoscopy to evaluate MH within a mean delay of 26 ± 17 months after IFX introduction. In these patients, the rate of MH was 50%(37/74). Demographic and clinical characteristics before IFX introduction were similar between CD patients with or without MH. Clinical remission rates at 3 to 6 months after IFX introduction were also similar between patients with and without MH (59% vs. 57%, p=ns). Looking for long-term CD outcomes, patients with MH had fewer hospitalizations (13% vs. 38%, Log-rank p=0.002), fewer major abdominal surgeries (3% vs. 27%, Log-rank p=0.002) than patients without MH. Patients with MH had also fewer therapeutic modifications (24% vs. 51%, Log-rank p=0.027), fewer discontinuation of IFX for inefficacy or intolerance (11% vs. 43%, Log-rank p=0.008) and fewer switch for another anti-TNF agent (3% vs. 22%, Log-rank 0.013) compared to patients without MH. In multivariate analysis, absence of MH was associated to the risk of hospitalization (RR= 3.6; IC 1.2-11.2) and major abdominal surgery (RR=8.0; IC 95%: 1.5-43.5) for patients with CD during follow up.

Conclusions: In our cohort, MH was achieved in half of CD patients treated with IFX as maintenance therapy and was associated with less hospitalization, surgery, treatment modification and discontinuation of IFX. Results of this study suggested that MH should be considered as an important therapeutic goal for CD patients treated with IFX.

P424
Th1 and Th17 response in relation with steroid response in Crohn's disease

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Background: Th1 and Th17 cells are increased in the mucosa of inflammatory bowel disease (IBD) patients. In Crohn's Disease (CD) peripheral Th17 cells are increased in late patients compared with newly diagnosed (Veny et al 2010). Increased Th17 cells are also

increased in the mucosa of the anastomosis in operated patients after recurrence (Zorzi et al 2013). Therefore, Th17 cells increase seems to be related with the perpetuation of inflammation and the lack of response of medical treatments, and could be useful for steroid response prediction.
Aim: Assess usefulness of Th1 and Th17 cells as steroid response predictors.
Methods: 21 CD patients (5 sensitive, 6 dependent and 5 refractory to steroids, and 7 refractory to all treatments), 7 ulcerative colitis (UC) and 20 healthy controls (HC) were included. Inflammatory bowel disease patients were included with active disease and before steroid administration. No patient were taking immunossuppresants (IIMs) or biologics. CD was considered disabling when there was a need for IMMs or biologics for disease control during the following 3 years follow-up (Th1 and Th17 cells were determined in mucosal and peripheral blood lymhocytes in unstimulated and stimulated (PMA/Ionomycin/Brefeldin-A) cultures with intracellular staining (IFN and IL117A) and flow cytometry.
Results: An increase in mucosalIFN (p=0.000) and IL17A (p=0.000) CD3+CD4+ producer cells was detected in CD patients compared to controls, in both stimulated and unstimulated cultures, but no differences were detected in relation to steroid response or the presence of disabling disease. In ulcerative colitis, an increase in mucosal IL17A CD3+CD4+ producing cells (p=0.031) was detected only in stimulated culture in comparison with HC.An increase in CD3+IFN+ (p=0.007), CD3+CD4+IFN+ (p=0.024) and CD3+IL17A+ (p=0.014) peripheral cells was detected in CD patients compared to controls. CD3+ IFN producing peripheral T cells from unstimulatedculture were increased in dependent and refractory patients in comparison to steroid responders (p=0.024)
Conclusions: A Th1 and Th17 response in CD was confirmed. A higher peripheral Th1 response in steroid refractoriness was found, but not discriminative enough to be used for diagnostic purposes.

P425
Endothelial function and cardiovascular risk in Inflammatory Bowel Disease in remission phase

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Background: Endothelial dysfunction has been reported in patients affected by inflammatory bowel diseases (IBD) in active phase, but not yet in remission.
Methods: We evaluated endothelial dysfunction by brachial artery flow-mediated vasodilatation (FMD), and subclinical atherosclerosis by assessment of common carotid intima-media thickness (CCA-IMT) in a cohort of patients with Crohn's disease (CD) or Ulcerative colitis (UC) in remission phase compared to healthy control subjects. The remission was evaluated by Crohn's disease activity index (CDAI) for CD and Mayo score for UC. ANOVA was performed to compare continuous variables and Pearson's r coefficient was calculated for correlation between disease activity and FMD or IMT.
Results: Fifty-eight patients with IBD were enrolled (29 males, aging 40 ± 15, 16 CD and 15 UC) and 40 healthy controls (16 males, aging 45 ± 15). FMD values for IBD in remission was similar to control group (8.38 ± 1.75 vs 9.39 ± 2.23; p=ns). No statistically significant difference was detected between CD (8.38 ± 1.75) and UC (9.64 ± 5.49). No statistically significant difference was found after adjustment for age, sex, body mass index, and family history of cardiovascular disease. Finally, no differences in IMT values between IBD in remission and control group was found, while significant inverse relationship between C reactive protein (CRP) and FMD was detected (r=-0.876; p <0.005).
Conclusions: IBD in remission revealed FMD values comparable to non-IBD population. CRP inversely correlates with FMD. Therefore, endothelial function is completely normalized during remission phase and this suggests the possibility of the reversal/arrest of atherosclerotic process.

P426
Disease phenotype, activity, and clinical course based on the C-reactive protein level at diagnosis in Crohn's Disease: results from the CONNECT study

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Background: C-reactive protein (CRP) is a surrogate marker of acute inflammation in Crohn's disease (CD). Disease course of CD is unpredictable and clinical manifestation of is heterogeneous with phenotypic change over time. Although several clinical factors, serologic, and genetic biomarkers may be used for the prediction of clinical course, definite prognostic factor has not been established. CRP is easily measurable noninvasive marker to evaluate disease activity, but there's controversy about the role for prediction of clinical course. Therefore, we designed a study to investigate whether CRP level at diagnosis is valuable for identification of disease phenotype, activity, and clinical course in CD.
Methods: We retrospectively analyzed 705 CD patients with measurable CRP level who were enrolled into Crohn's Disease Clinical Network and Cohort (CONNECT) study from 32 institutions. Those patients divided into CRP more than 20 or CRP less than 20 mg/L at diagnosis. Patient's demographic, clinical characteristics and use of immunosuppressive or biological agents were investigated. Disease location, behavior, hospitalization, and surgery were also analyzed based on the CRP. Logistic regression analysis was performed to evaluate predictive factor affecting hospitalization.
Results: Of 705 CD patients, 52.9% had CRP more than 20 mg/L at diagnosis. High CRP was associated with younger age at diagnosis, use of steroid at diagnosis, colonic or ileocolonic location, high score of CDAI, and active inflammation at colonoscopy (P<0.001, <0.001, <0.001, 0.001, and <0.001 respectively). In disease progress, patients with high CRP were found to have more stricturing feature (P=0.027). There were significant differences in use of 5-aminosalicylic acid, antibiotics, corticosteroid, azathioprine, and infliximab (P<0.001, < 0.001, <0.001, <0.001, and 0.023 respectively). Hospitalization was also higher in patients with high CRP.

Conclusions: Disease classification by CRP level at diagnosis is useful for evaluating disease phenotype, activity, and clinical course in CD. Strict follow-up strategy with early aggressive treatment could be considered in patients with high CRP.

P427
Fecal microbiota transplantation in refractory pediatric UC - preliminary data.

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Background: Ulcerative colitis is characterized by a dysregulated immune reaction and associated with fecal dysbiosis. Fecal Microbial Transplant (FMT), by changing the gastrointestinal microbiome of patients with UC, may be a potential therapeutic option. For Clostridium difficile infection FMT is an effective alternative treatment. This therapeutic option has been rarely explored in children with UC, however preliminary data have shown some effectivness of FMT in adults and children with UC. The aim was to assess the efficacy of FMT in children with refractory UC.

Methods: Four children, ages ranged from 10-17 years (3 girls) with moderate to severe UC defined by PUCAI, refractory to standard therapy (steroids, immunomodulators, cyclosporin, tacrolimus, anti-TNF) were treated with FMT. They received50 ml FMT via gastroscopy on 5 consecuitive days in first week and every other day in the second week (8 infusions in 14 days). Donors, not related to patients, were healthy and screened for HIV, HAV, HBV, HCV, HAV, EBV, Treponema pallidum, Clostridium difficile, ova & parasites. Patients were evaluated using PUCAI, CRP and fecal calprotectin on the day before the first infusion (0 week), and during follow up period at 2, 4 weeks post transplant. Study subjects were maintained on their pre-transplant medications and PPI was added during FMT treatment.

Results: Four patients with longstanding refractory UC received 8 infusions of FMT in 14 days. All patients had good tolerance and clinical response to FMT. We did not register any serious adverse effects. In 3 patients transient vomitting were observed in the first 2 days. All patients clinically improved (PUCAI). Inflammatory markers decreased in all patients (CRP and fecal calprotectin) at 2 week, but they rapidly increased in next 2 weeks without FMT administration (table 1). None of the patients achieved complete remission.

Conclusions: This study shows that in children with UC refractory to standard therapy, multiple dose of FMT via gastroscopy have clinical benefit but not remission in short-term observation. FMT was well tolerated and safe in active and longstanding pediatric UC. Long-term follow-up studies are required to fully assess effectiveness and safety of FMT as novel therapeutic option in pediatric UC.

P428
Rescue therapy with anti-TNF therapy in patients with Crohn's Disease and post-operative recurrence with intolerance or failure of thiopurines

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Background: The postoperative recurrence (POR) in Crohn's disease (CD) occurs in >75% within the first year after intestinal resection if no preventive treatment is started. Despite an early use of thiopurines, a 40% of patients presents POR one year after surgery. It is not well established what should be done in front of recurrent lesions because there are a few controlled studies about this setting. Aims: To describe the evolution of POR in pacients who receive anti-TNF agents as a treatment for POR.

Methods: We identified all the patients affected of CD with intestinal resection and ileocolic anastomosis who started anti-TNF therapies because of POR and not indicated as primary prevention. We defined endoscopic recurrence (ER) using Rutgeerts endoscopic score and we classified the recurrence as moderate (i2 Rutgeerts) or severe (i3 and i4 Rutgeerts) and Clinical recurrence (CR) as the development of symptoms that required changes in the treatment for CD. We followed the clinical and endoscopic evolution.

Results: 32 patients were included of whom 53% men; 53% ileum disease; 47% ileocolic disease; 43% stenosing patern and 40% penetrating pattern. We toke into account the three risk factors for POR which are: active smoking after surgery (60%), penetranting disease pattern and previous surgery (25%). 85% of patients have one or more risk factors. Before the main resection 62% of patients had been treated with thiopurines and 31% with anti-TNF agents. 72% started prevention with thiopurines after the main surgery and 16% with 5-ASA. Anti-TNF therapies had been started for moderate ER in 31% of patients and for severe ER in 69%. 87% of patients started infliximab and 13% adalimumab, and 74% maintained the initial anti-TNF. 88% used inmunosupressant treatment associated to anti-TNF agents, most of them the same which had been used previously. After a median follow up of 17 months since biological treatment had been started, we had imaging test in 29 out of 32 patients (80% with colonoscopy). 69% of cases had an

	gender	age (y.o.)	disease characteristic- Paris classification	maintain treatment	PUCAI	CRP mg/dl	calprotectin
					0 week; 2 week, 4 week		
1.	male	10	S1 E4	GCS, 5ASA	60→15→15	0.6→0.1→0.7	>1800; 1583; >1800
2.	female	16 1/2	S1 E4	GCS, 5ASA, AZA	70→40→45	3.7→2.1→4.0	824; 1562; >1800
3.	female	17	S1 E4	GCS, 5ASA, AZA	50→0 → 0	0.4→0.5→0.6	156; <100; <100
4.	female	17	S1 E4	GCS, 5ASA	15→0→0	0.7→0.6→0.44	>1800; 1500; 910

"clinical and laboratory data of patients"

improvement in the Rutgeert's score. Besides, a 60% had clinical improvement too. At the end of the follow up, 25% needed another intestinal resection, all of them had CR.

Conclusions: Anti-TNF therapies are a valid and alternative treatment for POR in patients in whom thiopurines had failed or had not been well tolerated. In spite of that, in at least a 25% of cases they will not be enough to avoid a new intestinal resection in a short-medium term. These data suggest that primary prevention with thiopurines associated to an early endoscopic monitoring could be a cost-effective strategy to prevent POR.

P429
Influence of Disease Course on Therapeutic Effect of IFX in Crohn's disease

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Background: Mucosal healing (MH) is an important therapeutic target of Crohn's disease (CD). Numerous clinical trials proved biologic therapies such as Infliximab (IFX) could not only induce and maintain clinical remission but also achieve mucosal healing. Studies from Adalimumab and Certolizumab suggested early disease had much better response than long disease course. The relationship between disease course and therapeutic effect of IFX is not clear. We performed this study to investigate whether disease course is a key factor influencing the efficacy of IFX.

Methods: CD patients (naive to both IFX and thiopurines) followed up in our center who treated with IFX not less than 6 shots of IFX were recruited since July 2012 to June 2014. Demographics and clinical variables were recorded. Mucosal healing rate and clinical remission rate of the first year as well as serum biomarker (High sensitivity C-reactive protein) at baseline, 2 weeks, 4weeks, 8 weeks and 52 weeks were evaluated. According to disease course, patients were divided into 3 groups as disease course< 2 years, disease course between 2-5 years and >5 years for further evaluation. Mucosal healing was assessed under endoscopy with SES-CD. A score< 2 suggested mucosal healing, otherwise unhealed. CDAI<150 was adopted as clinical remission.

Results: 61 patients (42 males and 19 females, mean age 23.66±9.64 yrs) were involved. 35 patients (57.4%) reached mucosal healing after one-year follow-up. The value of high sensitivity C-reactive protein deceased obviously at 2 weeks, 4 weeks, 8 weeks and 52 weeks on IFX treatment (P<0.001). 42 patients had a disease course less than 2 years and 29 of them (69%) reached MH after 1year follow-up; 14 patients had a disease course 2-5 years and 5 of them (36%) reached MH; 5 patients with disease course more than 5 years and only 1 of them reached MH after 1 year follow-up. Patients with a disease course< 2 years had a higher MH rate than the other two groups[disease course 2~5 years vs. < 2 years, P=0.028, OR 4.015, 95%CI (1.12-14.35); disease course >5 years vs. <2years, P=0.051]. Furthermore, compared with patients only treated with IFX for 6 shots, MH rate increased dramatically in patients who undertaken IFX more than 6 [26/37 vs. 9/24, P=0.011, OR 0.254, 95%CI (0.086-0.75)].

Conclusions: Patients with disease course <2 years had much higher rate of mucosal healing in the first year on IFX treatment. Moreover, compared to patients who had 6 shots of IFX, the mucosal healing rate was higher in patients received more than 6 shots. Our study suggests that an early use of IFX in CD patients and relatively longer therapeutic course may have more benefits to patients.

P430
Assessment of safety and efficacy of biosimilar infliximab in children with Crohn disease: a preliminary report.

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Background: Biosimilar infliximab (Remisma/Inflectra) was introduced into therapy in Poland and other selected European countries at the beginning of 2014. Biosimilar infliximab (BI) was authorised based on preclinical and clinical studies and is considered therapeutically equivalent in terms of safety and efficacy to the reference infliximab. We present first, to our knowledge, observation on the safety and efficacy of BI in children with Crohn disease.

Methods: A total of 12 children diagnosed and treated at 3 Polish hospitals with Crohn disease who started therapy with BI were assessed. Patients received BI 5 mg/kg at weeks 0, 2, and 6. Pediatric Crohn disease activity index (PCDAI) and laboratory values (CRP, ESR, platelet count) were assessed at qualification for the biological treatment and after induction treatment at week 10. Due to small number of cases, median and range of clinical values are reported for descriptive purposes only.

Results: Median age was 15.1 years (range 2-18). At BI start median PCDAI was 52.5 (range 5-65); CRP, ESR, platelet count values were 0.9 mg/dL (0.15-6.4), 18 mm (10-93), 327x109/L (235-602x109), respectively. Five out of 12 patients were previously treated with a biologics (4 with reference infliximab, 1 with adalimumab). Time of previous treatment was 6-59 months with biologic-free interval of 7-72 months. Treatment was discontinued in 2/12 patients (17%) after first BI dose due to lack of response, accompanied by adverse event in one patient and withdrawal of consent in second patient. In 10/12 patients (83%) response was observed as assessed by significant PCDAI and inflammation markers decrease. As of November 2014, 6 out of 12 patients (50%) received all 3 induction doses. For those patients, median initial PCDAI was 52.5 (15-62.5) and decreased to 5 (2.5-10) . Before treatment and at week 10 CRP, ESR and platelet count were 1.0 (0.15-6.4), 28 (16-93), 309x109 (255-553) and 0.2 (0.04-0.82), 16 (8-29), 263x109 (220-340), respectively. Adverse events during infusion were observed in 2/12 patients (17%) : one anaphylactic reaction leading to treatment discontinuation and one blood pressure rise that resolved after infusion rate lowering. In the latter case patient received all 3 doses of BI.

Conclusions: In this preliminary report BI appears to be safe and efficacious in inducing remission in Crohn disease paediatric patients. No unexpected safety and product quality issues were identified.

P431
Serology panel for prediction relapse after discontinuation of infliximab in patients with Crohn's disease achieving clinical remission

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Background: Stopping rules for anti-tumor necrosis factor (TNF) therapy are urgently needed. The identification of predictive markers identifying patients at low or high risk for relapse after stopping is therefore warranted. There are limited data concerning the role of non-invasive, serological factors as predictors of relapse after anti-TNF cessation in patients with Crohn's disease (CD). We investigated whether a novel serology panel for assessment of wound healing and repair can predict relapse after infliximab (IFX) cessation for clinical remission in patients with CD.

Methods: This was an observational, retrospective, single-center study. From an electronic database we identified 100 CD patients (57 luminal CD, 40 male, median age at diagnosis 25 years) who discontinued IFX for clinical remission. The majority of patients (n=84) continued on immunomodulators. Relapse was defined as the need to re-introduce medical therapy or surgery. The serology panel included serum TNFα, amphiregulin (AREG), epiregulin (EREG), heparin-binding EGF-like growth factor (HBEGF), hepatocyte growth factor (HGF), heregulin beta EGF domain (HRGB), betacellulin (BTC), epidermal growth factor (EGF), and transforming growth factor alpha (TNFα). These markers were determined in samples taken at the time of IFX discontinuation by Prometheus Laboratories (San Diego, CA). A test was considered positive if the titers were higher than the Q3 of the samples measurements: [TNFα (>12 µg/ml), AREG (>20 U/ml), EREG (>243 U/ml), HBEGF (>12 U/ml), HGF (>74 U/ml), HRGB (>33 U/ml), BTC (>235 U/ml), EGF (>88 U/ml), TNFα (>7 U/ml)].

Results: During a median (IQR) follow up of 9.7 (8.0-11.5) years, 48 out of 100 patients relapsed. A receiver operating characteristic (ROC) analysis did not identify predictive cut-off values for relapse after IFX discontinuation for any of the investigated serological markers. Univariate (Log-Rank) and multiple COX regression analysis revealed borderline significance for positive AREG in predicting relapse (p=0.066 and 0.068 respectively). However, multiple COX regression analysis for a sub-group of patients treated mainly for luminal disease, identified positive AREG as an independent factor predicting relapse after IFX cessation [n=34, p=0.008, HR: 8.1 (95%CI: 1.7-38.1), SN: 80%, SP: 52%, PPV: 22%, NPV: 94%].

Conclusions: Positive amphiregulin titers may be associated with relapse in patients who discontinue IFX for clinical remission. AREG is a member of the epidermal growth factor family which is highly expressed only in the active inflamed and not in the normal mucosa of CD patients.[1] Our results warrant further study of the role of serum AREG in mucosal healing and repair in IBD.

[1]

References:

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P432
Do tumor necrosis factor alpha antagonists reduce the development of advanced colonic neoplasia?

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Background: The aim of this study was to evaluate the effect tumor necrosis factor (TNF)-alpha antagonist on the development of advanced colonic neoplasia.

Methods: Our study consisted of 67 patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS), or psoriasis who used TNF-alpha antagonists and underwent colonoscopies after initial diagnosis. For each patient who used TNF-alpha antagonists, four age- (±5 years) and sex- matched controls were identified from patients with RA, AS, or psoriasis. We compared the prevalence of advanced colonic neoplasia between the two groups. Factors associated with advanced colonic neoplasia were analyzed.

Results: A total of 67 patients and 268 age-and gender-matched controls were identified. Etanercept was used in 47 patients (70.1%), infliximab in 8 patients (11.9%), and adalimumab in 12 patients (17.9%), respectively. Median duration of TNF-alpha antagonists' use was 23.7 ± 19.95 months. Two patients (3.0%) had advanced colonic neoplasia, including one colon cancer (1.5%) in TNF-alpha antagonists group. In contrast, 29 patients (10.8%) were diagnosed with advanced colonic neoplasia, including 10 (3.7%) colon cancers and 21 (7.8%) advanced adenomas in the control group. A case-control study revealed that the odds of detecting an advanced neoplasia among patients who used TNF-alpha antagonists were one fourth of the age- and sex- matched controls [OR, 0.254; 95% CI, 0.059 to 1.091; P = 0.048]. The use of TNF-alpha antagonists antagonist was an independent preventive factor for advanced colonic neoplasia (OR 0.20; 95% CI, 0.04 to 0.95, P = 0.043)

Conclusions: Further study is needed to demonstrate the chemopreventive effect of TNF-alpha antagonists in patients with inflammatory bowel disease.

P433
Efficacy of vedolizumab with concomitant corticosteroid or immunomodulator use in patients with ulcerative colitis from GEMINI 1

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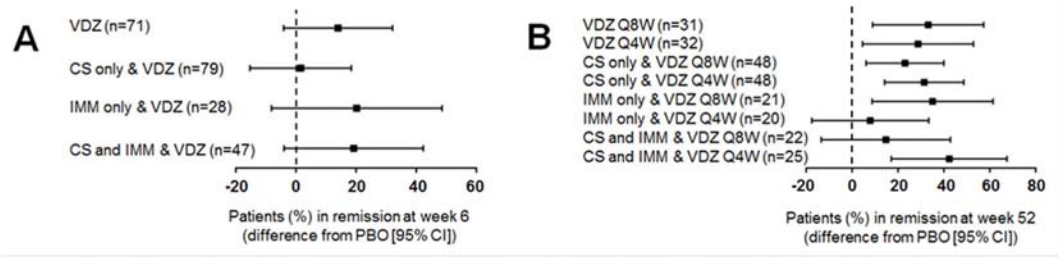
Background: The goals of therapy for ulcerative colitis (UC) include induction of remission, mucosal healing, and maintenance of clinical response. Vedolizumab (VDZ) is a monoclonal antibody to α4β7 integrin with efficacy and safety in patients (pts) with UC. In post

Figure. Percentage of VDZ-treated patients in clinical remission (difference from PBO) at week 6 (end of induction) and (B) week 52 (end of maintenance) by concomitant medication use at week 0 (baseline) in the ITT Populations



Abbreviations: CI, confidence interval; CS, corticosteroid; IMM, immunomodulator; ITT, intent-to-treat; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; VDZ, vedolizumab.
Clinical remission (secondary endpoint for induction and primary endpoint for maintenance) was defined as complete Mayo score of ≤2 points and no individual subscore >1 point.

hoc analyses of data from the GEMINI 1 trial (NCT00783718),[1] we evaluated the efficacy of VDZ in pts with UC who were receiving stable doses of concomitant corticosteroids (CS), immunomodulators (IMM), or both at baseline and experiencing a flare despite these treatments. The safety of VDZ with CS or IMM in these pts has been presented previously.[2]

Methods: GEMINI 1 consisted of 6 weeks (wks) of induction treatment with double-blind (DB) placebo (PBO) or VDZ (induction intent-to-treat [ITT] population) or open-label (OL) VDZ. VDZ responders at wk 6 were re-randomised in the 46-wk maintenance phase to DB PBO or VDZ every 8 or 4 wks (Q8W or Q4W) (maintenance ITT population). CS use was tapered on or after wk 6 in VDZ responders. In the United States, IMM use was discontinued at study entry for OL VDZ-treated pts and at wk 6 for pts on DB VDZ. Efficacy outcomes in the induction and maintenance ITT populations were stratified by use of CS or IMM or both at baseline of induction (wk 0).

Results: Of the 374 pts randomised to receive DB PBO or VDZ during induction, 37%, 12%, and 20% were taking CS or IMM, or both at baseline. Rates of clinical remission (Figure) and mucosal healing at wks 6 and 52, clinical response at wk 6, and durable clinical response and CS-free clinical remission at wk 52 were numerically higher with VDZ treatment compared with PBO, regardless of concomitant CS and/or IMM use at baseline.

Conclusions: The efficacy of VDZ during GEMINI 1 was similar among pts using CS and/or IMM at baseline and those who were not. The interpretation of data for maintenance treatment is limited by the small sample size and discontinuation of CS and IMM after induction. Because the study was not designed to address outcomes with concomitant medication, conclusions are preliminary, and further explorations of apparent synergy between VDZ and CS or IMM are warranted.

The clinical study was funded by Millennium Pharmaceuticals, Inc. (d/b/a Takeda Pharmaceuticals International Co.). Medical writing assistance was provided by inVentiv Medical Communications and supported by Takeda Pharmaceuticals International, Inc.

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P434
Clinical utility of routine measurement of Anti-TNF levels and their antibodies in inflammatory bowel disease (IBD)

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Background: Anti-TNF therapy is an effective option for IBD. Anti-TNF levels and antibodies may help in decision making in these patients. The effectiveness of serial measurement of anti-TNF levels and their antibodies in these subjects is unknown. Therefore, we evaluated the clinical benefit of 2 monthly measurement of these parameters in patient with IBD on maintenance anti-TNF therapy

Methods: All patients receiving maintenance anti-TNF therapy between June 2013 and June 2014 were included in the study. The trough levels and antibodies for infliximab and adalimumab were measured every 2 months. The impact of monitoring on clinical management was reviewed.

Results: Seventy nine (Inflximab n= 40, Adalimumab n=39) IBD patients were included in the study. Mean age was 39±14 years. Median duration of disease was 72 months. Antibodies against infliximab and adalimumab were found in 7 patients. Only one patient with antibodies had a therapeutic level. Of these 7 patients, anti-TNF were switched to the other ant-TNF agent in 3 with partial response, 2 underwent surgery and 2 discontinued the drug as their disease was in remission. In patients with therapeutic levels (n=53), disease activity was present in 17 (32%). Of these 17 patients 11 (64%) underwent dose escalation to achieve higher therapeutic levels resulting in complete response in 6 and partial response in 5 patients. Subtherapeutic levels were found in 22 (27%) patients; other than 6 patients with antibodies, dose escalation in 5 resulted in complete response in 3 and partial response in 2 patients, one discontinued due to joint pains, anti-TNF was continued without any modification in 10 of these patients as their disease was in remission and subsequent levels normalized in 7 of these 10 patients.

Conclusions: Most patients with active disease with subtherapeutic and therapeutic levels but without anti-TNF antibodies may respond to dose escalation. Development of antibodies allows early discontinuation or switching of anti-TNF. Accordingly we suggest routine monitoring of infliximab and adalimumab levels and their antibodies as they impact management of IBD patients.

P435
Maintenance of Remission with Partial Enteral Nutrition Therapy in pediatric Crohn's Disease: A retrospective study.

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Background: Exclusive Enteral Nutrition (EEN) is recommended as first line therapy to induce remission in pediatric Crohn's Disease (CD). A previous pediatric CD study showed that partial enteral nutrition (PEN) was associated with prolonged remission and better linear growth after EEN treatment. Several adult studies have showed the advantage of PEN in maintaining remission. Data on the ability of PEN in maintaining remission in pediatric CD is still lacking. We maintain all our CD patients on PEN (50% of total calories as polymeric diet) for at least one year.

Methods: We conducted a retrospective study in which we investigated the maintenance of remission in 44 pediatric CD patients who entered clinical remission on 6-8 weeks of EEN. To evaluate this, we have reviewed patients' charts and pooled demographic and follow-up data. In order to assess efficacy in maintaining remission we have used the Pediatric Crohn's Disease Activity Index (PCDAI), Physicians global assessment (PGA), laboratory parameters (Hb, ESR, CRP, albumin) and the growth data of each patient over a time period of approximately 12 months.

Results: The patients (27% female, mean age at diagnosis 11.8 (range 6.6-18.6) years) were followed up for a mean duration of 50 months. The mean remission length achieved on EEN treatment, followed by PEN was 9.6 months (range 0-36 months). Patients were maintained on PEN without concomitant medications for a mean time of 3.5 months. Concomitant medications during this period were: steroids (61%), thiopurines (84%), biologic treatment (32%), methotrexate (16%) and antiobiotics (45%). Mean BMI increased from 17.1 before EEN to 18.2 after EEN, followed by an increase to 19.0 after 6 months of PEN

Conclusions: PEN may be helpful in improving maintenance of remission and improves nutritional status. Further studies to assess efficacy are mandated.

P436
Efficacy and safety of azathioprine treatment in Asian patients with Ulcerative Colitis

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Background: To evaluate the efficacy (clinical efficacy and mucosal healing) and safely of azathioprine (AZA) treatment in Asian patients with ulcerative colitis (UC).

Methods: 85 patients with UC who were treated with AZA from 2003 to 2012 were reviewed. The indications for AZA use were as follows: (1) steroid dependent and steroid refractory disease; (2) AZA maintenance monotherapy for naive patients with severe disease; and (3) combination maintanence therapy (AZA + 5-ASA) .

Results: In steroid refractory/dependent group, the cumulative rate of clinical remission at 2 and 4 weeks after AZA use was 37.3% and 72.1%, respectively. The cumulative rates of mucosal healing for maintenance treatment at 6, 12 and 24 months were 10.2%, 22.2% and 34.0%, respectively. Factors associatetd with relapse for AZA maintenance therapy were age less than 40 years at diagnosis (OR=2.346, 95%CI: 1.112-4.949, p=0.025) and dose less than 50mg/d (OR=2.708, 95%CI: 1.213-6.046, p=0.015). 34 (40%) patients experienced adverse effects and 26 (30.6%) patients stopped or temporarily withdrew the use of AZA. Factors associated with adverse effects of AZA use were age of diseae onset older than 40 years (OR=2.074, 95%CI: 1.051-4.095, p=0.036) and combination use of 5-ASA (OR=3.579, 95%CI: 1.598-8.015, p=0.002).

Conclusions: AZA is an effective treatment for UC including clinical efficacy and mucosal healing in Asian patients. However, the adverse effects should be cautioned during the use of AZA.

P437
Short term prevalence of nodular regenerative hyperplasia of the liver in IBD patients treated with allopurinol-thiopurine combination therapy

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Background: Tioguanine has been associated with nodular regenerative hyperplasia (NRH) of the liver. Combination therapy of allopurinol and adapted dose conventional thiopurine leads to a pharmacokinetic profile partly comparable with that of tioguanine ((high 6-thioguanine nucleotides (6-TGN) and low 6-methylmercaptopurine (6-MMPR) concentrations)). Therefore, combination therapy of allopurinol and conventional thiopurines may induce NRH of the liver in a comparative way. We assessed short term prevalence of NRH in IBD-patients treated with allopurinol-thiopurine combination therapy.

Methods: This was an observational, single-centre cross-sectional study. All adult IBD-patients who were treated at least one year with allopurinol-thiopurine combination therapy were eligible. Subjects were identified at the Outpatients' clinic and they were consecutively invited to participate. All patients underwent a liver biopsy, and venous blood was drawn to measure haematological and hepatic parameters, including thrombocyte count and alkaline phosphatase, but also to determine thiopurine metabolite concentrations. Histopathology was assessed by an experienced hepatopathologist.

Results: Eighteen IBD-patients, of which thirteen were diagnosed with Crohn's disease were included. The median age at inclusion was 36 year (IQR 25-42). Combination therapy was initiated in nine patients as a result of elevated transaminase activities during thiopurine monotherapy. The median duration of combination therapy at inclusion was 24 months (IQR 20-28). The median 6-TGN and 6-MMPR level was 685 pmolx108 RBC (IQR 498-940) and 305 pmolx108 RBC (IQR 198-608). In none of the patients NRH was observed; sinusoidal dilatation was observed in four patients. No trombocytopenia was observed.

Conclusions: Short term prevalence of NRH in IBD-patients who were treated with a combination of allopurinol and low dose conventional thiopurine, was low, as in none of the included eighteen patients NRH was observed.

P438

Prospective, randomized clinical trial comparing the efficacy of two vaccines against hepatitis B virus (HBV) in inflammatory bowel disease (IBD) patients

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Background: Aims: To compare the success rate between two HBV vaccines in IBD patients: the traditional (Engerix ®) and a new vaccine with an adjuvant (Fendrix®). Secondary aim was to identify predictor factors of response to the vaccine

Methods: IBD patients with negative HBV serology and without previous vaccination against HBV were included in this multicenter study (EUDRA CT number: 2010-023947-14), and randomized 1:1 to receive Fendrix® or double doses of Engerix® at months 0, 1, 2 and 6. Anti-HBs concentration was measured 2 months after the 3rd and 4th doses

Results: 173 patients were included: 28% under immunosuppressants, and 35% under anti-TNF. 54% of patients received Engerix® and 46% Fendrix®; the main characteristics of patients (age, gender, type of IBD and treatment) were similar between the 2 groups. Overall, 43% of patients had response (pre-defined as anti-HBs ≥100 IU/l) after the first 3 doses (165 patients have received 3 doses up to now), and 71% after the completion of the vaccination (161 have completed the vaccination). 47% of patients that did not respond after the 3th dose, responded to the 4th vaccine administration (p<0.0001). The response rate after the 4 doses was 75% (95%CI, 63-84%) with Fendrix® vs. 67% (56-77%) with Engerix® (p=0.3; however, the statistical power for this comparison was only 30%); considering anti-HBs ≥10 IU/l (the standard threshold to define response), the success rate was marginally higher with Fendrix® than with Engerix® (88% [78-94%) vs. 77% [66-85%], p=0.06). In patients under anti-TNF, the response rate (anti-HBs ≥ 100 IU/l) after the 4 doses was 67% (47-83%) with Fendrix® vs. 45% (27-64%) with Engerix® (p=0.09); and considering anti-HBs ≥ 10 IU/l, the success rate was 80% (61-82%) with Fendrix® and 58% (39-75%) with Engerix® (p=0.06). In the multivariate analysis, older age (OR=0.9, p<0.0001), and the treatment with immunosuppressants (OR=0.12, p<0.01) or anti-TNFs (OR=0.09, p<0.0001) were associated with a lower the response rate to the vaccination. The type of vaccine -Engerix® or Fendrix®- was not associated with the response to the vaccination (OR=1.8, 95%CI=0.8-4). The frequencies of IBD flaring ups during the study period were similar in patients receiving Fendrix® and Engerix® (17% vs. 22%)

Conclusions: We could not demonstrate a statistically significant higher response rate of Fendrix® (single dose) over Engerix® (double dose) in IBD patients, although a beta error cannot be excluded. A 4-dose vaccine schedule significantly increases (over 40%) the response compared with a 3-dose regimen. Older age and the immunosuppressive and anti-TNF treatment impaired the success rate of the vaccine. The risk of flaring up is not increased with one vaccine compared to the other

P439

Deep remission as a predictor of clinical outcomes in vedolizumab-treated patients with ulcerative colitis

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Background: Deep remission (a combination of endoscopic and patient-reported outcomes) is an emerging treatment goal for patients with ulcerative colitis (UC). Vedolizumab (VDZ), a monoclonal antibody to α4β7 integrin, has demonstrated efficacy in achieving clinical remission and mucosal healing in patients with UC (GEMINI 1, NCT00783718).[1] In post hoc analyses of data from GEMINI 1, we investigated whether deep remission is a predictor of clinical outcomes and health-related quality of life (HRQoL) in patients with UC.

Methods: Responders to VDZ induction therapy at week (wk) 6 were re-randomised to placebo (PBO) or VDZ every 8 or 4 wks (Q8W or Q4W) for 46 wks (maintenance intent-to-treat [ITT] population). Clinical outcomes and HRQoL were evaluated at wk 52 in the maintenance ITT population who were in deep remission at wks 6 and 52. We selected 2 definitions of deep remission to represent a range of stringency: (1) Mayo endoscopic subscore=0, rectal bleeding subscore=0, and decrease or no change from baseline in stool frequency subscore or (2) Mayo endoscopic subscore=0 or 1, rectal bleeding subscore=0, and stool frequency subscore=0 or 1.

Results: All patients in the maintenance ITT population received VDZ during induction, and rates of deep remission at wk 6 (maintenance baseline) were comparable across treatment groups (Table 1). At wk 52, almost 3 times as many VDZ-treated patients were in deep remission

Table 1 Percentage of patients in deep remission at wks 6 and 52 (maintenance ITT population)

Week	Deep Remission	VDZ/PBO[a] n=126	VDZ/VDZ[a] Q8W n=122	VDZ/VDZ[a] Q4W n=125
	Yes/No	n (%)	n (%)	n (%)
Definition 1: Mayo endoscopic subscore=0, rectal bleeding subscore=0, decrease or no change from baseline in stool frequency subscore				
Week 6 (End of induction)	Yes	13 (10)	12 (10)	18 (14)
	No	113 (90)	110 (90)	107 (86)
Week 52 (End of maintenance)	Yes	11 (9)	33 (27)	35 (28)
	No	115 (91)	89 (73)	90 (72)
Definition 2: Mayo endoscopic subscore=0 or 1, rectal bleeding subscore=0, and stool frequency subscore=0 or 1				
Week 6 (End of induction)	Yes	55 (44)	62 (51)	64 (51)
	No	71 (56)	60 (49)	61 (49)
Week 52 (End of maintenance)	Yes	20 (16)	53 (43)	54 (43)
	No	106 (84)	69 (57)	71 (57)

Abbreviations: ITT, intent-to-treat; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; VDZ, vedolizumab; wk, week.
[a] All patients in the maintenance ITT population received VDZ at wk 0 and wk 2 in the 6-week induction phase.

Table 2 . Clinical and HRQoL outcomes at wk 52 in patients with or without deep remission (definition 2) at wk 6 (maintenance ITT population)

Week 52 Endpoints	Deep Remission[a] At Week 6	VDZ/PBO[b] n=55[c]/n=71[d]	VDZ/VDZ[b] Q8W n=62[c]/n=60[d]	VDZ/VDZ[b] Q4W n=64[c]/n=61[d]
	Yes/No	Patients, n (%) [95% CI]		
Clinical remission[e]	Yes	12 (21.8) [10.9, 32.7]	34 (54.8) [42.5, 67.2]	40 (62.5) [50.6, 74.4]
	No	8 (11.3) [3.9, 18.6]	17 (28.3) [16.9, 39.7]	16 (26.2) [15.2, 37.3]
Mucosal healing[f]	Yes	15 (27.3) [15.5, 39.0]	39 (62.9) [50.9, 74.9]	45 (70.3) [59.1, 81.5]
	No	10 (14.1) [6.0, 22.2]	24 (40.0) [27.6, 52.4]	25 (41.0) [28.6, 53.3]
CS-free remission[g]	Yes	5 (16.1) [5.5, 33.7]	17 (43.6) [27.8, 60.4]	24 (57.1) [41.0, 72.3]
	No	5 (12.2) [4.1, 26.2]	5 (16.1) [5.5, 33.7]	9 (29.0) [14.2, 48.0]
Deep remission[a]	Yes	11 (20.0) [9.4, 30.6]	34 (54.8) [42.5, 67.2]	38 (59.4) [47.3, 71.4]
	No	9 (12.7) [4.9, 20.4]	19 (31.7) [19.9, 43.4]	16 (26.2) [15.2, 37.3]
IBDQ total score >170	Yes	23 (41.8) [28.8, 54.9]	43 (69.4) [57.9, 80.8]	51 (79.7) [69.8, 89.5]
	No	24 (33.8) [22.8, 44.8]	27 (45.0) [32.4, 57.6]	34 (55.7) [43.3, 68.2]
EQ-5D VAS ≥7	Yes	31 (57.4) [44.2, 70.6]	52 (85.2) [76.3, 94.1]	49 (77.8) [67.5, 88.0]
	No	36 (50.7) [39.1, 62.3]	36 (60.0) [47.6, 72.4]	37 (61.7) [49.4, 74.0]

Abbreviations: CS, corticosteroids; EQ-5D, European Quality of Life-5 dimension; IBDQ, Inflammatory Bowel Disease Questionnaire; ITT, intent-to-treat; PBO, placebo; Q8W, every 8 weeks; Q4W, every 4 weeks; VAS, visual analogue scale; VDZ, vedolizumab; wk, week.
[a] Definition 2: Deep remission is defined as Mayo endoscopic subscore=0 or 1, rectal bleeding subscore=0, and stool frequency subscore=0 or 1.
[b] All patients in the maintenance ITT population received VDZ at wk 0 and wk 2 in the 6-wk induction phase.
[c] Patients in deep remission. Of patients using oral CS at baseline, 31 (VDZ/PBO), 39 (VDZ/VDZ Q8W), and 42 (VDZ/VDZ Q4W) were in deep remission. EQ-5D VAS was assessed in 54 (VDZ/PBO), 61 (VDZ/VDZ Q8W), and 63 (VDZ/VDZ Q4W) patients in deep remission.
[d] Patients not in deep remission. Of patients using oral CS at baseline, 41 (VDZ/PBO), 31 (VDZ/VDZ Q8W), and 31 (VDZ/VDZ Q4W) were not in deep remission. EQ-5D VAS was assessed in 71 (VDZ/PBO), 60 (VDZ/VDZ Q8W), and 60 (VDZ/VDZ Q4W) patients not in deep remission.
[e] Clinical remission is defined as complete Mayo score of ≤2 points and no individual subscore >1 point.
[f] Mucosal healing is defined as Mayo endoscopic subscore of ≤1.
[g] CS-free remission is defined as patients using oral CS at baseline who have discontinued CS and are in clinical remission at wk 52.

as were PBO-treated patients (Table 1). Compared with patients not in deep remission, patients in deep remission at wk 6 had better wk 52 outcomes (Table 2). Further, deep remission at wk 52 was aligned with better outcomes at wk 52 compared with no deep remission. Similar trends were observed with both definitions of deep remission.

Conclusions: Deep remission at wk 6 was a consistent predictor of positive outcomes at wk 52. More VDZ-treated patients were in deep remission at wk 52 compared with PBO-treated patients. Patients in deep remission at wk 6 or 52 had better clinical and HRQoL outcomes at wk 52 than those who were not in deep remission.

The clinical study was funded by Millennium Pharmaceuticals, Inc. (d/b/a Takeda Pharmaceuticals International Co.). Medical writing assistance was provided by inVentiv Medical Communications and supported by Takeda Pharmaceuticals International, Inc.

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[1] Feagan BG, (2013), Vedolizumab as induction and maintenance therapy for ulcerative colitis, N Engl J Med, 699-710

P440

Curcumin add-on therapy for induction of remission in mild-moderate active Ulcerative Colitis: A multi-center, prospective, randomized, double-blind, placebo-controlled trial

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Background: The phytochemical compound curcumin was reported to be effective in ameliorating chemically-induced colitis and for the maintenance of remission in ulcerative colitis (UC) patients*1*. The current study aimed to investigate curcumin's efficacy in inducing remission in patients with active mild-to-moderate UC.

Methods: This was an investigator initiated, multi-center, randomized, placebo-controlled double-blind study. Patients with active mild-to-moderate UC defined by a Simple Clinical Colitis Activity Index (SCCAI) score of ≥5 and ≤12, who failed at least four weeks of maximal (4 gram) oral 5-aminosalycilate (5ASA) therapy and a further two week run-in period of maximal oral and topical 5ASA therapy, were eligible. Patients were randomized to receive 3gr/day of curcumin capsules or identical placebo for one month as add-on to continued 5ASA treatment. The primary outcome was the rate of clinical remission (SCCAI ≤2) at week 4. Clinical and endoscopic responses were also recorded.

Results: Fifty patients entered the study out of 97 patients screened. In the intention-to-treat analysis, 14/26 (54%) of patients receiving curcumin achieved clinical remission at week 4 compared to 0/24 (0%) of patients receiving placebo (P=0.01, OR 42, 95% CI 2.3-760). Clinical response (reduction of ≥3 points in SCCAI) was achieved in 17/26 (65%) in the curcumin group versus 3/24 (12%) in the placebo group (P<0.001, OR13.2, 95%CI 3.1-56.6). Endoscopic remission (partial Mayo score ≤1) was observed in 8/21 (43%) of curcumin-treated patients compared to 0/16 (0%) of the placebo-treated patients (P=0.043, OR 20.7, 95%CI 1.1-393). Adverse events were rare and comparable between the two groups.

Conclusions: In our study curcumin as add-on to 5ASA therapy was superior to placebo for inducing clinical and endoscopic remission in mild-to-moderate active UC patients who failed 5ASA treatment. No apparent adverse effects were observed. Curcumin may be a safe and promising agent in the treatment of UC.

P441
Infliximab-Related Infusion Reactions: Systematic Review of Preventive and Management Practices

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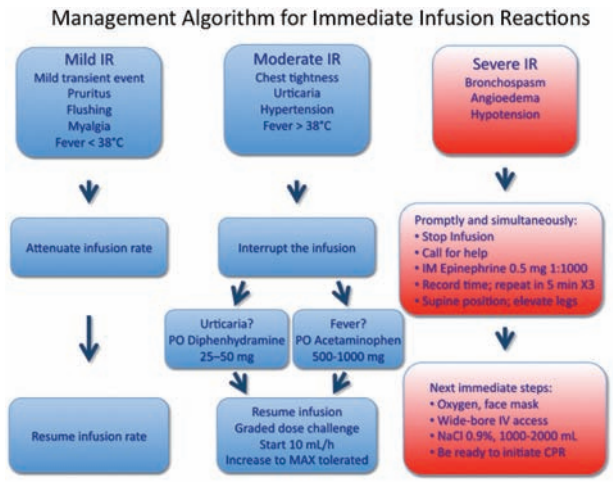
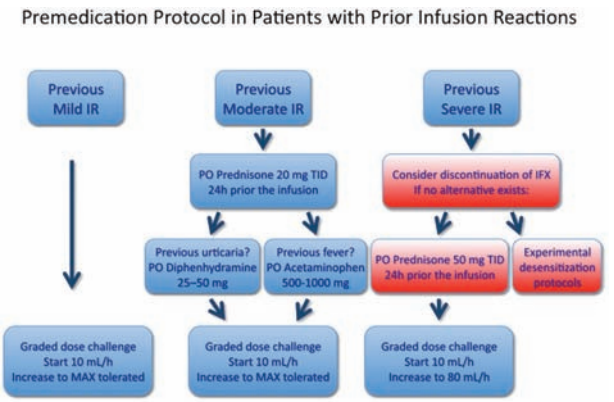
Background: Administration of infliximab (IFX) is associated with a well-recognized risk of infusion-related adverse events. The lack of a mechanism-based rationale for their prevention, combined with the absence of adequate, well-controlled studies has led to the use of diverse empirical administration protocols, each with its own rate instructions, choice of pre-administered preventive medications, and reaction-management algorithms. The aim of the present initiative was to reach a multicenter evidence-based consensus for the administration of IFX, with special emphasis on prevention and management of the infusion reactions.
Methods: We conducted extensive electronic searches of the PubMed and SCOPUS databases, from their earliest records through November 2014, for terms infliximab, anti-TNF, TNF-alpha, biologics, inflammatory bowel disease, Crohn's disease, ulcerative colitis, immunogenicity, infusion reactions, hypersensitivity, allergy, immediate reactions, late reactions, desensitization, and toxicity. We assessed and ranked - using Oxford Centre definitions of levels of evidence in treatment benefits format ("Does this intervention help?") - the quality of the best current evidence supporting: (1) preventive benefits of infusion rate protocols; (2) necessity and efficacy of primary preventive measures in unselected population and in special populations deemed to be particularly predisposed to infusion reactions (patients re-introduced with IFX following a prolonged drug-free interval; patients with high titers of ATI or progressive loss of response); (3) available management algorithms of ongoing immediate and late infusion reactions; (4) efficacy of graded dose challenge and premedication with corticosteroids, antihistamines, and/or antipyretics in patients with a history of infusion reactions.
Results: Local IFX administration practices presently in place in Israeli IBD tertiary care centers were collated, critically appraised against the evidence, and discussed with the involved medical teams.
Conclusions: The resulting consensus served as a basis for the development of a standardized administration protocol. The IBD Section of the Israel Gastroenterology Association recently adopted these recommendations and, in a special meeting, endorsed the updated, standardized protocols for implementation in Israeli adult and pediatric IBD Centers.





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Outcome of early surgery versus aggresive medical therapy in patients with newly diagnosed limited inflammatory/obstructive (A2/3L1B1/2) terminal Ileitis: A two-year, prospective, single-center, pilot study

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Background: Background: Data are scarce regarding the outcome of 'curative' early surgery (ES) versus 'aggressive medical therapy' [AMT, azathioprine (AZA) and anti-TNF biologics] for limited mixed inflammatory-obstructive Crohn's terminal ileitis (LMI/OTI). EST achieves removal of the affected segment and induces prolonged remission reserving immunosuppressives for patients at high-risk for recurrence. AMT can induce and maintain remission of CD but may be associated with serious adverse events and cannot guarantee long-term avoidance of surgery. Aim: To assess prospectively in a single-center pilot study the 2-year outcome of EST vs AMT in consecutive patients with LMI/OTI (phenotype A2/3L1B1/2).
Methods: Eligible were patients with newly diagnosed active (CDAI>180) LMI/OTI CD (despite treatment with 9mg/d budesonide for 6-8 weeks) and at high-risk for post-operative recurrence. LMI/OTI was defined as the combination of: a) raised inflammatory indices (leukocytes, platelets, CRP), b) involvement of < 25cm terminal ileum, characterized by a narrow lumen, ulcerated but slightly distensible bowel wall with pre-stenotic dilatation although

not purely stricturing disease at enteroclysis or MRI enterography, and c) inability to pass the colonoscope to the proximal unaffected ileum. After a thorough discussion, enrolled patients opted for AMT or EST (laparoscopic or open). EST patients received AZA (2.5mg/kg) for post-operative prophylaxis starting 14 days after surgery. AMT patients received standard doses of AZA and anti-TNF agents. Patients were followed for 2 years by physical examination and laboratory tests at bimonthly visits. Endoscopy was performed at 6, 12, and 24 months. Primary end-points were endoscopic remission (Rutgeerts score < or =1) for EST and avoidance of surgery for AMT.
Results: Between 2007 and 2011, 17 patients [7M:10F, mean age 24(18-67) years, 12 smokers] consented to undergo EST and 17 patients [8M:9F, age 26(17-68) years, 13 smokers] received AMT. 2 years after EST, 3/17 (18%) patients had endoscopic recurrence and switched to biologics; 82% patients were in endoscopic remission. On AMT, 10/17 (59%) patients underwent surgery for complications (bowel obstruction and/or abscess, n=5), lack of efficacy (n=3) or adverse events to therapy (n=2); seven patients were in clinical remission (3 in deep remission).
Conclusions: In this pilot study in consecutive CD patients selected by the A2/3L1B1/2 phenotype, EST appears to offer a better 2-year outcome than AMT. However, decisions should be taken on a case-to-case basis considering patient's age, life expectations, disease activity, relative degree of obstruction vs inflammation, and treatment morbidity. Large prospective trials are needed to evaluate longer-term outcomes.

P443
Soluble TNF serum levels during the induction phase in Crohn's Disease patients with anti-TNF treatment

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"Comparisons of TNF concentrations between patients that reached and those who did not reach remission"

Anti-TNF drug	Weeks	TNF pg/mL (remission)	TNF pg/mL (no remission)	p
Infliximab	0	5	8	0.04
	4	7	9	n.s.
	8	8	11	n.s.
	14	12	18	n.s.
Adalimumab	0	5	2	n.s.
	4	2.9	2.4	n.s.
	8	5	3.2	n.s.
	14	5.8	2.2	n.s.

Background: Aims: 1) To evaluate the correlation between TNF concentration and clinical activity in CD patients. 2) To assess the usefulness of measuring TNF serum levels to predict short-term remission with anti-TNF treatment. 3) To evaluate the correlation between TNF serum levels and short term remission in CD patients under anti-TNF treatment.
Methods: CD patients naïve to anti-TNF treatment were prospectively included in this multicenter study. Patients received 160/80 mg adalimumab (ADA) at weeks 0 and 2, and 40 mg every-other-week thereafter, or infliximab (IFX) 5 mg/kg at weeks 0, 2, 6 and 14. Remission was defined as a CDAI score < 150, and response as a decrease of >70 points, after 14 weeks of treatment. Clinical evaluation was assessed and blood samples were obtained at baseline and at weeks 4, 8 and 14. TNF serum levels were measured using a highly sensitive modified ELISA, Collaborative enzyme enhanced reactive immunoassay (CEER). ADA and IFX levels were measured using a homogeneous mobility shift assay (HMSA; Prometheus Lab, San Diego, United States). To study the correlation between TNF concentrations and remission at week 14, only patients with active disease at inclusion (CDAI>150) were considered. ROC curves were constructed and the area under the ROC curve (AUC) was calculated.
Results: 117 patients were included (47% had active disease at baseline, 52% received IFX and 48% ADA). Mean TNF levels were 5, 5.2, 5.5 and 8.4 pg/mL at baseline, weeks 4, 8 and 14 respectively. There was no correlation between CDAI score and TNF serum levels at any visit. Among patients with active disease, the AUCs of TNF to predict remission at week 14 were 0.50, 0.62, 0.66 and 0.48 at baseline and week 4, 8 and 14, respectively. Among patients who achieved remission with IFX, TNF levels were lower at baseline (5 vs. 8 pg/mL, p=0.04). However, TNF levels were similar between responders and non responders at the other visits (table 1).
Serum TNF levels were inversely and significantly associated with serum IFX levels at week 14 (data no shown). There were no differences in TNF serum levels between patients that reached remission and those who did not under adalimumab treatment (table 1)
Conclusions: TNF serum levels do not correlate with clinical activity in CD. Although basal TNF levels seem to be lower among CD patients that reach remission under IFX treatment, measuring soluble TNF does not seem useful for either predicting or monitoring anti-TNF treatment during the induction phase in CD patients.

P444
Successful allogeneic haematopoietic stem cell transplantation (HSCT) for refractory Paediatric Crohn's Disease without an identifiable genetic mutation - A case report

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Background: Remission in several autoimmune diseases has been reported after allogeneic haematopoietic stem cell transplantation (HSCT). There are only a few cases in the literature of curing IBD, following HSCT for coexisting conditions. We report a case of a male patient with severe early-onset Crohn's disease (CD) with no known genetic mutation, who underwent a successful matched unrelated HSCT.

Methods: A 9 year old boy born to non-consanguineous parents, diagnosed with ileo-colonic CD aged 4 years. He was initially treated with steroids, Azathioprine and Aminosalicylates over a 2 year period with only partial clinical response. There was no evidence of mucosal healing and the patient remained steroid dependent. At aged 6 year he underwent an emergency right hemi-colectomy with ileostomy formation with no improvement of his symptoms. Additionally his ileostomy prolapsed and ulcerated, causing him severe pain and bleeding. Infliximab was prescribed with some clinical response, but anaphylaxis led to a switch to Adalimumab. Although there was again some improvement, his symptoms persisted. The chronic use of steroids led to the development of severe hypertension, with extremely poor quality of life and poor to no school attendance. He additionally developed arthritis and debilitating pyoderma gangrenosum. Immune deficiencies and exclusions of known genetic mutations for early onset IBD were made. A multidisciplinary team meeting (Immunology, Gastroenterology and BMT) decided to proceed with a HSCT. Pre-transplant endoscopic assessment showed ongoing severe active oesophagitis and chronic colitis.

Results: The patient's pyoderma gangrenosum had healed 3 months post HSTC, an endoscopic assessment revealed only minor increase of intraepithelial cells in the lamina propria in the colon. 9 months post-transplant he was weaning Ciclosporin started for skin graft versus host disease (GvHD). 18 months post-transplant the patient had reconnection surgery with stoma closure. He is clinically well and his last endoscopy assessment showed no significant histological abnormalities. All his immunosuppression medication has been stopped; he has excellent energy levels and is eating a normal diet.

Conclusions: We report a successful allogeneic HSCT for severe refractory CD in a child, with no major complications of HSCT, now being off immunosuppression. We suggest that HSCT is a valid treatment option for patients with refractory CD presenting with poor quality of life, IBD-related complications, immunosuppressive treatment related complications and have exhausted conventional medical therapy. Careful selection of patients and discussion in multi-disciplinary teams is crucial to the success of this intensive treatment.

P445
Significance of non-alchoholic fatty liver disease in patients with Crohn's disease.

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Background: As reported by published studies, non-alcoholic fatty liver disease (NAFLD) has recently increased in Crohn's disease (CD). There are, however, no studies evaluating the significance on NAFLD in CD. This study demonstrates the frequency and impact of NAFLD on the disease course of CD.

Methods: CD patients who underwent abdominal ultrasound (US) from November 2008 to October 2014 were analyzed. CD patients with NAFLD by US were compared with those who had no evidence of NAFLD.

Results: This single center cross-sectional study included 300 CD patients with US; 65 (21.8%) had evidence of NAFLD by US imaging. The NAFLD group had lower CRP (0.58 vs. 2.18 (mg/dl), $P < 0.0001$) and significant higher remission (CDAI < 150) rate (75.9% vs. 53.7%, $P = 0.0024$). Age (42.0 vs. 35.5, P=0.0001) and body mass index (21.7 vs. 19.8, $P < 0.0001$) was higher and disease duration was longer (17.2 vs. 14.1 (years), $P = 0.028$) in NAFLD group. The effects of sex did not differ between groups. Multivariable analysis showed that NAFLD was an independent predictor of CRP negative (< 0.3mg/dl)(odds ratio (OR) 1.85; 95% confidence interval (CI) 1.03-3.37) and CDAI remission (OR 2.24; 95% CI 1.12-4.68).

Conclusions: NAFLD occurred in 21.8% of the CD population. NAFLD patients were in relatively better prognosis than those without NAFLD in CD course.

P447
Early initiation of adalimumab significantly diminishes post-operative Crohn's Disease recurrence, and is superior to immunomodulator therapy. Preliminary results from the POPART trial

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Background: A sizable proportion of Crohn's disease (CD) patients will undergo intestinal resection, but most will experience early endoscopic and clinical disease recurrence. Prevention of post-operative recurrence using a risk-stratified approach was recently demonstrated to be superior when anti-TNF agents were compared to placebo and immunomodulators, but the value of early anti-TNF in an all-comers patients population has not been examined to date. Aim: To evaluate the efficacy of an early unstratified approach comparing anti-TNF (adalimumab) and thiopurine (6-mercaptopurine, 6MP) therapy on the natural history of post operative CD recurrence. Aim: To evaluate the efficacy of an early unstratified approach comparing anti-TNF (adalimumab) and thiopurine

(6-mercaptopurine, 6MP) therapy on the natural history of post operative CD recurrence.

Methods: All CD patients undergoing a first ileocecectomy for inflammatory complications were prospectively recruited to the Post OPerative Adalimumab Recurrence Trial (POPART). Patients were randomized within 45 days to receive either adalimumab 160mg/80mg and then 40 mg every other week, or 6MP 1.5mg/kg/day. All patients underwent ileocolonoscopy at 6 and 12 months to asses for endoscopic recurrence as defined by the Rutgeert's score. Endoscopic remission was defined as a Rutgeert's score of i0-i1, while advanced lesions were defined as i2-i4.

Results: Nineteen patients have reached the 24 week time point. The mean ages of patients in the 6MP (n=8) and adalimumab (n=11) arms (30.5 ± 2.3 vs 34.4 ± 2.5 years, respectively) as well as the smoking status (1/11 vs3/8smokers/total) were comparable. Fifty percent (4/8) of the 6MP-treated patients had advanced lesions (i2), compared to only 9% (1 of 11) of the adalimumab-treated patients ($p<0.05$). Furthermore median fecal calprotectin levels were 186 in the 6MP (n=6) arm and 27 in the adalimumab arm (n=3), and adalimumab-treated patients gained more weight (6.5kg vs 3.5kg increase in the 6MP group, p=0.06) during the 24 weeks follow-up. CD activity index, histological scores, C-reactive protein, and quality of life as represented by the IBDQ score were comparable. Importantly, a Rutgeerts score of i2 was the most advanced score recorded in both groups, mostly due to discrete perianastomotic ulcers.

Conclusions: Early treatment of post operative CD patients with adalimumab is significantly superior to 6MP, regardless of risk stratification. Applying such therapy may modify the natural history of post-operative CD.

P448
How good are we at detecting and managing folate deficiency in inflammatory bowel disease?

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Background: Colorectal cancer (CRC) is the third most prevalent malignancy in the world and is the second leading cause of cancer death worldwide. Epidemiologic and clinical studies indicate that dietary folate intake and blood folate levels are inversely associated with colorectal cancer risk. Folate is involved in the biological methylation and maintenance of intracellular DNA synthesis, therefore, folate deficiency could potentially lead to cancer through disruption of these events. Patients with inflammatory bowel disease (IBD) have a higher risk of developing micronutrient deficiencies including folate in addition to a higher risk of developing CRC, and folate deficiency may synergistically add to this risk of CRC in these patients. Causes of folate deficiency in IBD include inadequate dietary intake, malabsorption and medication interactions. The aim of our study was to ascertain if folate was measured in our IBD patients and whether folate deficiency was corrected.

Methods: A single centre, retrospective analysis of IBD patients from a large district general NHS trust in North London was performed. Patients on methotrexate already receiving folic acid were excluded from the study. The data on demographics, diagnosis, treatment, folate levels and supplements from IBD patients were obtained from the local IBD database and electronic patient records.Folate deficiency was defined as a folate level of <3.1ug/ml.

Results: 333 patients with IBD were identified in the database. 8 patients were excluded from the analysis (4 patients on methotrexate and 4 with insufficient data). Of the 325 remaining patients, 159 were classified as Crohn's disease (CD), 153 as UC and 13 as IBD unclassified (IBD-U). Folate was checked in 222/325 (68.3%) of IBD patients. Folate deficiency was observed in 27/222 (12.2%) patients: 13/112 (11.6%) CD patients, 12/100 (12.0%) UC patients and 2/10 (20.0%) IBD-U patients. Of the 13 CD patients, 11 (84.6%) have ileal or ileocolonic disease. Folic acid was given to 15/27 (55.6%) patients with a folate deficiency. Only 7 out of these 15 patients had their folate levels rechecked and in all these cases an adequate treatment response with correction of folate levels was achieved.

Conclusions: In this study, almost a third (31.7%) of patients with IBD did not have their folate measured. Folate deficiency was not corrected in 45% of IBD patients in whom it was identified. This may suggest a missed opportunity to reduce the CRC risk in these patients with IBD who do not undergo folate measurement or correction if deficient. We recommend routine measurements of folate in all IBD patients under follow up and supplementing those who are deficient to further reduce the risk of CRC in this group.

P449
Anti-drug Antibodies Inhibit Neutralization of TNF-alpha in Infliximab Treated Patients with Inflammatory Bowel Disease (IBD)

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Background: Infliximab (IFX) trough levels (TL) as well as c-max levels have been positively associated with its efficacy and negatively with IFX immunogenicity in patients with IBD. Clearance of IFX is increased in the presence of anti-drug antibodies (ADA). However, to what extent ADAs impact the binding and neutralization of soluble TNF-alpha in vivo remains largely unknown. In this study we assessed the relationship between IFX-, ADA- and TNF-alpha levels at a mid-infusion visit and at trough in patients with IBD on maintenance therapy.

Methods: Serum samples from 90 consecutive patients with IBD (Crohn's disease: n=66, ulcerative colitis: n=24) on IFX maintenance therapy were obtained at mid-infusion visits and at trough. IFX and ADA were measured by a homogeneous mobility shift assay from Prometheus, which allows detection of ADA in the presence of IFX. Serum TNF-alpha was measured by a Collaborative Enzyme Enhanced immuno-Reactive (CEER) Assay.

Results: Patients had received a median number of 11 IFX infusions (range 3 - 71) with a median dose of 5.5 mg/kg (4.1- 10.9 mg/kg) before study entry. ADAs were detected in 18 pts at mid-infusion and in 21 pts at trough. In ADA positive pts median serum concentration of IFX was significantly lower than in ADA negative pts both at mid-infusion and at trough. Inversely, significantly higher serum concentrations of TNF-alpha were detectable in ADA positive pts at both visits (see Table1). At trough the TNF-alpha/IFX ratio was significantly higher in ADA positive patients (give data) than in

"Table1"

	Mid-infusion			Trough		
	ADA neg. n=69	ADA pos. n=21	p-value	ADA neg. n=69	ADA pos. n=21	p-value
IFX (µg/ml) median (range)	13.59 (3.2-35.2)	0.75 (0.08-16.37)	<0.0001	6.36 (range)	0.42 (range)	<0.0001
TNF-α (pg/ml) median (range)	5.5 (range)	10.2 (range)	0.04	7.5 (range)	25.6 (range)	<0.0001

those without ADA (give data, p<0.0001). No difference was seen in TNF-alpha levels when segregated by IFX serum levels alone. Interestingly, 3/10 (30%) ADA negative pts at mid-infusion with an IFX concentration below 8 µg/ml turned ADA positive at trough versus 1/36(3%) pts with an IFX concentration above or equal 8 µg/ml.
Conclusions: ADA detected in patients with IBD on IFX maintenance therapy impairs neutralization of soluble TNF-alpha and is associated with lower serum concentrations of IFX and higher levels of TNF-alpha both at mid-infusion and at trough. Our finding favours a strategy of a pre-emptive dose optimization in ADA positive patients due to insufficient control of inflammation.

P450
Poor recognition and management of iron deficiency anaemia in inflammatory bowel disease: a missed opportunity

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Background: Iron deficiency anaemia (IDA) is a common complication of inflammatory bowel disease (IBD) that has an impact on the patient's quality of life. IDA is caused by inadequate dietary intake, malabsorption of iron and iron loss through intestinal bleeding. Current guidelines recommend that all patients with IBD should be assessed for IDA and that iron supplementation be given as indicated. The aim of this study was to ascertain the prevalence of IDA in our IBD cohort, to look at whether iron replacement therapy (and in what form) was given and to assess treatment response.
Methods: A single centre, retrospective analysis of IBD patients from a large district general NHS trust in North London was performed. The local IBD database and electronic patient records (blood results and outpatient clinic letters) were used to collect data on patient demographics, diagnosis, screening parameters for IDA (Hb, Ferritin/transferrin saturation, CRP) and iron replacement therapy. The WHO definitions of anaemia were used (Hb<13g/dL in men and Hb<12g/dL in non pregnant women). Iron deficiency was diagnosed if ferritin <30 ug/L in quiescent IBD or <100ug/L in active IBD (CRP elevated) or transferrin saturation <16%.
Results: 333 IBD patients were identified in the database. 3 patients were excluded because of insufficient data as their care was transferred. 293/330 (88.8%) were checked for IDA using the screening parameters. 146/293 (49.8%) of this group were found to be anaemic. 101/146 (69.2%) had evidence of iron deficiency. 61/101 (60.4%) were treated using oral and/or intravenous (IV) iron preparations or blood transfusions. Most patients (50/61) received oral iron while 10 patients had IV iron (4 had failed oral therapy) and 6 had a transfusion. The recurrence rate of IDA was 21/50 with oral iron, 4/10 with IV iron and 4/6 with transfusions. We also noted that there were 39/184 patients (21.2%) with iron deficiency in the absence of anaemia. Only 3 of these patients were treated for iron deficiency.
Conclusions: The prevalence of IDA in our IBD group was close to 50%. Current practice in our trust does not comply with guidelines as only 60.4% of IDA patients were treated. Iron replacement therapy was mostly administered in the oral form. Recurrence of IDA was similar (about 40%) with both oral and IV iron therapy. There is little guidance on management of iron deficiency in the absence of anaemia and supplementation was not widespread in this group. Barriers to appropriate recognition of IDA including lack of routine monitoring and knowledge on iron data interpretation will need to be addressed to improve practice.

P451
Cost of hospitalisations among moderate-to-severe Ulcerative Colitis patients treated with adalimumab and conventional non-biologic therapies

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Background: Medical treatment options for patients with moderate-to-severe ulcerative colitis (UC) include conventional non-biologic therapies and biologic therapies, mainly tumour necrosis factor inhibitors. The economic burden of UC is substantial, owing partly to hospitalisation costs. The current study aimed to quantify the costs of hospitalisations among UC patients treated with adalimumab and with conventional non-biologic therapies in the United Kingdom (UK), Germany, France, Italy, Spain, and Canada.
Methods: An economic model was developed to estimate the annual hospitalisation costs for 1,000 moderate-to-severe UC patients, assuming they were treated with adalimumab or conventional non-biologic therapies. Rates of UC-related and all-cause hospitalisations for adalimumab and conventional non-biologic therapies among moderate-to-severe UC patients were derived from a publication summarising two Phase-III clinical trials of adalimumab (NCT00385736, NCT00408629)[1]. Unit costs per hospitalisation in the UK, Germany, France, Italy, Spain, and Canada were derived from the literature. All costs were inflated to 2013 in each country's respective currency.
Results: Treatment with adalimumab compared with conventional non-biologic therapies was associated with 101 fewer UC-related and 83 fewer all-cause hospitalisations per 1,000 UC-treated patients during a 1-year period. This finding translated to a UC-related annual cost savings of £292,160 in the UK, €190,528 in Germany, €256,453 in France, €615,221 in Italy, €433,536 in

Spain, and CAN$1,156,199 in Canada. Adalimumab-associated all-cause annual cost savings were £249,956 in the UK, €163,005 in Germany, €219,407 in France, €526,351 in Italy, €370,910 in Spain, and CAN$989,182 in Canada.

Conclusions: Treatment with adalimumab compared with conventional non-biologic therapy is associated with fewer UC-related and all-cause hospitalisations and with reduced costs among patients with moderate-to-severe UC.

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P452
Usability study of a smartphone-based patient monitoring system measuring Calprotectin for therapy follow-up

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Background: Inflammatory Bowel Disease (IBD) is a chronic inflammation of the gut presenting with phases of active inflammation, remission and relapses. IBD treatment goals are mucosal healing and persistent remission. Calprotectin measured in patients' stool samples is a well-established biomarker to measure the inflammatory activity in the gut. Periodical assessment of calprotectin levels is important to measure effectiveness of the treatment as well as predicting relapses. Until now affected patients send in their stool sample for laboratory analysis, leading to long time spans between sample collection and final test result. To ensure real-time information about the inflammatory activities in the gut for both, the clinician and the patient, we have developed a calprotectin home test, called IB*Doc*®. The IB*Doc*® consists of a stool extraction device (CALEX® Valve) and an immunochromatographic rapid test, which is measured using a smartphone App (CalApp®) controlling the phone's camera. Once the test is measured the result is sent to a webserver (IB*Doc*® Portal) allowing the treating physician immediate access to the result.

The objective of this study was to evaluate the usability of the IB*Doc*® calprotectin home test system with lay users in respect of handling both, the physical test components as well as the integrated software.

Methods: 25 voluntary healthy lay users (age 24-60 years) naïve to the IB*Doc*® system were trained to perform the test and asked to carry out a calprotectin stool test by themselves at home. The lay users then filled in a questionnaire based on 5-point Likert scale questions, free commentary sections and system usability scale (SUS). The SUS is commonly used in measuring and comparing the usability of integrated software systems.

Results: All 25 lay users were able to generate a calprotectin test result by themselves. 24 out of 25 users were able to collect and extract a stool sample with the CALEX® Valve device without major problems, and 22/25 were confident that the rapid test was performed correctly. When asked how easy it was to measure the test cassette with the smartphone, the users judged this question with an average score of 4.4 on a 5-point Likert scale. 21/25 users felt comfortable to use a smartphone for a medical test. The IB*Doc*® system reached a mean SUS score of 82 on a scale from 0 to 100. This SUS is well above the software industry's average of 68[1].

Conclusions: This study shows that calprotectin home testing using a smartphone as measuring system was well accepted among the tested lay users. The complexity of the application is low, the entire IB*Doc*® system can be considered very user-friendly and is easy to handle by lay users without prior knowledge or experience of immunochromatographic rapid tests.

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P453
Infliximab population pharmacokinetic modelling in patients with Inflammatory Bowel Disease (IBD): Patient factors influencing infliximab pharmacokinetics

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Background: There is a high interindividual variability in IFX pharmacokinetics (PK) and trough levels (TLI) in IBD. This is relevant because TLI influence response to therapy. The objective of the study was to evaluate factors affecting IFX exposure and pharmacokinetic variability in IBD.

Methods: Patient data were collected prospectively from patients on IFX between July´13 and March´14. Samples were collected before intravenous infusion at steady state. TLI and antibodies toward infliximab (ATI) were measured by ELISA (Promonitor®). Pharmacokinetic analysis based on the Fasanmade et al. PopPK model for Crohn disease (1) was carried out using Nonmem®7.2. TLI, individual peak levels (Cmax) and area under the concentration-time curve (AUC) were individually predicted and individual PK parameters were calculated (Bayesian approach) according to interindividual variance of the population PK model.

Results: 132 TLI and ATI were measured from 64 patients (25 ulcerative colitis, 39 Crohn's disease). TLI, dose-adjusted TLI and dose-adjusted AUC were significantly higher in patients without ATI and in those receiving IMM before initiating IFX. ATI formation was associated with a 26.8% increase in clearance (Cl) ($p< 0.00001$) whereas Inmunomodulators (IMM) significantly reduced Cl. Patients who initiated IMM before IFX therapy required their first dose escalation later than those who were not on concurrent IMM ($p=0.015$). When IMM were initiated before IFX, t1/2 was longer than when IMM were added throughout IFX therapy or no prescribed. A higher proportion of patients achieved TLI > 3 mg/L if serum albumin concentration (SAC) was >3.9 g/L. Smoking and SAC<3.9 were associated with an average 162% and 13% increase in Cl, respectively.

Conclusions: Inmunomodulators, SAC, presence of ATI and smoking status influence IFX pharmacokinetics. Patients who initiated IMM before IFX therapy could have better pharmacokinetic profile than patients without IMM or when IMM were added throughout IFX therapy. IFX dosing could be individualized according these variables in order to improve outcomes for IFX-treated patients with IBD.

P454
A protocol to avoid corticosteroids in Crohn's disease requiring luminal surgery

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Background: Corticosteroids (CS) are prescribed to control inflammatory and obstructive symptoms in Crohn's disease (CD). Preoperative CS are associated with higher risk of all complications post-operatively including sepsis, anastomotic breakdown and venous thromboembolic disease. High doses of CS also preclude a primary anastomosis.

Methods: In January 2013 we implemented a protocol to avoid CS administration or allow a rapid wean in patients requiring ileal/ileocaecal resection, with use of exclusive enteral nutrition (EEN) or parenteral nutrition (PN). Where tolerated, this also enables nutritional optimisation.

EEN (with either Modulen IBD Nestle or Fortisip Nutricia as tolerated, as tolerated) is prescribed to a target dose of 30kcal/kg, and sepsis controlled with intravenous, then oral antibiotics. This approach provides relief for obstructive symptoms and treats acute infection. If EEN is not tolerated due to ongoing obstructive symptoms, parenteral nutrition is considered or surgery is expedited. Patients on CS are advised to wean. This protocols primary aim is to avoid corticosteroid exposure for more than 4 weeks prior to surgery.

Patients requiring surgery were not offered this protocol if they had minimal symptoms, adequate nutritional status and not on CS.

Results: In total, 39 patients with CD had ileal/ileocaecal resection from January 2013 - September 2014.

17 were excluded from protocol implementation. 9 emergency surgeries all with penetrating and/or stricturing disease or suspected cancer; 4 operations on CS (45%). 8 patients with stable symptoms secondary to fibrotic stricture (4 on biologic, 4 on immunomodulator) and adequate nutritional status not requiring CS.

22 patients with acute symptoms suitable for above protocol, all with penetrating and/or stricturing disease. 8 patients on pre-existing CS. 7 successfully weaned off CS for more than 4 weeks with EEN, 1 did not tolerate, and proceeded to surgery on CS. 11 patients successfully treated via protocol to avoid CS (7 with EEN / 4 with PN). 3 patients did not tolerate/declined EEN and proceeded to expedited surgery avoiding CS.

Where the protocol was implemented, CS administration was not required (14/14 patients, 100%) and wean >4 weeks successful in majority (7/8 patients, 87.5%). CS exposure was limited to 1 patient via protocol (4.5%).

Conclusions: The above protocol provides and alternative approach to control acute symptoms in patients requiring ileal/ileocaecal resection, avoiding CS exposure and optimising nutrition. The implementation of the protocol requires close liaison between gastroenterologists, colorectal surgeons and dietetics. The protocol should not delay emergency operations.

P455
Need and predictors of colectomy for Ulcerative Colitis patients in the biologic therapy era. A real life experience in a tertiary referral center

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Background: Since its introduction on 2005, anti-TNF therapy has been increasingly used in patients with moderate or severe ulcerative colitis (UC) and the natural history of the disease has changed dramatically. With our study we aimed to examine how the colectomy rate has changed from the prebiologic to the biologic eras, while we tried to identify predictors of colectomy in these patients.

Methods: Adult patients with a diagnosis of ulcerative colitis who subsequently underwent an urgent or elective colectomy for medically refractory disease in our hospital between October 1998 and October 2014 were identified. We retrospectively analyzed data on patients with UC receiving infliximab, adalimumab and golimumab from October 2006 to October 2014 while the need for colectomy was also calculated and compared to the one observed between October 1998 to October 2006 when biologic therapy was not available.

Results: From October 2006 to October 2014, 122 patients with ulcerative colitis were followed up in our Department. The mean age of this patients' group was 44±15 years and 65 were males (53.27%), while 32 patients had pancolitis, 55 had left sided colitis and 35 had proctitis. Out of these patients, 46 received therapy with an anti-TNF agent (infliximab n=31, adalimumab n=10, golimumab = 5) because of steroid refractory (n=26, 56.52%) or steroid dependent disease and/or failure of immunomodulator therapy (n=20, 43.47%). Finally 11 patients have been subjected to colectomy (9.01%). As regards the period from October 1998 to October 2006, 77 UC patients were followed up in our Department. The mean age of this patients' group was 51±19 years and 38 were males (49.35%), while 21 patients had pancolitis, 39 had left sided colitis and 17 had proctitis. From these patients 19 have been subjected to colectomy (24.67%). According to the statistical analysis high CRP values (CRP > 5mg/L) and severe endoscopic lesions at initial presentation (Mayo endoscopic score = 3) were associated with the risk of colectomy (Risk Ratio=1.95, 95%CI 1.15-4.02 and Risk Ratio=3.57, 95%CI 1.75-10.02, respectively).

Conclusions: The total incidence rate of colectomy for medically refractory ulcerative colitis has declined substantially since 2006, paralleling the increased use of anti-TNF therapy in this patient population. High CRP values and severe endoscopic lesions at initial presentation are associated with the risk of colectomy.

P456
First observations of the use of biosimilar infliximab for treatment of ulcerative colitis in paediatric population.

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Background: Biological treatment in ulcerative colitis (UC) is employed after the failure of standard treatment. Introduction of biosimilar infliximab (INF) (Remsima/Inflectra) in European Union allows gaining first experience with this medicine in children with ulcerative colitis. Biosimilar infliximab was authorised in all indications on the basis of in-depth review of preclinical and clinical data. However, the use in children with ulcerative colitis was not reported previously.

Methods: Six patients starting treatment with biosimilar infliximab Remisma (5 mg/kg) was assessed at week 10 after receiving 3 doses at weeks 0, 2 and 6. Disease activity (PUCAI) and laboratory values (CRP, ESR, platelet count) was assessed at the start of the biological therapy and at week 10. Mean and range of clinical values is reported.

Results: Median age of 6 patients was 12.3 years (range 8.5-17.5). Mean PUCAI before infliximab initiation was 47.5 (range 5-80). Mean (range) CRP, ESR and platelet count before initiation were 1.8 mg/dL (0.03-8.1), 24 mm (5-33) and 370x109/L (260-530x109). For one patient it was the second course of biological treatment (3 doses of the reference INF received 9 months ago. For 2 patients (33%) treatment was discontinued, in 1 due to lack of response after first dose (disease flare), in second due to anaphylactic reaction during dose 3 infusion. For the latter patient that was the second course of infliximab treatment. As of November 2014 3 patients (50%) received 3 doses and were evaluated at week 10. For these patients initial values of PUCAI, CRP, ESR and platelet count were not different than for all 6 patients. After 3 doses of biosimilar infliximab PUCAI values decreased to 28.3 (range 5-50). CRP, ESR and platelet count were 0.3 (0.02-0.68), 20 (10-28) and 418x109 (236-706), respectively.

Conclusions: Initial observations point to efficacy and safety of biosimilar infliximab in the treatment of pediatric patients with ulcerative colitis. Further studies with larger patient groups are required. Data for more patients and longer observation time will be collected and presented.

P457
Anti-TNF therapy successfully improves anemia in Inflammatory Bowel Disease - Results from a tertiary referral center

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Background: BACKGROUND: Anemia is a frequently overlooked complication of inflammatory bowel disease (IBD) but studies have reported a prevalence ranging from 6% to 74%. In IBD, anemia results from a combination of complex mechanisms, though iron deficiency and inflammation play major roles. Anemia has been associated with increased healthcare utilization and reduced quality of life in IBD patients.

AIM: Our primary goal was to determine the prevalence of anemia in active Ulcerative Colitis (UC) and Crohn's Disease (CD) and determine the impact of anti-TNF therapy on hemoglobin levels. We also assessed possible predictors of response.

Methods: METHODS: We retrospectively reviewed patients with moderate to severe UC and CD followed in our institution assigned to start anti-TNF therapy. Prevalence of anemia was determined prior to starting Infliximab (IFX) or Adalimumab (ADA) and after one year of therapy. Patients who discontinued anti-TNF therapy before the end of study were excluded. Anemia was defined as a hemoglobin level lower than 12 g/dL in women and 13 g/dL in men.

Results: 211 patients (182 CD, 29 UC) met our inclusion criteria. Anti-TNF therapy included IFX in 161 patients (138 CD, 23 UC) and ADA in 50 patients (44 CD, 6 UC). At baseline 85 patients were under immunomodulation (76 CD, 9 UC).

The overall prevalence of anemia in our population at baseline was 33.2%. Hemoglobin levels were inversely correlated with C-reactive-protein (CRP) levels at baseline (Spearman's rho -0.183, p<0.001). A negative CRP (<0.5 mg/dL) had a positive predictive value of 74.7% for the absence of anemia.

There was no statistically significant association between the presence of anemia at baseline and IBD subtype (p=0.31), gender (p=0.4) and immunomodulation therapy (p=0.121).

After one year of therapy there was a statistically significant decrease in the prevalence of anemia (33.2% vs. 11.0%, p<0.005). CRP levels were significantly lower in patients who corrected anemia (1.27 mg/dL vs. 0.62 mg/dL, p=0.002). Combined immunomodulation had no impact on response (p=0.29).

Conclusions: CONCLUSIONS: Anemia is a common complication in IBD. Anti-TNF therapy is associated with a decrease in the prevalence of anemia and levels of CRP in moderate to severe IBD. This effect supports the importance of inflammation in the pathogenesis of anemia.

P458
Cutaneous events during anti-tumour necrosis factor (anti-TNF) treatment at a London Inflammatory Bowel Disease (IBD) centre

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Background: Anti-TNF agents are important in the treatment of IBD. Studies have reported paradoxical skin inflammation in patients receiving anti-TNF therapy: Cleynen reported 22.5%[203/922] patients on infliximab (IFX) developed a skin problem (58% psoriaisiform or eczematous)(1) and a smaller study by Wlodarczyk, reported 60% to have skin manifestations (44% psoriaisiform, 22% eczema)(2).

Methods: We aimed to identify IBD patients at our hospital that developed skin pathology attributed to anti-TNF therapy. All IBD patients currently receiving anti-TNF therapy were asked to complete a questionnaire. 50%[117/233] patients responded.

Results: 117[64 male] IBD patients, 77%[90/117] on IFX and 23%[27/117] on adalimumab, responded. Median age[range] 40[19-78]years. 83%[97/117] white Caucasian, 9%[11/117] Asian, 3%[4/117] Afro-Caribbean and 3%[4/117] other. 86%[101/117] had Crohn's disease, 9%[10/117] ulcerative colitis and 5%[6/117] indeterminate colitis.

34%[40/117] had a skin complaint whilst on anti-TNF, of which 26%[31/117] attribute it to the anti-TNF agent (21%[19/90] IFX;

44%[12/27] adalimumab). Of those 31, 74%[23/31] were taking concurrent IBD medication: 45%[14/31] aminosalicylate; 54%[17/31] thiopurine; 3%[1/31] methotrexate; 6%[2/31] corticosteroid.

77%[24/31] of those with skin complaints thought secondary to anti-TNF therapy had a formal opinion from a clinician (38%[9/24] by a dermatologist). 38%[9/24] had eczema, while 21%[5/24] had a cutaneous infection (either fungal, viral or bacterial), 1[4%] had drug induced systemic lupus erythematosus (SLE), and 1[4%] psoriasis. 33%[8/24] could not recall the diagnosis, however the most common descriptors chosen were crusty, dry, red itchy skin, appearing mostly on face and legs (those with eczema described dry, crusty, red itchy skin mostly on face, legs and arms).

58%[18/31] required treatment: 89%[16/18] topical treatment; 39%[7/18] steroids; 28%[5/18] antibiotic/antifungal/antiviral treatment; 11%[2/18] non-steroidal treatment for dermatitis; 39%[7/18] could not recall the treatment. 50%[9/18] continued to have the skin complaint following treatment.

6%[2/31] had to stop anti-TNF due to the skin complaint: the patient with impetigo discontinued adalimumab, while the patient with drug-induced SLE switched from IFX to adalimumab.

Conclusions: We report similar figures (26%) to larger studies of skin complaints in patients on anti-TNF therapy(1). Inflammatory skin disease (eczema) was the commonest skin complaint seen in our cohort. The majority of patients had their skin complaint reviewed by a medical professional and in only 2 cases was anti-TNF therapy stopped. Medical, specifically early dermatological, review is advised to direct treatment and prevent anti-TNF withdrawal (1).

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P459
Characteristics of Pediatric Crohn's Disease in a Tertiary Center in China according to Paris Classification

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Background: Paris Classification was recently validated to better characterize inflammatory bowel disease (IBD), especially pediatric IBD. In contrast to the Montreal classification which all patients <17 years were grouped as A1, the Paris classification recognizes Crohn's disease (CD) patients aged <10 years as A1a and those 10-17 years as A1b. A few retrospective studies have analyzed the incidence and phenotype of pediatric CD according to the new classification whereas data was limited in Chinese. So the present retrospective study aimed to analyze the characteristics of pediatric Crohn's disease in Chinese population according to Paris classification.

Methods: Consecutive patients (Age <17 years) diagnosed as CD in our IBD center from January 2007 to July 2014 were enrolled. Diagnosis was based on the latest ECCO guideline. Clinical data was collected and the phenotype was classified according to the Paris classification.

Results: Ninety-two patients were included, which account for 21.9% of all CD patients diagnosed during the same period. Among them, 22(23.9%) were diagnosed before 10 years old (A1a group). 70(76.1%) were diagnosed between 10-17 years old (A1b group). In the A1a group, there were 2 L1 (9.1%), 2 L2 (9.1%), 8 L3 (36.3%), 7 L3L4b (31.8%), 1 L1L4b (4.5%), 2 L3L4aL4b (9.1%).In the A1b group, there were 3 L1(4.3%),12 L2(17.1%),51 L3(72.9%), 4 L3L4b(5.7%).The upper gastrointestinal tract involvement was significantly higher in A1a group($P<0.05$). 6(27.3%) patients behaved as penetrating behavior and 1 with stricture(4.5%) in A1a group, while in A1b group,10 patients(14.2%) behaved as penetrating behavior and 19(27.1%)with stricture($P<0.05$). The proportion of perianal involvement was 6(27.2%) in A1a group and 38(54.2%) in A1b group ($P<0.05$). The proportion of growth retardation was significantly higher in A1a group (59.2v.s. 28.6%, $P<0.05$). During the first year after disease diagnosis, 2 patients with penetrating behavior in A1a group experienced intestinal surgery and 1 patient in A1b group experienced intestinal surgery because of stricture.

Conclusions: The phenotype of pediatric CD may be different between different age groups. Those with early on-set seemed to be with more extensive distribution, higher risk of upper gastrointestinal tract involvement as well as growth retardation. The Paris classification is a useful tool to discriminate the very early onset pediatric CD who believed to have different pathogenesis from other age group. Further study should be conducted to determine if this stratification would predict prognosis and benefit our treatment strategy.

P460
Efficacy and Safety of Granulocyte/Monocyte Apheresis in Active Ulcerative Colitis Using an Adsorber Device Based on Cellulosic Filaments

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Background: Granulocyte/monocyte apheresis (GMA) is an emerging therapeutic option in ulcerative colitis (UC). The efficacy and safety of a recently introduced adsorber device based on cellulosic filaments (Immuloc® sorbent) was studied for the treatment of active UC.

Methods: Eligible patients in two different centers had to have a clinical activity index according to Rachmilewitz (CAI) > 4 points at baseline. Over a period of 5 consecutive weeks, patients enrolled received 5 to 10 GMA at a blood flow rate of 30 ml/min for 60 to 120 min. CAI, endoscopical index (EI) and C-reactive protein (CRP) were assessed at baseline, after the treatment period and at the end of the observation period.

Results: Of 33 patients totally enrolled, 27 were eligible for the per protocol population (PPP). 3 patients had to discontinue the study early and 3 met an exclusion criterion before treatment initiation. The median baseline CAI and EI of the PPP were 8 (range 5 to 17 points) and 9 points (6 to 12 points), respectively. Nine patients presented mild, 14 moderate (CAI ≥ 8-10 points; EI ≥ 7 points) and 4 patients severe UC (CAI ≥ 11 points; EI ≥ 7 points). At the end of the treatment period, remission (CAI < 4 points) was achieved in 16 patients (59.3 %) and response (reduction in CAI or in CAI plus

EI of ≥ 3 points) in 5 patients (18.6 %). Six patients (22.2 %) did not respond to GMA. At the end of the 4-5-week follow-up period, 12 patients were still in remission and 5 patients fulfilled the criteria for response. The mean baseline CRP of 12.02 mg/L decreased to 5.38 mg/L after treatment and was 6.09 mg/L at the end of the follow-up period (not statistically significant). The treatments were overall well tolerated with only mild therapy related adverse symptoms, such as temporary headache, dizziness, and nausea, in only few patients.

Conclusions: The vast majority of patients with active UC benefits from GMA, which is well tolerated with only few side effects. The highly favorable risk to benefit ratio makes GMA with the Immuloc® sorbent a promising therapeutic option even in patients with severe UC.

P461
Therapeutic requirements and health resources in the treatment of clinically active ulcerative proctitis

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Background: In population-based studies, ulcerative proctitis (UP) accounts for more than 25% of of ulcerative colitis (UC) patients and presents clinical, distinctive clinical outcomes and therapeutic approaches as compared to left-sided and extensive UC. Aim: To describe the clinical outcomes, therapeutic requirements and the use of health resources for treatment of active UP.

Methods: We identified all the patients with UC limited to the rectum as maximum disease extent. Clinical information was recorded including patients' evolution and treatments provided for each episode, specifying galenical drug used.

Results: Out of 687 patients with UC, 101 (15%) had UP, with no further evidence of proximal progression. Median age at diagnosis was 38 years (IQR 29-49), average time of follow up was 8 years (3-14). The most common treatment schedule for disease activity was topical 5ASA in monotehrapy in 66% (mostly suppositories), followed by oral 5ASA monotherapy in 33% of patients, whereas 30% of patients were managed with combination therapy (oral+topical, topical+topical). Steroids were used topically in 26% of cases: In 8% of cases oral prednisone was used, and 10% used oral beclomethasone (mostly only one course per patient). Only 4% required hospital admission due to UP activity.

Conclusions: Active UP requires a low use of healthcare resources. In clinical practice, 5ASA suppositories are the most used treatment, suggesting a high degree of confidence by prescribers. However, oral 5ASA, topical corticosteroids and combination of any of them, are also frequently used for the management of active UP.

P462
A single factor of compliance may not be sufficient to improve outcomes in Ulcerative Colitis

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Background: While some factors, such as once-daily dosing of mesalazine (OD), have indicated better compliance, in real-life healthcare, it is still unclear if a single factor of compliance can improve the patient outcome.

Methods: A total of 520 patients (47 % females) aged between 16 and 82 years with ulcerative colitis (UC) were included in a prospective study which was conducted in 113 private gastroenterology specialist practices throughout Germany. All patients were treated with mesalazine. Compliance was rated by the patients using a visual analogue scale (VAG) ranging from 0 (I have taken all medication correctly) to 10 (I have taken no medication).

The severity of UC was rated according to the UCDAI; follow-up took place for up to 12 months and included several patient visits. Results are given as median/range and differences were calculated using chi²-testing.

Results: In active UC, compliance improved during the study and was better at the end in the OD group compared to divided dosing (DD) (90.5 % vs. 79.9 %).

Patients in remission reported very good compliance at the start of the observation (OD: 84.1 % vs. DD: 82.4 %), which slightly improved with OD (88.9 %) but not with DD (82.1 %).

The UCDAI was 6 in patients with active disease in both groups (OD, DD) and dropped to 2 with OD as well as with DD. In the remission group, the UCDAI dropped from 3 to 2 with DD, while it increased from 2 to 3 with OD. The average UCDAI at visits A, B and C in patients with bad compliance (<=70 %) was 5.7 (4.8 - 6.7) (median/range) in comparison to 5.3 (5.0 - 5.5) (median/range) in patients with good compliance.

Conclusions: In real-life healthcare, a single factor such as daily dosing has only modest effects on compliance and no significant effects on outcome. Better compliance improves outcomes in patients with active disease and in those in remission.

P463
Achieving Remission in Paediatric Inflammatory Bowel Disease (pIBD): Data on Mono- vs. Combination Therapy using the ImproveCareNow (ICN) Data Base

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Background: The main objectives for managing children with Crohn's disease are to improve quality of life, promote growth, and prevent disease complications by maintaining remission. At the same time medications have significant side effects. A variety of treatment in Paediatric IBD is available either as monotherapy or combination therapy.

The aim of this study using our ICN database was to review the latest management of our pIBD patients identifying the number of patients currently in clinical remission and the treatment we are using to achieve our goal. Our centre joined the ICN collaboration in 2010 to benchmark our outcomes against at present 66 other pIBD Centres looking after a total of over 18 000 pIBD patients.

Methods: We retrospectively reviewed our ICN data base of 285 patients diagnosed with IBD at our tertiary Paediatric

Gastroenterology Centre. All patients were diagnosed with IBD according to standard clinical and histopathological criteria. We looked into each patient's last clinic appointment.

Results: We identified 206 patients (male n=117, aged 5-17 years, median 11y), 60% had Crohn's Disease (CD), 22% Ulcerative Colitis (UC), 18% IBD unclassified (IBDU.

80.5% (166) were in clinical remission, 15% had mild symptoms, <5% moderate to severe

In the clinical remission group 55 patients (33%) were on monotherapy, as follows: Aza/6-MP n=28, 5 ASA's n=16, MTX n=5, Infliximab n=3, Adalimimab n=3

107 (64.5%) on combination therapies: Aza/6MP and 5 ASA n=45, Aza/6MP and Infliximab n=16, Aza and Adalimumab n=5, MTX and Infliximab n=1, MTX and Adalimumab n=3, MTX and 5 ASA n=3, AZA and 5 ASA and Infliximab n=11, AZA and 5 ASA and Adalimumab n=6, Others n=17.

4 patients (2.5%) were not on any medication.

No difference in remission rate was seen across CD, UC and IBDU patients.

Conclusions: Overall 80.5% of our patients were in clinical remission, of whom one third were on monotherapy only.

Our ICN database is a valuable tool in capturing our remission rates on mono- and combination therapies, alerting us on treatment failures.

P464
Short- and Long-term Outcomes of Acute Severe Ulcerative Colitis in Korea: The 1999-2005 cohort

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Background: No studies have evaluated the long-term outcomes of acute severe ulcerative colitis (ASUC) in non-Caucasian populations. The purposes of this study were to evaluate short- and long-term outcomes of Korean patients with ASUC.

Methods: We retrospectively analyzed 99 patients with ASUC who satisfied the Truelove and Witts' criteria between 1999 and 2005. The short-term outcome parameter was colectomy rates during the index hospitalization, and the long-term outcome parameters were rates of colectomy and re-hospialization after discharge from the index hospitalization.

Results: During the index hospitalization, 16 of 99 patients (16.2%) underwent colectomy: 6 of 71 responders (8.5%) to intravenous steroids on day 3 versus 10 of 28 non-responders (35.7%) assessed using the Oxford Index (odds ratio, 6.02; 95% confidence interval, 1.93-18.80; P = 0.002). Among 83 patients who avoided colectomy during the index hospitalization, 13 patients (15.7%) underwent colectomy during a median duration of follow-up of 10.5 years (range, 0.3-15.4 years), producing cumulative probabilities of colectomy at 1, 5, 10, and 15 years after discharge of 2.4%, 10.1%, 14.3%, and 23.0%, respectively. In addition, 34 patients (40.1%) experienced a re-hospitalization for UC during follow-up with 1- 5- 10- and 15-year cumulative probabilities of 12.2%, 31.2%, 41.9%, and 48.6%, respectively. The cumulative probability of colectomy tended to be lower in complete responders on day 7 of intravenous steroid therapy than in the others: 3.7% versus 13.9% at 5 years, and 7.6% versus 18.2% at 10 years (P = 0.100). The cumulative probability of re-hospitalization was significantly lower in complete responders on day 7 of intravenous steroid therapy than in the others: 20.5% versus 37.5% at 5 years, and 31.4% versus 48.2% at 10 years (P = 0.043).

Conclusions: Assessment of the degree of response to intravenous steroids is helpful in predicting short- and long-term outcomes of ASUC. Korean patients with ASUC may have better short-term and long-term prognoses than Westerners, as indicated by the lower colectomy rate.

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P465
Inadequate immunisation against viral hepatitis B and no detected cases of hepatits C infection among patients with Inflammatory Bowel Disease

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Background: Hepatitis B (HBV) vaccination, screening for HBV vaccine-induced seroprotection and screening for hepatitis C (HCV) infection are recommended in patients with inflammatory bowel disease (IBD).

Methods: The aim of the study was to assess the immune status for HBV and HCV in Polish IBD patients. We examined 98 patients aged 18-91 yrs (mean 38 years; 55 men) with IBD hospitalised in the Department of Gastroenterology and Hepatology from November 2013 to March 2014. We did not included in the study patients with previously documented HBV or HCV infection. There were 61 patients with colitis ulcerosa (62%) and 37 (38%) with Crohn's disease; mean IBD duration was 8 years. In all patients antiHBsAb, antiHBcAb, HBsAg, and antiHCVAb were determined. Additionally, patients completed a questionnaire comprised of demographic data, IBD medical history and HBV vaccination history. The level of antiHBsAb ≥ 10 IU/l was considered as immunity to HBV infection. Patients with positive antiHBcAb or HBsAg were considered as HBV infected. Patients with positive antiHCVAb were considered as HCV infected (current or past infection). The chi-square test was used for cross-classification tables.

Results: Among 54 IBD patients who reported previous HBV vaccination, we detected 6 new cases of HBV infection. Overall, we found HBV infection in 13 patients. Forty three subjects (44%) had antiHBsAb level lower than 10 IU/l. In the subgroup of 48 vaccinated and non-infected patients 43 (90%) had the recommended level of antiHBsAb ≥ 10 IU/l and only 21 (44%) reached a cut-off level of 100 IU/l. There were no differences in the uptake of hepatitis B vaccine with regards to differing educational levels (p=0.44) and place of residency (p=0.68). We did not detect any positive antiHCV antybodies result.

Conclusions: HBV vaccine uptake is moderate despite the recommendations. All patients with IBD, even if previously HBV vaccinated, should be tested for antiHBsAb and in the case of non-response to vaccination, markers of HBV infection should be checked. Patients with IBD may need booster doses in order to maintain antiHBsAb levels ≥10 IU/l. Gastroenterologists should be more involved in HBV vaccine promotion to improve hepatitis B immunisation coverage.

P466
Not all penetrating events are the same: differences and similarities in patients with or without entero-urinary fistulas.

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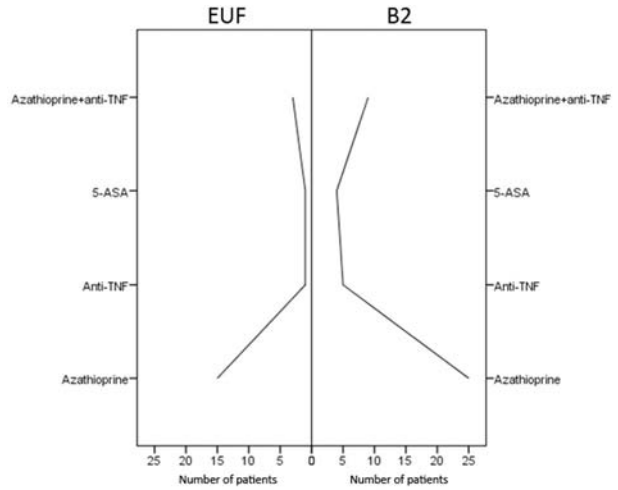
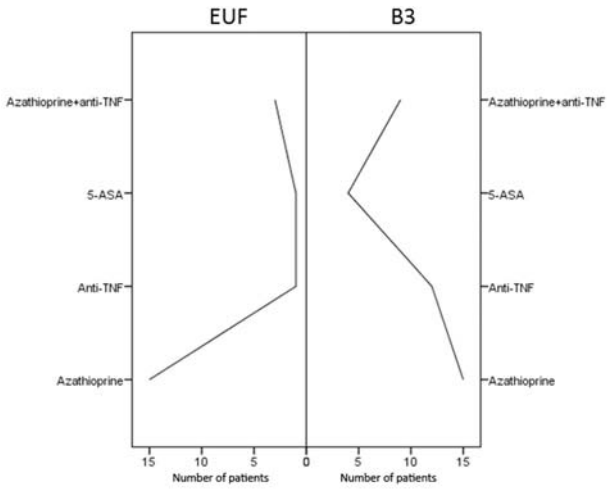
Background: Entero-urinary fistulas (EUF) are a rare manifestation of Crohn's disease (CD) observed in 2-8% of patients. The authors aimed to evaluate the response to treatment of patients with EUF in comparison with others with penetrating and stenosing phenotype (B2 and B3 according to the Montreal classification.

Methods: Retrospective single-center analysis of 21 patients with the diagnosis of EUF. Each patient with EUF was compared with 2 patients with B2 phenotype and 2 patients with B3 phenotype. They were randomly selected from inflammatory bowel disease database (www.gedii.pt) and they had the same extent of disease, smoking status, perianal disease and age at diagnosis.

Results: A total of 105 patients were included: EUF (n=21); B2 group (n=42); B3 group (n=42). Patients with EUF had a median age at diagnosis of 29.0 (IQR: 20.5-37.0) and were followed-up for a median of 11.0 years (IQR: 6.0-19.0). The EUF diagnosis was performed 15.0 months (IQR: 2.0-55.0) after CD diagnosis and all the patients were submitted to surgery, mainly ileocolectomy (71.4%). Comparing B3 group with patients with EUF, the former was more steroid dependent and resistant (52.4% vs. 19.0%, p= 0.009) and needed anti-TNF therapy more frequently (59.5% vs. 28.6%, p=0.016). Moreover, B3 patients had a poorer response to anti-TNF therapy without remission free of steroid therapy in comparison with EUF patients (92.1% vs. 16.7%, p<0.001). EUF patients did not differ from B2 group regarding anti-TNF therapy (p=0.956) and steroid dependence or resistance (p=0.141). The current therapy of patients with EUF is very similar to patients with B2 group (graphic 1) and differ from patients with penetrating phenotype (graphic 2).

Conclusions: Surgery seems to be a good therapy choice for patients with EUF as their response to CD treatment after surgery appears not to differ to B2 patients.





P467
Systematic Review and Meta-Analysis: Infliximab or Ciclosporin as Rescue Therapy in Patients with Severe Ulcerative Colitis Refractory to Steroids

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Background: Acute severe steroid-refractory ulcerative colitis (UC) carries a poor prognosis and requires optimal management. A systematic review and meta-analysis were conducted to assess ciclosporin and infliximab (IFX) as rescue agents in patients with steroid refractory UC.

Methods: A literature search identified studies that investigated IFX and ciclosporin in steroid-refractory ulcerative colitis patients. The primary outcome was short term response to treatment. Secondary outcomes included the rates of colectomy at 3 months and 12 months, adverse drug reactions, postoperative complications in those who received rescue therapy but underwent colectomy subsequently, and mortality. Odds ratios (OR) with 95% confidence intervals (CI) are reported.

Results: Overall, eleven studies with 988 participants were eligible for inclusion. Among two randomized controlled trials with 145 patients, no significant difference was seen with IFX compared to ciclosporin with regards to treatment response, and 3-month or 12-month colectomy. Among non-randomized studies with 843 eligible participants, IFX was associated with significantly higher rates of treatment response (OR 2.99 (95% CI 2.99-4.30)) and lower 12-month colectomy rate (OR 0.38 (95% CI, 0.17-0.85)), with no significant difference seen in 3 month colectomy rate (OR 0.71 (95% CI, 0.26-1.89) compared to ciclosporin. There was no significant difference between IFX and ciclosporin in adverse drug-related events, postoperative complications, or mortality.

Conclusions: In the management of steroid refractory severe UC, no definitive preference between IFX and ciclosporin exists based on randomized trials, but non-randomized studies suggest IFX is associated with better treatment response and lower risk of colectomy at 12 months.

P468
Appendectomy is associated with an increased risk of colonic neoplasia in Ulcerative Colitis

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Background: Appendectomy is usually considered as a protective factor of ulcerative colitis (UC). Currently clinical trials are testing appendectomy to treat UC. Original results of experiments performed in a murine model of UC-like colitis (IL10/Nox1 mice) showed that appendectomies provoked an un-expected high rate of early colonic neoplasia. The purpose of this study was to determine if previous appendectomy in patients with UC was associated with high risk of colonic neoplasia.

Methods: This is a retrospective study including all the consecutive UC patients who required colectomy in two French referral university centers between 2001 and 2011. Medical records and colon specimens of the 232 consecutive UC patients were analyzed. UC features and previous appendectomy were retrospectively collected. Presence of the appendix, high-grade dysplasia or colon cancer, and colitis severity on the surgical specimens of colectomy were assessed blindly by gastro-intestinal pathologists.

Results: Among 232 UC patients who underwent colectomy, 15 had previous appendectomy and 39 had colonic high grade dysplasia (HGD) or cancer. Among patients with previous appendectomy 5 had colon cancer (33%) and 4 HGD (27%) versus 12 with colon cancer (5.5%) and 18 with HGD (8.3%) in the non-appendectomy group. Previous appendectomy was the highest independent risk factor of colorectal neoplasia in UC [p=0.005, OR=17.16 (CI 3.5-84.2)]. Primary sclerosing cholangitis, already identified as a risk factor of colonic neoplasia in UC subjects was also found [p=0.002, OR=4.46 (CI 1.7-11.6)].

Conclusions: Murine data on a new model of UC-like colitis showed that appendectomy, for a non-inflamed appendix, triggered colonic carcinogenesis. Our study identified previous appendectomy as a strong independent risk factor of colonic neoplasia in UC patients. We recommend: 1- to stop current clinical trials testing appendectomy as a treatment for UC, as long as larger data on this risk are not available, and 2- to screen carefully UC patients with previous appendectomy.

P469
Accelerated treatment strategy in Inflammatory Bowel Diseases: Is it associated with a change in the disease course?

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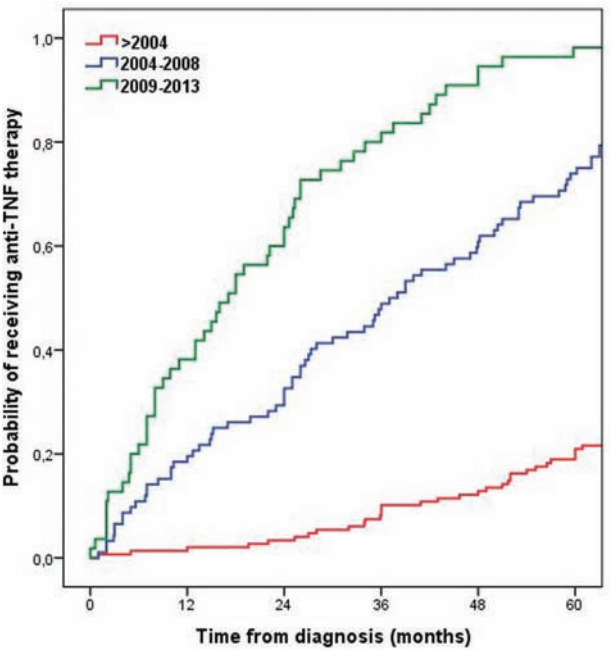
Background: Evidence from new clinical trials in inflammatory bowel diseases (IBD) suggests that tight disease control and early aggressive therapy is associated with superior outcomes in patients with poor prognostic factors. The aim of the present study was to investigate the evolution of the treatment strategy and probability of resective surgery/colectomy in three IBD-centers according to the era of diagnosis

Methods: Data of 352 consecutive anti-TNF treated IBD patients (CD/UC: 296/56, males: 48.3%/42.9%, 1st anti TNF infliximab/adalimumab: 300/52, median age at diagnosis: 22/25.5 years, follow-up from diagnosis: 8.5/5.5 years, complicated disease behavior and ileocolonic location in CD: 48% and 57.1%, extensive location in UC: 39.3% at diagnosis) were analysed. Both in- and outpatient records were collected and comprehensively reviewed.



"Figure 1. Probability of receiving anti-TNF therapy according to the year of diagnosis"

Results: The time to anti-TNF, immunosuppressives and steroids was significantly and progressively shortened in both CD (pLogRank<0.001 for all, Figure 1) and UC (pLogRank<0.003 for all) according to the era of diagnosis (A: <2004, B: 2004-2008, C: 2009-2013).

Mean time to anti TNFs and immunosuppressives was 123.8/76.6, 40.8/16.8 and 20.5/8.8 months in CD in Groups A, B and C (pANOVA<0.001, pScheffeA.vs.B/C<0.001). Of note, since 2008, a harmonized, mandatory, tight monitoring strategy was applied in anti-TNF exposed patients including CDAI-PDAI assessment, laboratory evaluation (including CRP) at least every 3 months and endoscopy/imaging at least every 12 months requested and regularly controlled by the National Health Fund (OEP). Despite similar disease phenotype, the era of diagnosis was not associated with the time to resective surgery or colectomy (pLogRankCD=0.08, pLogRankUC=NS) in the total cohort. However, need for resective surgery decreased over time in CD patients treated with infliximab as 1st anti-TNF (pLogRank=0.034) and in patients with perianal disease (pLogRank=0.04), but not according to disease location or initial disease behavior.

Conclusions: An accelerated treatment strategy was observed in this referral IBD cohort. Further data are required to determine whether accelerated treatment strategy is associated with superior long-term outcomes in IBD.

P470
Changes in serum through levels of infliximab during treatment intensification but not in anti-infliximab antibody detection are associated with clinical outcomes after therapeutic failure in Crohn's disease

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Background: It is recommended to intensify the infliximab (IFX) regimen in case of inadequate treatment effect in patients with Crohn's disease. IFX trough concentrations and formation of anti-IFX antibodies (Abs) are associated with clinical efficacy of IFX, but these parameters are subject to change over time. This study therefore explored if changes in IFX and anti-IFX antibodies (Abs) during IFX intensification applied at treatment failure associated with clinical outcomes.

Methods: This was a post hoc analysis of a randomized controlled trial which had included 69 Crohn's disease patients with symptomatic IFX treatment failure defined as CDAI ≥220 or ≥1 draining perianal fistula.(1) The current study included 42 patients (35 luminal, 4 fistulizing, 3 both) who had received an intensified IFX regimen with infusions of 5 mg/kg every 4 weeks throughout the 12-week study period. Trough serum IFX and anti-IFX Abs were measured by homogeneous mobility shift binding assay (HMSA) (2) and functional cell-based reporter gene assay (RGA) (3) at treatment failure and end of trial.

Results: After 12 weeks of intensified IFX regimen, 21 patients (50%) had regained clinical response. While IFX levels at manifestation of treatment failure were comparable between responders and non-responders at week 12, the overall increase in IFX during treatment intensification was significantly higher among the responders (RGA: 8.8 µg/ml vs. 3.0, p=0.035; HMSA: 9.9 µg/ml vs. 4.7, p=0.040). Furthermore, ROC analysis of change in IFX trough levels during IFX intensification differentiated patients by clinical outcome: AUC^{ROC}_{RGA} 0.75 [0.53-0.97], p=0.035; AUC^{ROC}_{HMSA} 0.74 [0.53-0.95], p=0.042. All responders exhibited IFX increase ≥2.6 µg/ml (sensitivity 100%, specificity 50%). Anti-IFX Abs were detected at time of IFX treatment failure in 13 patients (32%) by HMSA, and in 6 (15%) patients by RGA (all of which were positive by HMSA). Anti-IFX Abs detected by HMSA were often non-functional (62% had simultaneous IFX detection) and generally became undetectable during IFX intensification (89%). However, even functional anti-IFX Abs detected by RGA became undetectable (100%).

Conclusions: Increased IFX exposure during treatment intensification associates with improved clinical outcomes indicating underlying pharmacokinetic issues in a subgroup of patients. However, non-pharmacokinetic mechanisms of treatment failure are also common and other biologic agents than TNF-inhibitors should be considered here. Anti-IFX Abs become undetectable during treatment intensification and seems of limited prognostic value in this situation.

(1) Steenholdt et al. Gut (2014)
(2) Wang et al. J Immunol Methods (2012)

P471
Infliximab trough levels are lower in patients with acute severe, compared to moderate-severe ulcerative colitis patients

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Background: Infliximab is effective as salvage therapy for patients with steroid refractory acute severe ulcerative colitis (ASUC). Moderately-severe colitis (MSUC) is defined as an ulcerative colitis exacerbation which requires infliximab therapy, although not severe enough to require hospitalization. Data comparing infliximab trough levels (TL) in patients with ASUC versus MSUC are scarce. Our aim was to examine whether infliximab drug and anti-infliximab antibodies (ATI) TL during induction differ between patients with ASUC and MSUC.

Methods: Infliximab and ATI TL 14 days after the first 5mg/kg infusion were compared in hospitalized ASUC and MSUC patients. Response status and immunomodulator use were matched. Continuous and categorical variables were analyzed using the Mann-Whitney U-test and Fisher's exact test, respectively.

Results: Fourteen patients with intravenous steroid refractory ASUC treated with infliximab 5mg/kg "salvage" therapy were compared to 14 matched MSUC controls. Mean infliximab TL at day 14 were significantly lower in patients with ASUC compared to MSUC (8 ± 5.5 versus 18.5 ± 11.4 mcg/ml, p=0.015). ATI formation rate (50%vs.21%, p=0.24) did not differ between the groups, although there was a trend for higher ATI levels (4.7 ± 5 vs. 2.6 ± 4.7 mcg/mleq, p=0.13) among the ASUC patients. Four patients (2 ASUC and 2 MSUC) were primary non-responders to infliximab. However, infliximab level at day 14 did not differ between responders and non responders (14.2 ± 10.6 vs. 7.3 ± 6.9 mcg/ml respectively, p=0.2).

Conclusions: Lower infliximab TL in patients with ASUC compared to MSUC may possibly be due to a higher inflammatory burden and/or increased drug clearance, perhaps via fecal loss of infliximab. Controlled trials are required in order to determine whether an a-priori intensified infliximab induction therapy would result in higher drug levels and thus an improved outcome in ASUC patients.

P472
Risk of relapse after anti-TNF discontinuation in Inflammatory Bowel Disease: A meta-analysis

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Background: The discontinuation of anti-TNF treatment in Crohn's disease (CD) and ulcerative colitis (UC) patients after achieving remission could be considered due to safety and cost issues. However, the convenience of this strategy is presently unknown.

AIM: To assess the risk of relapse after anti-TNF discontinuation, to evaluate the factors that could affect this risk, and to calculate the response to re-treatment with the same anti-TNF after relapsing in CD and UC patients.

Methods: *Inclusion criteria:* Studies evaluating the incidence of relapse after anti-TNF [infliximab (IFX), adalimumab (ADA), or certolizumab pegol (CZP)] discontinuation in patients with CD and/or UC that reached, at least, clinical remission at the time of withdrawal of anti-TNF. *Search strategy:* Bibliographical searches in PubMed, Embase and Congresses up to October 2014. *Data synthesis:* Percentage of relapse after anti-TNF withdrawal; meta-analyses were performed using the inverse variance method. *Subanalyses:* according to type of disease, type of CD (luminal or fistulizing), anti-TNF drug, and the reason to stop anti-TNF (clinical and/or endoscopic remission).

Results: 26 studies were included. Six studies reported mixed results with ADA-IFX, and 20 of IFX. The risk of relapse after anti-TNF discontinuation was 44% for CD (95%CI=36-51%; I^2=76%; 23 studies; 720 patients), and 41% for UC patients (30-53%; I^2=53%; 9 studies; 159 patients). In CD, the relapse rate at short-term (6 months after the discontinuation of the anti-TNF) was 35%, at medium-term (12 months) 36%, and at long-term (60-125 months) 49%. These results were highly heterogeneous (I^2=71-88%). In UC, there were 33% of relapses 12 months after the discontinuation of the anti-TNF (2-65%; I^2=93%; 3 studies; 94 patients). In CD, when the anti-TNF was stopped considering only clinical remission, the relapse rate after 1 year was 39%, decreasing to 26% when endoscopic remission was also required. This subanalysis could not be performed in UC due to lack of data. None of the other studied factors were associated with relapse risk. Re-treatment with the same anti-TNF in those patients who relapsed, induced remission in 79% (66-92%; 8 studies; 255 patients) of them; respective figures for CD and UC were 83% (62-100%) and 85% (62-100%)

Conclusions: One-third of both CD and UC patients in remission under anti-TNF treatment relapsed 1 year after discontinuation of the drug. In CD patients, when the criteria for discontinuation was clinical remission, 39% of relapses were reported, but only 26% when patients had also endoscopic remission. Response to retreatment with the same anti-TNF was generally favourable (80% remission) in patients who relapsed after discontinuation.

P473
Antibodies to infliximab, body weight and low serum albumin levels increase clearance of infliximab, a population pharmacokinetic study in 324 IBD patients

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Background: Factors suggested to influence the pharmacokinetics (PK) of infliximab (IFX) in patients with inflammatory bowel disease (IBD) have mainly been derived from clinical trials or computer modelling, clinical data are scarce. Therefore we aimed to study the real-life PK of IFX in a large historical cohort of IBD patients and to identify patient, disease and treatment characteristics that influence serum concentrations and clearance of IFX.

Methods: In this cross-sectional study all measurements (November 2004 - August 2014) of IFX serum concentrations in IBD patients collected in a tertiary referral center were identified. Medical charts of these patients were reviewed for patient, disease and treatment characteristics. IFX serum concentrations and antibodies to IFX (ATI) had been measured using an ELISA and antigen binding test

(radioimmunoassay, Sanquin Laboratories). PK was analysed by nonlinear mixed-effects modelling and described using a 2-compartiment PK model. All influential covariates were combined into a full model.

Results: A total of 734 distinct IFX concentrations measurements were included, comprising data from 324 IBD patients (mean 2.27 measurements). Disease extent was scored based on the Montreal classification for 252 Crohn's disease patients (L1:53/252, L2:79/252, L3: 120/252) and 72 ulcerative colitis patients (E1: 6/72, E2: 26/72, E3:40/72). 318/324(98%) of patients were anti-TNF naïve at start of IFX. Mean dose of IFX was 5.49 mg/kg (SD 1.39). ATI were detected in 100/324 (31%) patients. Mean (inter individual variability) values for clearance, central and peripheral volume of distribution were 0.34 L/day (74%), 12.8 L (98%) and 15.1 L (153%). Disease extent did not affect PK. Body weight and anti-IFX antibodies were identified as independent covariates (P<0.001) increasing clearance (mean (SE)) by 2.76 (14.1) fold and 6.04 (10.3) fold respectively, whereas serum albumin had a -0.69 (22.2) fold inverse impact on clearance. Because serum CRP values tended to change rapidly after initiation of treatment, and use of concomitant immunomodulators was often intermittent, these factors could not be evaluated as independent covariates although the administration of continuous concomitant immunomodulators was associated with a decrease in clearance.

Conclusions: Antibodies to infliximab, body weight and low serum albumin levels increase clearance of infliximab.

P474
Anti-TNFα treatment efficacy in prevention of postoperative recurrence in Crohn's disease depends on previous exposure to anti-TNFα agents

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Background: Almost 50% of Crohn's disease (CD) patients will need surgical resection during their follow-up. Infliximab and adalimumab are effective to prevent postoperative recurrence in CD patient naïve from anti-TNFα antibodies (anti-TNF). The effect of previous exposure to one or more anti-TNF before surgery on prevention of postoperative recurrence by these agents is still unknown. The aim of our study was to investigate the efficacy of anti-TNF to prevent CD postoperative recurrence according to previous exposure to these drugs.

Methods: We performed a retrospective analysis of CD patients, followed in a tertiary referral centre, who underwent surgical bowel resection and prophylactic treatment with anti-TNF between January 2005 and June 2012. Infliximab, adalimumab and certolizumab pegol were considered as prophylactic treatments if started within three months after surgery. Endoscopic recurrence, defined as a Rutgeerts score ≥ i2 and clinical recurrence, defined as physician judgment were evaluated one year after surgery and also during the follow-up.

Results: Fifty-seven consecutive CD patients with bowel resection, anastomosis and prophylactic treatment with anti-TNF were included in the study. Twenty two patients (39%) had prior intestinal resection for CD and a majority (45, 79%) were treated with at least one anti-TNF before surgery. Twenty-four (42%) received two or more anti-TNF before surgery and 12 (21%) patients were naïve from anti-TNF. Thirty-nine (67%) patients had a surveillance colonoscopy one year after surgery. At one year, the global endoscopic and clinical postoperative recurrence rates were 42% (17/39) and 19% (11/57), respectively. According to previous exposure to anti-TNF, patients with two or more anti-TNF before surgery had a higher one-year endoscopic recurrence rate compared with patients that received one and zero anti-TNF before surgery (62%, n=13/21 vs. 31%, n=4/13 vs. 20%, n=1/5). Also, patients with two or more anti-TNF before surgery had a higher rate of clinical recurrence compared with patients receiving less than two anti-TNF before surgery (37%, n=9/24 vs. 12%, n=4/33, p=0.05). In multivariate analysis, smoking (HR=3.2; IC 95%: 1.2-7.8) and previous exposure to two or more anti-TNF (HR=4.3; IC 95%: 1.3-14.0) were significantly associated to the risk of clinical postoperative recurrence in CD patients.

Conclusions: Previous exposure to two or more anti-TNF agents was associated to a higher risk of postoperative recurrence in CD patients receiving prophylactic treatment with anti-TNF. This study suggested that previous exposure to anti-TNF should be taken into account when managing prevention of post-operative recurrence in CD patients.

P475
What is our success on complex perianal fistulae healing under optimal medical treatment ending up with ileostomy?

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Background: Our aim was to determine overall success rate of ileostomy in patients with complex perianal fistulas (Cpfis) that are under optimal medical Tx (MedTx) with anti-TNF based regimens combined with antibiotics and/or azathioprine (AZA) and find out predictors of ileostomy.

Methods: IBD patients' charts between 1999-14 retrospectively were reviewed. There were 60/762 (8%) CD patients with Cpfis. All patients were treated with different combinations of antibiotics, azathioprine (AZA) and anti-TNFs but our aim was to put them on triple MedTx if there was no drug intolerance. In case of an abscess, drainage and seton were applied remaining between 3 to 6 mo. in case of no recurrence. Tx success was stratified as complete discharge cessation or additional closure of external orifice, and ultimately radiological disappearance by MRI. In case of MedTx failure a diverting stoma was applied. Age, sex, disease duration, location, behaviour, rectal involvement, age at fistula onset, fistula duration, number of fistula, smoking, number of setons, time with seton, total durations of drugs, and type of surgery were noted. Each patient's fistula status at the last visit was noted. Ileostomy procedure only was performed after recommendation of our IBD council together with the patient's acceptance

Comparisons between complex perianal fistulae patients with and without ileostomy

	Patients with ileostomy (n=16)	Patients without ileostomy (n=44)	P
Age	41.12 ± 13.78	35.54 ± 10.53	NS
Age at fistulae onset	35.43 ± 13.78	31.79 ± 9.92	NS
Sex (Female-Male)%	69%-31%	32%-68%	0.01
Disease duration(yrs)	13.25 ± 6.7	7.54 ± 6.71	0.005
Fistula duration (mo)	69.81 ± 35.61	38.93 ± 24.47	0.000
Number of fistulae tracts	2.25 ± 1.13	1.72 ± 0.78	0.048
Time spent under seton (mo)	28.6 ± 17.74	15.73 ± 10	0.006
Rectal involvemen t(%)	81	48	0.02
Luminal activity (%)	83	39	0.011

Results: There were 60 Cpfis pts., 25(42%) being female with a mean age of 37.03 ± 11.63 yrs. Sixteen out of 60 patients (27%) underwent an ileostomy after MedTx failure but none of them due to anal stricture or incontinence. Overall success rate after ileostomy was 8/16 (50%) but radiological healing rate was just 4/16 (25%). The need for ileostomy significantly was more common among women and patients with rectal involvement and luminal active disease despite optimal MedTx. The duration of CD and fistulae, number of fistulae and time under seton significantly were higher among patients ending up with ileostomy (Table 1). Cox-regression analysis disclosed none of the above mentioned parameters as independent predictors of an ileostomy.

Conclusions: This study stresses the actual ongoing problem with complex perianal fistula closure in CD despite evolving MedTx modalities even when ending up with diverting stoma. However, we can not ignore the possibility of ileostomy related optimal results regarding the fistula closure in early cases who are under better clinical and endoscopic conditions.

P476
EArly SurgerY or Immunosuppression - EASY study

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Background: Crohn's disease (CD) can be treated medically or surgically. Surgery was considered the last option. Immunomodulators have shown efficacy in maintaining remission and surgery by using bowel sparing techniques and laparoscopic approach improved earlier recovery and morbidity. Studies addressing the timing of surgery or medical treatment are scarce. Aims: Our aim was to compare the outcome in CD patients submitted to immunomodulators or surgery in the first six months after diagnosis.

Methods: It is a national, multicentric study on CD patients diagnosed and followed for more than three years and submitted to immunomodulators (index episode) or surgery (index episode) in the first six months after diagnosis. Disability was defined as: one surgery or hospitalization in the first five years after the index episode or more than one surgery or two hospitalizations in the follow-up, more than two courses of corticosteroids per year, corticosteroid dependency, or resistance, needed of switch of the first immunomodulator or anti-TNF, or appearance of clinical events after index episode (fistula, abscess, stenosis, perforation or anal disease).

Results: With a follow-up of 12.6 years (IQ:7.9;41.4) 615 patients were analysed. It was possible to identify four cohorts with different outcome: A-patients submitted to surgery in the first 6 months after diagnosis without any immunosuppression thereafter, B- patients submitted to surgery in the first 6 months after diagnosis and under immunosuppression within the first two months after surgery, C-patients submitted to surgery in the first 6 months after diagnosis and in immunosuppression only after the second month after surgery, and D- those under immunosuppression in the first 6 months after diagnosis and without any surgery in this period. In the table are shown the main outcomes.

Conclusions: Patients older than 40 years and with ileal disease the surgery was the best option with regards disability, however early introduction of immunomodulators showed to be the best strategy in bowel sparing.

P477
Biological Therapy Is Able To Modify The Disease Progression of Crohn's Disease Preventing Its Long-Term Associated Disability - A Study Performed By Using The Lèmann Score

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Background: Crohn's disease (CD) is a chronic inflammatory bowel disorder characterized by an alternation of remission and relapse phases. Even during periods of clinical remission a subclinical inflammation persists, reflecting a progressive, destructive disease course in the later phases of the disease. Surgical resection of bowel is the ultimate manifestation of bowel damage. Recently a new score, the Lèmann Score

"200"

	Cohort A N=95	Cohort B N=46	Cohort C N=205	Cohort D N=269	p
A3 (>40 years) (%)	38	13	25	12	0.001
Location (L1) (%)	64	38	52	35	0.001
Disability (%)	22	78	77	72	0.001
Disability A3+L1 patients (%)	15	75	82	69	0.001
Surgery + abdominal events (%)	9	12	48	31	0.001
Steroids (%)	21	30	44	27	0.001
Anti-TNF (%)	4	30	29	40	0.001
Hospitalization rates (per person per year)	0.04	0.28	0.13	0.21	0.001
Surgery rates (per person per year) Without index surgery	0.02	0.07	0.06	0.04	0.001
Surgery rates (per person per year) With index surgery	0.12	0.25	0.15	0.04	0.001
Re-operation (%)	17	30	39	3	0.001

(LS), has been proposed in order to assess the cumulative structural damage to the bowel in different CD patients. Limited data are present assessing the value of this instrument in measuring the effect of various medical therapies on the progression of bowel damage.

The aim of our observational study was to evaluate the effect of various medical therapies on the progression of bowel damage by using the Lèmann Score : Group A, biological therapy, Group B immunomodulation therapy, Group Cmelamine therapy.

Methods: In this retrospective study we included consecutive CD patients who were followed up at our IBD Unit. All patients underwent every tree month clinical assessment with measurement of disease status based on HBI index, and every year or before in case of disease relapse bowel magnetic resonance imaging and a colonoscopy. Patients were divided on the basis of drug administered during the follow-up period: Group A: biological mono-therapy; Group B, azathioprine therapy; Group C: melamine therapy. We calculated the LS at the beginning and end of follow-up period.

Results: We included 88 patients (39 F/49M, mean age 43.5 range 19-79) with a median follow-up of 26 months. At the start of the observational period the median LS in group A, B and C was respectively 7.05 (2.5-292.3), 4.2 (0.6-159.6) and 4.1 (0.6-202.6). At the end of the follow-up the median LS in group A, B and C was respectively 17.05 (1.3-292.3), 7 (0.6-209.6) and 6.7 (1-206.5). Evaluating the difference of LS between the beginning and end of follow-up period, we observed that the delta was higher ($p<0.05$) in Group A (median delta LS 0.0, range 3.1; -24.3) compared to Group B (median delta LS -1.55, range -1.2;-83.3) and Group C (median delta LS 0.0, range 0.0;-79.2). Moreover no statistical difference was found between Group B and Group C ($p=0.3$)

Conclusions: Our data suggest that the use of biological therapy rather than Azathioprine and melamine changes the cumulative structural damage to the bowel and, therefore, modifies the disease progression of CD, preventing its long-term associated disability.

P478
Vitamin D status and response to anti-tumor necrosis factor-alpha therapy in inflammatory bowel disease

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Background: Vitamin D has immune modulating potential in inflammatory bowel disease (IBD) and might have a synergistic effect on anti-tumor necrosis factor- α (anti-TNF α) therapy. We wanted to investigate whether pre-treatment P-25-hydroxyvitamin D (25-vitD) levels affect IBD-patients' response to anti-TNF α therapy.

Methods: We performed a retrospective, single-centre study on all IBD-patients receiving anti-TNF α therapy from 2011 to 2014. Seventy-eight patients were included (57 with Crohn's disease (CD), 21 with ulcerative colitis). We collected patients' 25-vitD status, clinical scores (Harvey Bradshaw Index (HBI), Simple Clinical Colitis Activity Index and Short Health Scale (SH)) and inflammatory markers prior to and 6, 14, 22 and 52 weeks after treatment initiation. Patients were categorised according to their 25-vitD status as either insufficient (25-vitD < 50 nmol/L) ("D-low") or sufficient (25-vitD > 50 nmol/L) ("D-normal"). Data were analysed using a mixed model.

Results: At baseline, D-low patients (n = 15) had more active disease than D-normal patients (n = 63) estimated by CRP (4.1 times higher, 95% CI: 2.0 - 8.1 ($p < 0.001$)), albumin (0.91 times lower, 95% CI: 0.86 - 0.98 ($p < 0.05$)) and HBI for CD patients (3 points higher, 95% CI: 0.6 - 5.4 ($p < 0.05$)) (figure 1). At this point, SCCAI, SH, haemoglobin and f-calprotectin did not differ significantly between the two groups. Initially, both groups responded equally to anti-TNF α treatment, but after 14 weeks the D-low group had higher CRP and f-calprotectin levels than did the D-normal group (3.1 times higher, 95% CI: 1.4 - 7.1 ($p < 0.01$)) and (5.6 times higher, 95% CI: 2.1 - 15.5, ($p = 0.001$)) respectively. CRP continued to be higher in the D-low group at week 22 (3.1 times higher, 95% CI = 1.2 - 7.7 ($p < 0.05$)) and these patients also reported a worse quality of life than D-normal patients (SH 7.5 points higher, 95%CI: 0.3 - 14.8 ($p < 0.05$)). After one year the two groups had responded equally to anti-TNF α therapy.

Conclusions: Vitamin D insufficiency is associated with increased disease activity in IBD and a poorer response to anti-TNF α therapy from week 14-22. Clinical studies are needed to clarify whether vitamin D supplementation will improve the response to anti-TNF α therapy.

P479
Factors Associated with Development of Endoscopic Stricture in Patients with Crohn's Disease Treated with Infliximab

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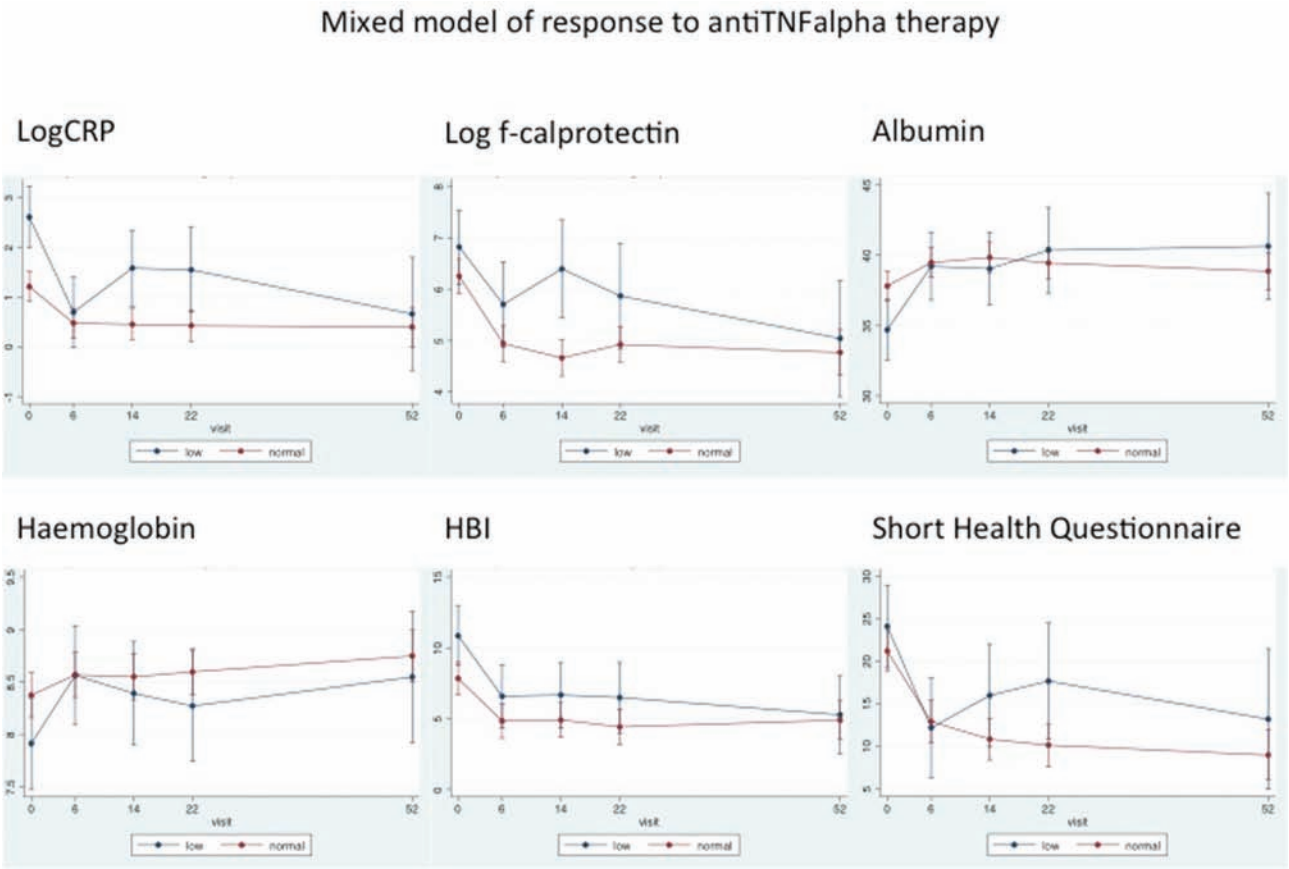

"Mixed model of response to anti-TNF-alpha therapy"

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Background: Controversy exists that whether rapid luminal healing in Crohn's disease (CD) with infliximab increases the risk of intestinal stricture. Data from TREAT and ACCENT I did not suggest that infliximab therapy increased risk of developing intestinal obstruction. The aim of our study was to identify risk factors associated with endoscopic stricture, a more objective index of intestinal stenosis, in CD patients treated with infliximab.

Methods: This was a case-control study. Established CD patients who received infliximab therapy between September,2007 and June,2014 were divided into two homogeneous arms: endoscopic stricture group and control group The primary outcome was development of endoscopic stricture. The duration of follow-up was calculated from the first time of infliximab treatment up to the time of detection of endoscopic stricture, loss of follow-up or the end of study (October 20, 2014).Cox regression analysis was used to evaluate risk factors associated with endoscopic stricture.

Results: Among 88 patients who received infliximab therapy, 17 patients (19.3%, 8.45 events/100 patient-years) developed intestinal stricture after a median follow-up of 19.5 (IQR, 7.7-47.8) months. The cumulative rates of endoscopic stricture were 17%, 26% and 31% at 1, 3 and 5 years, respectively. Independent risk factors associated with development of endoscopic stricture in CD patients treated with infliximab were new immunomodulator use(HR=9.892, 95% CI, 1.852-52.844, P=0.007) and CRP level(HR=1.044, 95% CI, 1.022-1.067, P<0.001). Smoking, age, disease area, disease duration, CDAI, prior bowel surgery, perianal lesion and extraintestinal manifestation, new corticosteroids use new infliximab use, times of infliximab infusion and cumulative infliximab dose were not associated with endoscopic stricture.

Conclusions: For CD patients treated with infliximab, factors associated with subsequent development of endoscopic stricture were new immunomodulator use and CRP level. New infliximab use, times of infliximab infusion and cumulative infliximab dose were not associated with endoscopic stricture.

P480
Efficacy of switching to pH-dependent release formulation of mesalazine at 3.6 g/day from time-dependent release formulation of mesalazine at 4.0 g/day in patients with Ulcerative Colitis

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Background: In Japan, two different mesalazine formulations, namely pH-dependent release formulation at 3.6 g/day (pH-3.6 g) and time-dependent release formulation at 4.0 g/day (Time-4.0 g) can be administered for high-dose mesalazine treatment of ulcerative colitis (UC). However there are few reports on the efficacy of switching to pH-3.6 g in UC patients who do not sufficiently respond

to Time-4.0 g. The aim of this study was to analyze the efficacy of switching to pH-3.6 g in UC patients treated with Time-4.0 g.

Methods: Retrospective data was collected from active UC patients who switched to pH-3.6 g because of an insufficient response to Time-4.0 g between January 2010 and November 2013 at the IBD Center, Sapporo Kosei General Hospital, Japan. We excluded patients with a Lichtiger's clinical activity index (CAI) score of ≤ 4 and those who received additional medical treatments within 4 weeks before switching to pH-3.6 g. The efficacy switching to pH-3.6 g was evaluated by the decrease in scores on the CAI. The CAI scores were calculated at baseline, 4 weeks and 8 weeks. Remission was defined as a decrease in the CAI scores to ≤ 4. Prognostic factors related to the remission rate at 8 weeks were evaluated using univariate analysis.

Results: Of the 46 patients (mean age, 40.4 years), 27 were females. The mean duration of the disease was 8.9 years, and the mean CAI score was 6.0 at baseline. Eighteen patients had total colitis, 21 had left-sided colitis and 7 had proctitis-type colitis. Concomitant treatment with both immunomodulators (azathioprine or 6-mercaptopurine) and local mesalazine was administered in 10 patients. Previous treatment included administration of prednisolone in 10 patients. The CAI score at 4 weeks from baseline significantly decreased from 6.0 ± 1.3 to 4.8 ± 2.6 (P = 0.001). The remission rate at 4 and 8 weeks were 50% for both. No significant prognostic factor related to the remission rate at 8 weeks was identified in univariate analysis. However, remission rate tended to decrease for patients previously treated with prednisolone (36%). In addition, the remission rate of the 10 patients to whom local mesalazine was administered was high (70%).

Conclusions: Switching to pH-3.6 g in UC patients not sufficiently responding to Time-4.0 g is effective and should be attempted even if local mesalazine is administered. However, switching to pH-3.6 g from Time-4.0 g may have little effect on UC patients previously treated with prednisolone.

P481
A Scandinavian prospective observational study of iron isomaltoside 1000 treatment: Clinical practice and outcomes in iron deficiency anaemia in patients with IBD

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Background: Iron deficiency is a frequent complication in inflammatory bowel diseases (IBD) with negative effects on quality of life. Appropriate iron substitution is crucial. The objective of this study was to prospectively collect data for treatment routine, efficacy and safety of iron isomaltoside 1000 in IBD patients.

Methods: This observational study included 149 IBD patients, 82 with Crohn's disease (CD) and 67 with ulcerative colitis (UC), treated with iron isomaltoside 1000 at 10 sites in Denmark, Norway and Sweden. Data for iron treatment, blood tests and adverse drug reactions (ADRs) were recorded from August 2013 to October 2014.

Results: Of 149 patients 69 were male and 80 female with a mean age of 41.7 (17-75) years and a mean body weight of 74.1 (45-137) kg. Four percent had received oral iron, and no patients had blood transfusions or erythropoietin before treatment with iron isomaltoside 1000. Two patients did not receive the full prescribed dose and were excluded from the efficacy analysis. Mean baseline levels of haemoglobin (Hb), ferritin and transferrin saturation (TSAT) were 11.6 g/dL, 24.2 micrograms/L and 9.7 %, respectively. The treatment resulted in a mean increase from baseline to the first blood test follow-up of 1.4 g/dL for Hb, 113 micrograms/L for ferritin and 8.4 % for TSAT ($p < 0.001$ for all three parameters) during a mean time of 7.2 weeks following treatment. There were no significant differences between the CD and UC groups. The mean Hb increase for patients with baseline Hb below 10 g/dL was 3.2 g/dL and for all patients with anaemia at baseline 1.7 g/dL ($p < 0.001$). The mean administered iron dose in the study was 1010 mg. The mean dose that would have been needed for full iron correction was higher than the mean dose administered, 1363 mg using the simplified dosing table and 1100 mg using the Ganzoni formula, respectively. A total of 95 % were treated at one single visit. Ferritin of 100 micrograms/L was reached in only 49 % of patients and 27 % were still anaemic after treatment. Six (4 %) ADRs were reported. Three (2 %) were described as acute infusion reactions. The other events were fever, headache, nausea and skin reactions. All patients with ADRs had an uneventful recovery.

Conclusions: This study demonstrates good efficacy and tolerability of iron isomaltoside 1000 in IBD patients treated for iron deficiency. Although the patients had significant increases in Hb, more than one in four patients was still anaemic after iron treatment. Combined with the finding of iron doses given being lower than the estimated iron need, this suggests that doses of iron routinely given in clinical practice are lower than needed for full iron correction.

P482
Infliximab population pharmacokinetic modelling in patients with Inflammatory Bowel Disease: estimation of individual pharmacokinetic parameters and trough levels prediction

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Background: Infliximab (IFX) trough levels (TLI) exhibit a high interinviduals variability in inflammatory bowel disease (IBD) patients. This variability is relevant because there is a relationship between TLI and clinical efficacy of IFX in both Crohn Disease (CD) and ulcerative colitis (UC). Two-compartment population pharmacokinetic models (PopPK) using data from pivotal trials have been developed in CD and UC. The main objective of the study was to estimate individual pharmacokinetic (PK) parameters and predict TLI

Methods: Patient data were collected prospectively from patients treated with IFX between July 2013 to March 2014. Blood samples were collected before intravenous infusion at steady state. TLI and antibodies toward infliximab (ATI) were measured by enzyme-linked immunosorbent assay (ELISA) (Promonitor®). Covariates included in final popPK models, C reactive protein (CRP) and smoking were recorded. Individual PK parameters were estimated on the basis of previously developed popPK models and TLI, Cpeak and AUC were individually predicted using the Bayesian posthoc option. Pharmacokinetic analysis was carried out using Nonmem® 7.2

Results: 64 patients (39 CD 25 UC). 132 TLI and ATI were measured. 132 TLI and ATI were measured. Mean TLI was 317 mg/L

(54%<3 mg/L); of the 113 samples taken in patients who were negative for ATI, 4.4% had undetectable TLI, whereas of the 19 samples taken in patients positive for ATI, 84.2% had undetectable TLI. Mean predicted TLI (IPRED) was: 2.92 mg/L. Mean estimated peak levels and AUC were 115,53 mg/L and 26447.41 mg/h/L, respectively.The comparison between IPRED and observed TLI values using the PopPK model for CD led to a non-significant overall mean relative bias of -3.99% and an acceptable precision of 18.96%. IPRED correlated with observed TLI (coefficient 0.985, p<0.0001). No correlation was found between IPRED and observed TLI using the PopPK model for UC. Individual (Bayesian estimates) PK parameters (mean) were: central clearance (Cl) 7.68 ml/kg/day, volume of distribution (central) (Vd) 50.61 ml/kg, half-life (t1/2): 11.41 days

Conclusions: PopPK model for CD proposed by Fasanmade AA et al (1) adequatly predicts TLI and estimates individual PK parameters in both CD and UC patients. The model may be useful to individualize doses according to patient factors influencing IFX PK

1. Fasanmade AA et al. 2011.
2. Fasanmade AA, et al. 2009

P483
ABO blood group in monitoring response to infliximab treatment for Crohn's Disease

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Background: The variation of ABO blood group is reported as a potential genetic risk factor for Crohn's disease (CD). However, its role in Chinese patients with CD was still unknown. The present study aimed to investigate the distribution of ABO blood group in Chinese patients with CD, and also to explore its impact on response to infliximab for CD.

Methods: Patients with CD were consecutively recruited in The First Affiliated Hospital, Sun Yat-sen University from between 2007 and 2014. Patients receiving infliximab therapy were under follow-up. ABO blood group antigen and Rh factor were characterized on peripheral blood samples. The distribution of ABO blood type in CD and its correlation with the response to infliximab were evaluated using unconditional logistic regression analysis.

Results: Of 293 patients with CD, 119 patients were type O (40.6%), 80 type A (27.3%), 75 type B (25.6%), and 19 type AB (6.5%).

The odds ratio of CD in type O patients was 0.95 (95% CI, 0.55~ 1.68; P = 0.5) compared to all other blood types, while it was 0.82 (95% CI, 0.45~ 1.52; P = 0.32) in type A patients, and 1.21 (95% CI, 0.36~4.11; P = 0.5) in type AB patients. Overall 109 patients with CD received the treatment of infliximab in our centre. At 1 year (54w), 70 patients (66.0%) responded to induction therapy. Patients with CD with type AB blood (OR = 8.17, 95% CI, 1.530~ 43.641; P = 0.014) had an advantage to achieve mucosal healing, while patients with CD with type A blood appeared to had a high risk of loss response (OR = 0.372, 95% CI, 0.148~0.935; P = 0.036).

Distribution of ABO group in patients with Crohn's disease and the general population.

	Blood type			
Group	O	A	B	AB
Patients with Crohn's disease, No. (%)	119 (40.6)	80 (27.3)	75 (25.6)	19 (6.5)
Chinese Han population, %	42	31	22	5

Conclusions: ABO blood type had no influence on the CD risk in Chinese population. Patients with type AB had a better response to infliximab whereas those with type A appeared to had a risk of loss response to infliximab for CD. Further study involving more patients would confirm this finding.

P484
Is topical therapy necessary for patients with acute mild and/or moderately active extensive or left-sided Ulcerative Colitis treated with mmx-mesalazine? A pilot, single-center, faecal calprotectin-guided study

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Background: According to the ECCO guidelines patients with mild-to-moderately active extensive or left-sided ulcerative colitis (UC) should be treated with combined oral and topical mesalazine(COTP). However, these guidelines were based almost exclusively on studies with slow-release and/or pH-dependent release mesalazine. MMX-mesalazine (MMX-M) allows preferential delivery of 5-ASA especially in the left colon. Therefore, question arises whether topical therapy is still needed for patients treated with MMX-M. Aim: To assess in a prospective, single-center, pilot study whether adding topical 5-ASA therapy improves the remission rates achieved by MMX-M monotherapy.

Methods: Eligible were patients >18 years, with active mild and/or moderate extensive (E-UC) or left-sided (LS-UC) UC. Patients with proctitis were excluded. Patients with mild UC received 2.4g/day and patients with moderate UC received 4.8g/day MMX-M for 8 weeks. Clinical response and remission rates were assessed by the partial Mayo score at weeks 2 and 6 and the full Mayo score at weeks 4 and 8. Faecal Calprotectin (FC) tests (Quantum Blue, Bühlmann, normal values <50microg/g faeces) were performed at weeks 0, 4 and 8.

Results: Twenty six patients [15 male - 11female, mean age 28 (range 18-65) years, 5 smokers, 14 with LS-UC and 12 with E-UC, and Mayo score 6.5 (5-9)] received 2.4g MMX-M for mild (n=15) and 4.8g/day MMX-M for moderate (n=11) UC. After 8 weeks, 21/26 (81%) patients were in clinical and endoscopic remission (Mayo score=0). There were no significant differences in remission rates between patients with E-UC and LS-UC. Remission rates increased progressively by week 8 (31%, 54%, 69% and 81% at weeks 2, 4, 6 and 8, respectively) and are comparable to the known remission rates achieved by COTP. FC ranged from 72 to >300 microg/g of faeces at baseline but decreased gradually to < 50microg/g in the 21 patients in remission at week 8. Five of 26 (19%) patients did not achieve clinical remission (Mayo score 5-8, FC levels >100microg/g faeces). A significantly higher correlation was seen for FC than CRP with Mayo scores (P<0.001).

Conclusions: High levels of clinical remission were achieved by MMX-M monotherapy in this single-center pilot study in E-/LS-UC patients with mild and moderate disease without any differences between E-UC and LS-UC. FC may be used to follow clinical response. Adding topical therapy may not further increase remission rates at a clinically meaningful (cost-effective) difference than MMX-M monotherapy but this should be better addressed in large scale clinical trials.

P485
Pregnancy and its outcomes in female IBD patients.

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Background: Inflammatory Bowel Disease (IBD) typically affects patients during their child-bearing years. Reproductive issues are a key area of concern for female patients. The aim of this study was to determine the outcomes of pregnancy in femaIe IBD patients.
Methods: This was a retrospective study were female patients with IBD were recruited from 5 different European centres. Patients were interviewed through a purposely designed questionnaire.
Results: 233 patients were recruited (mean age 40 SD±11.9). The mean age of diagnosis was 31.4 years (SD±11.2). 85.5% patients with ulcerative colitis (UC) had a Montreal classification of E2 or E3. Most Crohn's disease (CD) patients (64.7%) had non-stricturing and non-penetrating disease.
There were a total of 224 pregnancies. 17.2% were pregnant twice, 6.44% were pregnant three times and 1.72% reported 4 pregnancies each. 26.6% had one pregnancy. 63.8% of pregnancies were before the diagnosis of IBD.
There were 0.96 life births/woman (0.82 life births/woman - CD; 1.02 life births/woman - UC) recorded in this study. There was no significant difference in patents with UC or CD. 54.0% of pregnancies were unplanned. This was higher in those who were pregnant after being diagnosed with IBD (p<0.0001). 8.6% of patients reported fertility issues. 9% of patients had an exacerbation of their IBD during pregnancy. Delivery was by caesarian section in 30.8% and by vaginal delivery in 69.2%. Mode of delivery (caesarian) was influenced by the underlying IBD in 12.0%.
Delivery was uncomplicated in the majority of patients (92.0%). Most patients had their delivery between 38 and 40 weeks gestation (81.6%). Mean birth weight was 3.34 kg (1.90 - 4.70kg; SD 0.395). Most births resulted in healthy babies (94.6%). One infant had congenital anomalies (0.44%). 1.34% suffered from developmental delay. 1.75% had low birth weight and 0.89% were born prematurely. One patient (0.45%) suffered a stillbirth. In those having suffered low birth weight, only one patient was on biologic therapy. Her IBD wasn't well controlled prior to pregnancy and her pregnancy wasn't planned. The mother of one baby who suffered preterm birth had exacerbations of IBD during pregnancy and needed hospital admission. 29 miscarriages were reported in this study.
54.4% of IBD patients breastfed their infants.
Conclusions: Although a lower birth rate and breast-feeding rate was present among IBD patients when compared to European data, the rate of low birth weight, caesarian section, still birth and pre-term births was actually lower than the rest of the European population. This data demonstrates that well controlled IBD is an important factor prior to pregnancy and its medications are safe during pregnancies

P486
Assay of infliximab trough levels and of total antibodies to infliximab in the management of loss of response

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Background: Optimization of infliximab therapy in inflammatory bowel disease (IBD) patients who lose the clinical response is currently performed empirically. The assay of antibodies to infliximab (ATI) and infliximab trough levels (TL) could be helpful in the clinical decision.
Methods: We collected sera from 102 IBD patients on maintenance infliximab. Fifty-five patients had experienced a loss of response (LOR) and most of them (45/55) had the infliximab dose already been optimized at 7.5 to 10 mg/kg. As a control group we studied 47 patients in stable clinical response (CR). Blood was drawn for ATI, TL and C-reactive protein (CRP) assay immediately before the next infliximab infusion. We assayed ATI and TL by an ELISA kit (Immundiagnostik AG, Bensheim, FRG). ATI were expressed as arbitrary units (AU)/ml (a level of 10 AU/ml is considered as positive for antibody presence in the serum). TL were expressed as ug/ml. The subsequent clinical decisions were made blinded to ATI and TL levels. Clinical activity and CRP were also assessed after 12 months.
Results: Fifty-one patients had Crohn's disease and 51 had ulcerative colitis. Twenty-three were on concomitant immune modulators (IM). Median ATI were 24,5 AU/ml (IQR 7,4 to115,8) and 66 (65%) had ATI score higher than 10 AU/ml, while median TL were 2,3 ug/ml (IQR 0 to 5,6). ATI and TL were negatively correlated (Spearman's rho -0,579, p<0.0001). ATI were lower in the patients on concomitant IM, as compared to those not (median 10,6 AU/ml, IQR 5,5 to 48,6 versus 27,5 AU/ml, IQR 7,8 to 128,3, p= 0,045 by Mann-Whitney test). Mean TL were lower in the patients with LOR and standard infliximab dosage (0,49 ug/ml) as compared to those on optimized dosage (2,96 ug/ml) and those on CR (2,59 ug/ml) although these differences were not statistically significant. ATI levels were significantly higher in the LOR group as compared to the CR (40,8 AU/ml, IQR 9,8-189,7 versus 11,4 AU/ml, IQR 6,5 to 82,3, p = 0,037 by Mann-Whitney test). A ROC analysis detected a cut off value of ATI for CR at 12 months of < 26,3 AU/ml (AUC 0,693, 95% CI 0,594 to 0,780, p= 0,0033) with sensitivity of 64% and specificity of 75%. The same analysis for TL detected a cut off of >2,08 ug/ml for predicting CR at 12 months with 56,4% sensitivity and 70,8% specificity (AUC 0,628, 95% CI 0,527 to 0,722, p= 0,038). Among patients with LOR, 62% had ATI > 26,3 AU/ml, as compared to 32% of those maintaining the response (p=0,003 by Fisher's exact test). A significant correlation was detected between ATI and CRP levels both at baseline (Spearman's rho 0,218, p= 0,0287) and after 12 months (rho 0,284, p= 0,0043).
Conclusions: Prospective studies will determine the utility of these cut off values in the management of LOR to infliximab in IBD.

P487
A Study of Optimal Screening for Latent Tuberculosis in Patients with Inflammatory Bowel Disease

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Background: Reactivation of latent tuberculosis infection (LTBI) in patients with IBD, secondary to treatment with anti-tumour necrosis factor (TNF)- α agents, can lead to serious and life-threatening illness. No gold standard exists for the detection of LTBI and there is conflicting evidence within the inflammatory bowel disease (IBD) literature regarding the best screening strategy for LTBI. The aims of our study were to 1) assess whether the addition of an interferon-gamma release assays (IGRA) to a tuberculin skin tests (TST) would improve the detection of LTBI, 2) evaluate the concordance of the TST and IGRA and 3) assess the impact of various demographic, diagnostic and treatment factors on the each test.

Methods: Consecutive IBD patients being considered for anti-TNF-α treatment underwent testing with a TST, IGRA (QuantiFERON Gold In-Tube) and chest x-ray (CXR). All patients completed a self-administered questionnaire. The association of both tests with demographic factors, LTBI risk factors (including CXR), BCG vaccination and immunomodulator (IM) therapy were evaluated using Fisher's exact test, and agreement between the TST and IGRA was evaluated using the kappa statistic.

Results: One hundred and fifty-five consecutive IBD patients (131 Crohn's disease, 22 ulcerative colitis and 2 indeterminate colitis) underwent testing with both TST and IGRA. Six patients had indeterminate IGRA results and were excluded from the analysis. Twenty-four (18%) patients had a history of BCG vaccination. Twenty-eight patients (19%) had at least one risk factor for LTBI, including four (3%) with an abnormal CXR. One hundred and two patients (70%) were taking immunosuppressive therapy at time of inclusion. Nine patients were TST positive (6%) and 7 patients (5%) were IGRA positive. Concordance between TST and IGRA was 91.9% (but $\kappa = 0.21$), with only 2 patients being positive for both tests. Neither test was affected by age, gender or BCG vaccination. In bivariate analysis, the presence of risk factors for LTBI was found to positively influence TST results (OR 19.8, 3.9-102.1), but not IGRA. IGRA was negatively influenced by IM therapy (OR 0.06, 0.007-0.5), but not TST. Four of the five patients who were IGRA positive but TST negative were treated or advised to begin treatment for LTBI by a respirologist.

Conclusions: IGRA was negatively influenced by IM therapy, while the presence of risk factors for LTBI was found to positively influence TST results. There is fair agreement between positive TST and IGRA results. The addition of IGRA to the standard practice of TST and CXR increased the number of cases presumed to have LTBI and influenced management. Given these findings, dual testing with TST and IGRA should be considered in IBD patients.

P488
Virus associated hemophagocytic syndrome: rare but serious complication of azathioprine treatment in patients with Crohn´ s disease

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Background: The course of Epstein - Barr virus (EBV) infection is mostly asymptomatic or presented as infectious mononucleosis. The fulminant EBV infection and EBV - associated immune based syndromes are poorly described rare complications of patients with inflammatory bowel disease (IBD) and related immunosuppressive therapy. In immunocompromised individuals a severe course of the EBV associated disease cannot be excluded. Virus associated hemophagocytic syndrome (VAHS) is a severe life-threatening condition mostly connected to EBV infection in formerly EBV naive patients. VAHS is considered to be a specific clinical condition for which histiocytary proliferation with hemophagocytosis and the symptoms like hepatosplenomegaly, lymfadenosis and intermittent fever are typical.

Methods: We analyzed 2 cases of EBV-naive patients with Crohn´ s disease long-term treated with azathioprine and eventually corticosteroids for the suspicion of secondary bone marrow supression. Early onset of VAHS and fatal clinical outcome followed in both of them.

Results: Both patients (aged 29 and 22 years) were treated with azathioprine (2.5 mg/kg/ day) for Crohn´ s disease with ileal involvement. They were admitted for fever, malaise and lymfadenosis with the suspection on infectious mononucleosis. Their clinical condition further deteriorated after onset of corticoid therapy (80 mg/day) initiated for the suspicion of secondary bone marrow suppression and presented as fulminant liver failure followed by kidney failure. The laboratory analysis described viral capsid antigen (VCA) IgM and IgG positivity and nuclear antigen (EBNA) IgG negativity. Despite intensive therapy (based on mechanical ventilation, continuous renal replacement therapy, continuous veno-venous hemofiltration) they died within 32 and 33 days respectively after onset of VAHS.

Conclusions: VAHS is a rare but potentially lethal complication of primary EBV infection. Concomitant immunosuppressive therapy in IBD patients significantly increases the risk of fatal clinical outcome. We are the first to describe VAHS and azathioprine treatment association. Therefore, EBV status should be assessed in patients before introduction to azathioprine. In patients with VAHS administration of high dosed corticoids could deteriorate the condition.

P489
Faecal microbiota transplantation via nasogastric route for the treatment of recurrent and antibiotic refractory Clostridum Difficile infection: The UK experience

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Background: Faecal microbiota transplantation (FMT) has been shown to be a highly effective and safe treatment strategy for recurrent and antibiotic refractory Clostridium Difficile infection (CDI). This procedure has mainly been reported to be carried out in the United States, Canada and several European countries however experience using the nasogastric (NG) route is as yet limited. Nasogastric / nasoduodenal administration has been shown to be a safe and effective mode of administration of FMT and was the route for delivery in the only RCT that demonstrated its efficacy for recurrent CDI. We present our clinical experience using this mode of treatment in patients who underwent FMT for CDI via a NG tube over a one year period.

Methods: Patients underwent FMT for CDI at the University Hospital Birmingham and Heart of England Foundation Trust from March 2013 to September 2014. Donors were selected from a cohort of screened volunteers and processed stool was administered via the

nasogastric route to patients who had either recurrent or antibiotic refractory CDI. Demographic data, antibiotic treatment, biochemical markers, stool frequency and type were collected for each patient. CDI cure was defined as less than 3 unformed bowel movements (Bristol Stool Chart type 1 - 5) per day for 2 consecutive days.
Results: A total of 23 patients underwent FMT of which 11 were for antibiotic refractory CDI and 12 for recurrent CDI. Twenty one patients (91%) achieved a CDI cure rate after a single FMT. Of the 16 patients with a 12 week follow up period 14 patients (88%) suffered no recurrence of CDI post FMT. One patient who relapsed following an initial response to FMT had a second FMT with a further response prior to relapsing before 90 days. Three patients died within 90 days of the FMT with one as a result of refractory CDI that failed to respond to FMT, however there were no deaths directly associated with FMT. The main side effect reported was constipation in three patients and abdominal discomfort in one patient.
Conclusions: In the largest UK series to date we have demonstrated that FMT administered via nasogastric route is a highly effective, safe and tolerable therapy for recurrent and antibiotic refractory CDI. The manipulation of gut microbiota represents a promising new therapeutic option that warrants further investigation in the treatment of gastrointestinal disease. Our data, in conjunction with recent safety/acceptability information of orally delivered capsules for FMT reinforces the possibility of either the nasogastric or even oral route of delivery for treatment. Either of these is, of course, much easier than nasoduodenal or colonic delivery.

P490
Comparative analysis of the cost of maintenance treatment of Ulcerative Colitis with different compound preparation of mesalazine

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Background: Introduction: Mesalazine is effective in the induction and maintenance of remission in patients with mild/to moderate Active Ulcerative Colitis (UC) without significant differences between different forms of release. Maintenance dose varies from 1.5-3 grams/day and cost per gram of mesalazine varies between different available agents.
Aim: Analyze the average cost of the maintenance treatment of remission for one year in patients with UC in relation to the type of mesalazine used.
Methods: This is a retrospective multi-center study of historical cohort of UC patients in clinical remission and monotherapy with oral mesalazine.
Patients were included from 4 centers with left side UC/Extensive UC in sustained clinical remission at least for one year before they were included in the analysis. Mesalazine evaluated by commercial register were: Claversal®, Lixacol®, Pentasa®, Salofalk®, Mezavant MMX® and Salazopirina® (SZP). Age, sex, date of diagnosis, Montreal classification in diagnosis, mesalazine/patient dose and gr/mesalazine price were recorded. The global average dose and individual for each compound preparation of mesalazine were calculated estimating cost/day and annual cost (cost/day/365 days). Prices are PVP+IVA (RRP + VAT) and are taken from the General Council of official colleges of pharmacists. https://botplusweb.portalfarma.com/botplus.aspx
Results: 283 patients (137 women), Average age 38.5 (8-81). There were no differences in demographic characteristics, extension of disease and severity at diagnosis of patients in the different groups of mesalazine. Patients medicine (drug): SZP 14(5%), Lixacol 19 (7%), Salofalk 37 (13%), Mezavant 64 (23%), Pentasa 74 (26%), Claversal 72 (26%). Average dose of Mesalazine: 2.64gr (0.8-4.8). Cost/day of mesalazine adjusted to dose(***): SZP® 0.96***; Claversal® 1.28***; Lixacol® 1.70***; Salofalk®2.29***; Pentasa®2.35***; Mezavant® 4.70***. Cost/year for each different analyzed mesalazinas (***): SZP 350.79***; Claversal® 467***; Lixacol® 627.80***: Salofalk®834.07***; Pentasa® 854.40***; Mezavant® 1697.97***.TABLE 1.
Conclusions: 1) Medical compounds under different name and label of oral mesalazine are equally effective in maintenance of remission in UC but the annual cost varies significantly depending on the type of mesalazine used.

P491
"Now I know I'm not alone": Participating in a disease-specific summer camp improves the quality of life of young people with Inflammatory Bowel Disease

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Background: Inflammatory bowel diseases (IBD) are often diagnosed at a young age. Recent British [1] and European [2] surveys have shown IBD can affect confidence, self-esteem, educational achievement, and career development. Camps may provide a means of overcoming these problems caused by IBD: two previous studies of IDB-specific summer camps for children and adolescents in the USA showed beneficial effects on psychosocial adjustment and health-related quality of life [3] [4] . A survey was conducted to find out the effects of summer camps for European young people with IBD.
Methods: European summer camp participants from previous years were invited to complete an online survey about whether the camp

Gender	n	%
Male	20	36.4%
Female	35	63.6%
Age at first camp		
12-14	1	1.8%
15-18	12	21.8%
19-24	19	34.5%
25-29	16	29.1%
30+	7	12.7%
Country of camp attended		
Portugal	25	45.5%
Netherlands	7	12.7%
Switzerland	6	10.9%
More than one	4	7.3%
Other	13	23.6%

"Table 1: Demographics of respondents"

	n	%
Attending the camp improved my confidence in dealing with IBD		
Strongly disagree	3	5.5%
Disagree	0	0.0%
Agree	19	34.5%
Strongly agree	32	58.2%
Don't know or cannot answer	1	1.8%
Attending the camp improved my acceptance of my IBD		
Strongly disagree	2	3.6%
Disagree	0	0.0%
Agree	23	41.8%
Strongly agree	29	52.7%
Don't know or cannot answer	1	1.8%
Attending the camp improved my overall quality of life		
Strongly disagree	3	5.5%
Disagree	3	5.5%
Agree	22	40.0%
Strongly agree	22	40.0%
Don't know or cannot answer	5	9.1%
What in the camp experience was the most supportive for you?		
Activities	9	16.4%
Counselors	8	14.5%
Fellow campers	35	63.6%
Something else	3	5.5%
Would you recommend the camp to other people with IBD?		
Yes	54	98.2%
No	1	1.8%

"Table 2: Participant responses"

improved their confidence in dealing with IBD, their acceptance of IBD, and their overall quality of life. They also answered open-ended questions about what about the camps they enjoyed most. Participation was anonymous. The survey was accessible from May to October 2014.

Results: Fifty-five people who attended camps between 2010 and 2014 completed the survey. Demographics are shown in Table 1. Table 2 reports the responses.

For many participants, meeting other IBD patients was the most enjoyable experience: "Interacting with other IBD patients who had a complete understanding of what each other was going through", "Possibility of talking shameless about my problems", "The knowledge that I'm not the only one with IBD". Meeting peers had concrete beneficial effects: "The contact with all other campers inspired me to start new things in my life, things like going back to school, which I was afraid and hesitant to do before. Before the camp I was without job or school, sitting ill at home whole day. People who were more ill than I was and who still did a lot served as a great example of all the things I could still do!" Most respondents (98.2%) would recommend camps to other people with IBD.

Conclusions: Attending a summer camp and meeting other IBD patients was beneficial to most young people who completed the brief survey. However, the survey was susceptible to response bias because the small proportion who responded may have been more positive about the camps than all participants. Future studies should improve response rates.

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P492
Resolution of factor XI (FXI) deficiency in refractory Ulcerative Colitis (UC) after surgery: A case report

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Background: Coagulation abnormalities in acute inflammatory conditions such as sepsis are well recognised. Chronic inflammatory conditions, such as Inflammatory Bowel Disease, have the potential to induce a coagulopathic or procoagulant state with potential devastating consequences.

Methods: We present the case of a 14 year old male with severe UC, FXI deficiency and an acute cerebrovascular event. We report resolution of FXI deficiency post colectomy and restorative surgery for UC.

Results: The patient presented with two-week history of headache, vomiting, altered consciousness and left leg weakness, one year after diagnosis of severe UC refractory to combination immunosuppressive therapy. MRI changes were in keeping with Right Middle Cerebral Artery ischaemic stroke. There was no radiological evidence of systemic vasculitis, APTT was prolonged (67.3s; N:26-38s), FXI (13 IU/dl; N:50-150), Thrombocytopenia post stroke (lowest 76) with subsequent gradual recovery. Lifelong aspirin anticoagulation was commenced. No neurological sequelae were observed. UC remained uncontrolled despite escalation to non-conventional immunosuppression.

Patient underwent subtotal colectomy and ileostomy formation with good results. Lowest FXI levels documented pre-operatively (8 IU/dl) and treated with FXI concentrate. Congenital FXI deficiency was excluded by patient genetic and parental FXI testing. Spontaneous normalisation of FXI within 2 years of surgery (FXI>50 IU/dl) with no further complications.

Conclusions: Clinicians should recognise the haematological implications of UC, especially in cases refractory to medical therapy. In our patient, FXI deficiency was secondary to uncontrollable gastrointestinal inflammation and normalised after definitive surgical treatment. FXI deficiency was a likely contributing factor in this patient's stroke.

P493
Adding 5-Aminosalicylate to Immunomodulators Showed No Additional Benefit in Crohn's Disease

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Background: The use of 5-aminosalicylate (5-ASA) in Crohn's disease (CD) has provoked many debates in recent years. However, a significant number of doctors used 5-ASA as combination with immunomodulators (IMM) because of lack of evidence that 5-ASA has no additional benefit over IMM monotherapy for control of CD. This study was conducted to investigate whether concomitant therapy with both 5-ASA and IMM is better than IMM monotherapy in terms of the long term efficacy in CD.
Methods: Between January 1991 and May 2014.a total of 106 patients treated with IMMs only were identified, and were compared with 318 matched patients (1:3) treated with concomitant therapy during the same periods retrospectively. All the patients have been on IMMs or IMMs with 5-ASA more than 3 months at Asan medical center, Seoul, Korea. Kaplane Meier analysis was used to estimate the cumulative probability of receiving oral corticosteroids, anti-TNF agents, resectional surgery, and disease- related hospitalization.
Results: The median length of follow-up for patients was 57.6 months (Range, 192.0 or IQR, 28.8). The cumulative probabilities of steroid use were 0.3%, 24.9%, and 75.8% in 5-ASA+IMM group, and 0%, 31.2% and 87.8% in IMM only group at 1, 5, and 10 years respectively (p = 0.187). And, the cumulative probabilities of anti-TNF use at 1, 5, and 10 years were 0 %, 12.9 %, and 49.4 % in 5-ASA+IMM group, and 0 %, 20.6% and 63.2% in IMM only group (p = 0.107) respectively. Furthermore, surgical resection rate and disease related hospitalization rate were comparable between the groups. Drug-related adverse events occurred similarly in the both groups (p = 0.799).
Conclusions: Adding 5-ASA to IMM showed no additional benefit in terms of steroid use, anti-TNF use, resectional surgery and disease related hospitalization.

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Exploring the efficacy of weight-based dosing of thiopurine therapy in relation to metabolite levels at week 12 in patients with Inflammatory Bowel Disease

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Background: Traditionally patients commencing on thiopurine therapy in IBD have been dosed according to their body weight with data showing less than 70% achieve long term steroid free remission. The ability to measure thiopurine metabolites has shown that 6- thioguanine nucleotide (6-TGN) levels inversely correlate with disease activity and patients with sub-therapeutic concentrations are less likely to achieve remission. Also very high 6-TGN concentrations risk myelotoxicity and hepatic nodular regernative hyperplasia whilst 6-methyl mercaptopurine (6-MMP) concentrations above 5700 pmol/8 x 108 correlate with hepatotoxicity [1] .
Methods: The primary aim of this study was to assess how effective weight based dosing is in achieving therapeutic 6-TGN levels after 12 weeks of therapy in patients commencing thiopurines for the first time at our institution for both Crohn's and Ulcerative Colitis between Oct 2013 and July 2014. The incidence of potentially toxic thiopurine levels was also assessed along with symptoms, MCV, LFTs and disease activity indicies. All patients with normal TMPT levels were dosed at 2.5mg/kg (azathioprine) or 1.5mg/kg (mercaptopurine) with any dose adjustments made clinically based on blood results and symptoms.
Results: From 37 patients (19 male) at week 12 on stable thiopurine weight based therapy 15 (41%) did not achieve therapeutic 6-TGN concentrations. 7 (19%) were under-dosed, 6 (16%) were overdosed and 2 (6%) preferentially metabolised to excessive 6-MMP levels. Disease activity indices, faecal calprotectin, MCV and routine blood monitoring for leucopenia and abnormal LFTs did not consistently correlate with metabolite levels at week 12.
Conclusions: Weight-based dosing does not appear to be an accurate method for establishing patients on thiopurine maintenance therapy and this may explain the previous perceived lack of efficacy of thiopurines in a significant number of patients. MCV cannot be used as a surrogate for sufficient 6-TGN levels at week 12 and of the 2 "shunters" neither had significantly abnormal LFTs highlighting the need to identify these group using metabolite monitoring to enable allopurinol co-prescribing. The lack of correlation with disease activity likely reflects the patients having recently completed a reduction course of steroids at week 12 and that thiopurines themselves are not induction agents. Starting patients on weight-based dosing plus metabolite monitoring at week 12 to achieve therapeutic ranges may increase long term maintenance rates and increase the safety of treatment by preventing toxicity and a long term outcome study is warranted.

References:

[1] Chouchana L et al, (2012), Dr, Alimentary Pharmacol Ther

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Azathioprine versus mycophenolate mofetil in combination with anti-TNF alpha agents in the management of Crohn's disease

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Background: Combination therapy of biologics and immunomodulators is sometimes necessary in chronically active Crohn's disease to achieve remission and prevent further complications. Treatment escalation in patients who are intolerant to thiopurines can be very challenging as there are few alternative immunosuppressive agents. In this study we evaluate mycopheonalte mofetil in combination with an anti-TNF alpha agent in patients who are intolerant to azathioprine.
Methods: 17 patients under double immunosuppression (mycophenolate mofetil + biologic) were compared to 29 randomly chosen patients with an azathioprine-based combination therapy. The indication for treatment escalation was chronically active Crohn's disease. Treatment response was compared between both groups, defined by a drop of Crohn's diseases activity index (CDAI) of 70 and 100 points, respectively.
Results: The median follow up time for all patients was 12 months. In the mycophenolate mofetil group five patients (29.4%) discontinued due to adverse events. Eight patients (47.1%; CDAI -70) and four patients (23.5%; CDAI -100) achieved treatment response, respectively. In the azathioprine group two patients (6.7%) discontinued treatment due to lack of improvement. 11 patients (37.9%; CDAI -70) and 8 patients (27.6%; CDAI -100) had a response to the double immunosuppression, respectively. Treatment response for both groups (CDAI -70, p=0.757; CDAI -100, p=1) was comparable.
Conclusions: Mycophenolate mofetil could be a treatment option in combination with biologics in patients with chronically active Crohn's disease who are intolerant to thiopurines.

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Prevalence and reasons for drug non-adherence in a European cohort of ulcerative colitis patients: The UCandME survey

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Background: Non-adherence to medical treatment represents a major issue in patients with inflammatory bowel disease (IBD). Studies assessing the prevalence and associated causes of non-adherence in patients with ulcerative colitis (UC) in Europe remain scarce. We aimed to assess the prevalence and specific reasons for non-adherence in a prospective cohort of mild-to-moderate UC patients.

Methods: Five European UC experts developed a questionnaire that was administered to UC patients in 6 European countries (Sweden, Norway, Finland, Denmark, United Kingdom, and Spain). The questionnaire consists of 54 questions, including several questions addressing specifically adherence to UC medication. Patients completed the questionnaire online via a secured website. The Morisky score was calculated to evaluate drug adherence.

Results: A total of 372 UC patients completed the survey (mean age 42.3 ± 13.9 years, 50% females, mean disease duration 10 years). Current disease location was in 24% proctitis, 45% left-sided colitis, 22% pancolitis, and in 9% unknown. At time of questionnaire completion, 47% of patients were on a specific diet, and 31% took alternative medicine to treat their UC. Nine out of 10 of patients were concerned about the preservation of their health, 68% believed in preventive treatments, and 66% thought they "should do more to be healthy". Based on the Morisky scale, 60% of patients were identified to have a low adherence, 33% had medium adherence, and only 7% had high adherence. In the last three months before the survey, 36% had never forgotten to take their medication, 30% forgot it once to two times, 18% forgot it 3-5 times, and 16% forgot it 6 and more times. The following reasons for drug non-adherence were identified: 51% of patients "forgot to take the drugs", 22% of patients "found it inconvenient to take the drugs", 21% stopped the drugs because of feeling better, 20% wanted to prevent drug-related side effects, 19% feared side-effects, 15% feared addiction to drugs for UC treatment, 14% noted that the drugs to treat UC were too expensive, 9% thought they were not in need of the drugs, 5% had doubts that the drugs would work, and 3% indicated not to know how to use the drugs (multiple answers possible).

Conclusions: Non-adherence to drugs is frequent in patients with mild to moderate UC, only 7% of them being highly adherent in this European survey. The most frequent reason for non-adherence was "forgetting to take the drug". Interventions to target patient adherence should take into account their specific health beliefs and offer a reminder system for regular drug intake.

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Surgery and hospitalization in inflammatory bowel disease - what has changed in the last 25 years? - Overview of clinical practice in a tertiary referral center

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Background: Crohn's Disease (CD) and Ulcerative Colitis (UC) are subtypes of Inflammatory Bowel Disease (IBD) often requiring both medical and surgical management. Anti-TNF drugs have represented a major breakthrough in the medical treatment of moderate to severe UC and CD. More than half of IBD patients will require surgery during their lifetime. Therefore, both hospitalization and surgery are important outcomes and major drivers of healthcare costs in these patients.

Our aim was to evaluate the changes in number and length of hospitalizations and surgical procedures in IBD patients after the introduction of anti-TNF therapy in 2005.

Methods: Retrospective study of patients with CD and UC followed in a tertiary referral center over a period of 25 years (July 1989- October 2014). Patients were divided into two cohorts: patients admitted to hospitalization before 2005 (A) and after 2005 (B). Endpoints included number and length of hospitalizations and surgeries. Statistical analysis was performed with SPSS v 20.0 IBM statistics.

Results: During the follow-up time there were a total of 5541 hospitalizations - 3662 (66%) in CD and 1879 (34%) in UC, averaging 222 hospitalizations per year. These included 2298 patients - 1365 (59%) with CD and 933 (41%) with UC. The number of hospitalizations increased over time: 2483 (44.8%) in cohort A and 3058 (55.2%) in cohort B. However, the mean length of hospitalizations slightly decreased (10.4 ± 14.5 days versus 9.5 ± 15.4 days, p= 0.029). There was no statistically significant difference when comparing patients with CD and UC separately (9.5 ± 14.0 days versus 8.8 ± 14.4 days, p = 0.149 and 12.1 ± 15.24 versus 11.1 ± 17.35 days, p = 0.173, respectively). Patients with UC had longer lengths of hospitalization (11.5 ± 16.4 versus 9.1 ± 14.2 days, p=0.0001).

During this time period 593 surgeries were performed: 338 (57%) in the last ten years, averaging 23 per year.

The length of hospitalization in patients admitted for surgical procedures was significantly different between the two time cohorts (21.2 ± 21.3 versus 17.8 ± 17.5 days, p=0.038).

Conclusions: In our series, there was a clear tendency for an increase in the number of hospitalizations and surgeries in the last ten years in both patients with UC and CD. However, the length of hospitalizations was significantly shorter. Interestingly the length of hospitalizations were longer in patients with UC.

Possible reasons for these results are explained by both an increased awareness of IBD and the introduction of both immunomodulation and anti-TNF therapy.

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Final Results of SOLE study: Focus on patient adherence/satisfaction and their correlation with patient worries

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Background: A large "Survey on Quality Of Life in Crohn's PatiEnts (SOLE)" was conducted in Italy on subjects with active Crohn's disease (CD) with the aim of assessing health-related QoL over a 12-month period and determining the relationship between QoL and disease activity, patient satisfaction and treatment adherence.
Methods: Adults with active moderate-to-severe CD [Harvey Bradshaw Index (HBI) ≥ 8] were prospectively recruited in 38 IBD centres, over a 12-month observation period (2012-2013), with visits scheduled at baseline, and at 3, 6 and 12 months. Treatment adherence, disease-related worries, and treatment satisfaction were assessed with Medication Adherence Report Scale (MARS-5), Rating Form of Inflammatory Bowel Disease Patient Concerns (RFIPC) and Treatment Satisfaction Questionnaire for Medication (TSQM) respectively. Patients were categorized as fully or partially adherent (MARS score =25 or <25 respectively). For data analysis we used a multilevel mixed-effect linear regression model taking into account the visits and either HBI and therapeutic management or MARS and RFIPC.
Results: 552 patients with active CD (51% males, mean age 41.3 ± 13.7 y, range 18-84 y) were recruited and showed a remarkable mean HBI score reduction (from 10.3 at baseline to 4.4 at 12 months). The HBI reduction was related to biologic drugs use (adalimumab, p=0.012; infliximab, p=0.004) and follow-up visits progression (p<0.001). Mean (±SD) MARS score at baseline was 22.7 ± 4.2; it remained stable during the study (23.3 ± 3.5, 23.6 ± 3.1, and 23.5 ± 3.2 at 3, 6, 12 months respectively). Patients with full adherence (=25) represented 44,4% of the total population at baseline and gradually increased through the study (57.5% at 12 months). Mean RFIPC total score in patients with high adherence was significantly lower than in patients with low adherence (p<0.001) in all the study visits. This was confirmed for each RFIPC subdomain score: [body stigma (p<0.001), complications (p=0.002), sexual intimacy (p<0.001), and impact of disease (p<0.001)]. Mean TSQM score increased from 50.1 at baseline to 59.2 at 12-month visit (p=NS) and was significantly associated with a reduction of the mean RFIPC total score, and withall its subdomain scores (p<0.001 for all, calculated with Pearson's correlation coefficient).
Conclusions: SOLE is the first study so far to have evaluated Italian CD patients adherence, and it is one of the largest Italian observational study in this field. During SOLE, the disease activity decrease was significantly affected by visit progression and biologic drugs use. Fully adherent patients were significantly less worried about their disease than those with low adherence.

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Individualized therapy is long-term cost-effective compared to dose intensification in Crohn's disease patients failing infliximab

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Background: Infliximab (IFX) treatment failure in patients with Crohn's disease is generally handled by intensifying the IFX regimen. However, an alternative strategy defined by an algorithm based on serum IFX and anti-IFX antibody measurements to identify reasons for failure and corresponding interventions has been proposed. In a randomized controlled trial, we observed substantial cost reductions after 12 weeks when using this algorithm as compared to IFX intensification, and without negative influence on symptom control.(1) The current study primarily investigated long-term cost outcomes at time of the week 20 follow-up study visit and after 1 year. In addition, clinical outcomes were assessed at week 20.
Methods: Predefined follow-up from a 12-week, single-blind, clinical trial where Crohn's disease patients with IFX treatment failure (CDAI ≥220 or ≥1 draining perianal fistula) were randomized to IFX intensification (5 mg/kg every 4 weeks) (n=36), or algorithm-defined interventions in form of IFX intensification, change to adalimumab, or use of pharmaceuticals other than TNF-inhibitors (n=33). Patients were treated at the discretion of the physician from week 12 onwards. Blinding was maintained until week 20. Accumulated costs, expressed as mean costs per patient, were based on the Danish National Patient Registry. Data were analyzed in the following populations: intention-to-treat (ITT) (n=69), per protocol (PP) (n=55), per protocol completion at end of trial week 12 (PPCw12) (n=45) or end of follow-up week 20 (PPCw20) (n=29). NCT00851565.
Results: At the scheduled follow-up visit at week 20, response (CDAI reduction ≥70 point or ≥50% reduction of active fistulas) and remission rates (CDAI ≤150 or closure of all fistulas) were similar in all study populations between patients treated by the algorithm or by

IFX intensification (p>0.05). However, the sum of health care costs related to Crohn's disease was substantially lower (31%) for patients randomized to algorithm-based interventions than IFX intensification in the ITT population: €8,652 vs. €12,490; p<0.01. In the PP and PPw12 populations, costs at week 20 were even lower (49% and 50%) in the algorithm group: €6,335 vs. €12,490; p<0.01; and €6,171 vs. €12,364; p<0.01. In the PPCw20 population, costs were reduced by 60% in algorithm-treated patients: €5,113 vs. €12,881; p<0.001. The observed relative cost reductions (i.e. percentages) remained stable from week 20 until reassessment after one year, and were similar also when evaluating total health care costs irrespective of relation to Crohn's disease.

Conclusions: Economic benefit of algorithm-based interventions at IFX failure is maintained throughout one year.

(1) Steenholdt et al. Gut (2014

P500
Evolution after anti-TNF drug discontinuation in patients with inflammatory bowel disease (IBD): a multicenter long-term follow-up study.

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Background: The discontinuation of anti-TNF treatment after achieving remission in IBD patients could be considered due to safety and cost issues.

Aims: 1) to assess the risk of relapse after anti-TNF discontinuation; 2) to identify the factors associated with relapse; 3) to calculate the response rate to re-treatment with the same anti-TNF, and 4) to evaluate the safety of re-treatment with these drugs

Methods: Retrospective, observational, multicenter study conducted at 90 Spanish centers. Crohn's disease or ulcerative colitis patients who had been treated with anti-TNFs and in whom these drugs had been withdrawn after achieving clinical remission, were included. Follow-up time after anti-TNF discontinuation was at least 6 months. Long-term maintenance of remission was estimated using Kaplan-Meier curves. Cox-regression analysis was performed to identify predictive factors for relapse.

Results: At present, 311 patients have been included (53% women, mean age 42 y, 68% Crohn's disease). The reasons for anti-TNF discontinuation were: 62% medical decision, 21% adverse events, 12% patient desire, and 5% remission after top-down strategy. The median follow-up time was 24 months. The median time to relapse after anti-TNF discontinuation was 15 months, and the cumulative incidence of relapse was 37% (95%CI=32-43%): 4% at 6 months, 24% at 1 year, 37% at 2 years, 40% at 3 years, and 53% at 5 years after anti-TNF withdrawal. The incidence rate of relapse was 19% per patient-year (15-22%). At the time of anti-TNF discontinuation, endoscopy was performed in 49% of patients; of these, 88% had a normal endoscopy and 12% had mild activity. 66% of patients continued with an immunomodulator (IMM; AZA/MP/MTX) after discontinuing the anti-TNF. In the univariate analysis, the variables associated with a higher relapse risk were: female gender (p<0.02) and lack of maintenance of an IMM after anti-TNF discontinuation (p<0.01). In the multivariate analysis, the only variable associated with the risk of relapse was the treatment with IMMs after anti-TNF discontinuation (lower risk; HR=0.5, 95%CI=0.3-0.7). The incidence rate of relapse when an IMM was prescribed was 15% per patient-year. 72% of patients who relapsed were re-treated with the same anti-TNF; 68% of them achieved remission after induction, and 80% at the end of follow-up; 4 patients (5%) presented adverse events, all mild.

Conclusions: The incidence rate of relapse after anti-TNF drug discontinuation in IBD patients that were in remission was 19% per patient-year. The only predictive factor for relapse was the lack of IMM maintenance treatment after anti-TNF is stopped. Re-treatment of relapse with the same anti-TNF was effective (80% remission) and safe.

P501
Relationship between measures of infliximab exposure and clinical outcome of infliximab intensification at therapeutic failure in Crohn's disease

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Background: It is recommended to intensify the infliximab (IFX) regimen in case of flare of Crohn's disease during ongoing IFX maintenance therapy, as it is assumed that drug exposure often is insufficient in this situation. The relationship between drug exposure and clinical outcome has thus far primarily been assessed using the serum IFX concentration obtained immediately prior to the next IFX administration (C_{trough}). This study explored if alternative pharmacokinetic (PK) measures provide additional information and more accurately link IFX exposure with clinical outcomes.

Methods: Post-hoc analysis of randomized controlled trial which included 69 Crohn's disease patients with symptomatic IFX treatment failure (CDAI ≥220 or ≥1 draining perianal fistula).(1) Patients who had received an intensified IFX regimen with infusions every 4-6 weeks throughout the 20-week study period were included in the present study (n=30). Clinical outcome assessed by CDAI was evaluated at all study visits (weeks 0, 4, 8, 12, and 20). Individual PK parameters were estimated using a predefined population PK model (2) combined with each patient's IFX dosing regimen and C_{trough} determined by radioimmunoassay at time of manifestation of IFX treatment failure.(1) Based on these parameters, complete concentration-time profiles were simulated. NCT00851565.

Results: In this cohort, no overall association was observed between different PK measures of IFX exposure and clinical outcomes. Assessed models comprised: (a) IFX concentration at time of CDAI evaluation, area under the drug concentration-time curve (AUC) of the 1-3 preceding dosing intervals, and cumulated AUC (cAUC) during IFX intensification linked to CDAI; (b) cAUC between CDAI measurements linked to change in CDAI; (c) cAUC during IFX intensification linked to CDAI change from baseline; (d) AUC of prior IFX maintenance therapy linked to baseline CDAI. However, when patients were stratified according to clinical response type (i.e. response vs. response followed by relapse vs. no response), notable trends in most models indicated that increased IFX exposure associates with lowered disease activity in the subgroup of patients with clinical response.

Conclusions: Clinical outcome of applying an intensified IFX regimen at therapeutic failure only relates to increased IFX exposure in a subgroup of patients. This observation supports that pharmacodynamic mechanisms, with a shift to a non-TNF driven disease phenotype, often play a role in IFX treatment failure. Introduction of biologic drugs with different therapeutic targets may prove a favorable alternative to switching between TNF-inhibitors in selected subgroups.

(1) Steenholdt et al. Gut (2014)
(2) Fasanmade et al. Clin Ther (2011)

P502
Predictors of bad response to infliximab in Ulcerative Colitis patients (ECIA study. ACAD)

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Background: AntiTNF use is one of the last options of medical ulcerative colitis (UC) treatment before colectomy. ACT studies demonstrated its efficacy. Costs and side effects are disadvantages. We want to identificate: 1. predictor factors for stopping infliximab (IFX) treatment because IFX failure and 2. predictor factors for colectomy.

Methods: Retrospective and multicenter study including every UC patient treated with IFX in 10 Spanish centers from June 2003 to May 2014. 187 patients were included. Time from IFX induction to data extraction was 43±27 months. Included variables were related to UC extensión, severity, treatments before IFX, INM intolerance, INM resistance, IFX indication, concomitant use of immunomodulators (IFX+INM), IFX response, intensification, IFX interruption, date and reason, colectomy and colectomy date. Binary logistic regression analyses and Cox regression analyses were used for predictor of both variables: IFX interruption because insufficient response and colectomy. Results were expressed as odds ratios and hazard ratios.

Results: 26% of patients had IFX treatment stopped because no or loss of response. 16% of patients underwent colectomy. Independent predictor factors for IFX interuption because an insufficient response were: INM resistance (OR 2,899 IC 1,166-7,212 p 0,022), previous use of leukocitapheresys (LA) anytime before IFX (OR 3,322 IC 1,172-9,416 p 0,024), use of tacrolimus o cyclosporine (TC) anytime before IFX (OR 2,542 IC 0,950-6,802 p 0,063) and INM+IFX (OR 0,342 IC 0,121-0,963 P 0,022). Cox regression model demonstrated that corticosteroid use during IFX induction (HR 1,973 IC 1,002-3,887 p 0,049) and INM+IFX (HR 0,415 IC 0,222-0,777 p 0,006) were independent predictors of IFX interruption because insufficient response. Predictor factors fo colectomy were LA treatment anytime before IFX (OR 3,001 IC 1,075-8,379 p 0,036), severe cortico-resistant flare (OR 2,408 IC 0,952-6,092 p 0,061) and INM+IFX (OR 0,342 IC 0,121-0,963 P 0,022). Cox regression model demontraated severe cortico-resistant flare (HR 2,522 IC 1,080-5,880 p 0,032) and INM+IFX (HR 0,355 IC 0,159-0,792 p 0,011) were independent predictors of colectomy.

Conclusions: LA and TC treatments anytime before IFX, corticoisteroid treatment during IFX induction, severe cortico-resistant flare and IFX monotherapy predict an interuption of IFX treatment because of no or loss of response and colectomy.

P503
Infliximab and adalimumab serum levels predict probability of mucosal healing

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Background: The optimal target anti-TNF drug level that correlates with control of intestinal inflammation in IBD patients is still poorly defined. We aimed to define infliximab and adalimuamb serum levels that distinguish patients with mucosal healing (MH) from those with ongoing inflammation.

Methods: We conducted a retrospective study of 135 IBD (107 Crohn's disease, CD, 28 ulcerative colitis, UC) patients treated with infliximab (n=75) or adalimumab (n=60) maintenance therapy, who underwent lower endoscopy at a tertiary medical center. Infliximab/adalimumab drug levels were measured in temporal relation to endoscopy, and correlated with inflammatory markers (CRP) and with endoscopic evaluation of disease activity (SES-CD and MAYO scores for CD and UC respectively).

Results: Median drug levels (DL) were significantly higher in patients with MH vs. patients with endoscopically active disease, for both infliximab and adalimumab therapy (4.3 vs. 1.15 µg/ml, p=0.0002, 6.2 vs. 3.1 µg/ml, p=0.044, respectively). Patients whose CRP normalized under treatment, similarly had higher median DL than those who did not (4 vs. 2 µg/ml, p=0.022 for infliximab, 5.7 vs. 2.2 µg/ml, p=0.015 for adalimumab, respectively). Infliximab DL above 5.8 µg/ml (AUC=0.75, p<0.0001) and adalimumab levels above 7.4 µg/ml (AUC=0.68, p=0.03) had 85% specificity for achieving MH. Incremental gain analysis demonstrated that 50% of patients achieved MH when infliximab serum levels were above 4µg/ml and 75% reached MH with levels above 8µg/ml, whereas for adalimumab 50% and 75% of patients achieved MH when DL were above 7.5 and 10mcg/ml, respectively. Higher anti-TNF levels (infliximab DL above 8µg/ml or adalimumab DL above 10mcg/ml) were associated with only a negligible incremental increase of MH percentage.

Conclusions: Infliximab and adalimumab serum levels were significantly associated with MH. Infliximab DL above 5.8µg/ml and adalimumab DL above 7.4µg/ml had 85% specificity for MH, whereas increasing infliximab DL above 8µg/ml or adalimumab DL above 10mcg/ml conferred little additional endoscopic benefit.

P504
Clinical outcomes associated with switching or discontinuation of anti-TNF inhibitors for non-medical reasons

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Background: Anti-tumor necrosis factor (anti-TNF) agents are an important treatment option for Crohn's disease (CD), ulcerative colitis (UC), rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriasis (Ps), and psoriatic arthritis (PsA). However, patients with a stable response to anti-TNF therapy may discontinue or switch treatments for non-medical reasons such as cost reduction. We evaluated real-world clinical outcomes associated with non-medical switching of anti-TNF therapies in the US.

Methods: An online, physician-administered chart review collected data on patients with a diagnosis of CD, UC, RA, AS, Ps, or PsA who had response for ≥6-months to an anti-TNF therapy.

Table 1. Study Period Treatment Response: Discontinuers vs. Continuers

	Odds Ratios and Incidence Rate Ratios			
	Unadjusted	P-value	Adjusted	P-value
Patients with at least one disease flare	3.38	<0.001 *	3.34	<0.001 *
Mild	1.62	<0.001 *	1.65	<0.001 *
Moderate	4.97	<0.001 *	5.49	<0.001 *
Severe	6.55	<0.001 *	5.55	<0.001 *
Number of disease flares	1.82	<0.001 *	1.91	<0.001 *
Mild	1.60	<0.001 *	1.67	<0.001 *
Moderate	2.02	0.003 *	2.36	0.003 *
Severe	2.22	0.014 *	3.48	0.011 *

Notes: *P-value <0.05

Table 2. Study Period Healthcare Resource Utilization: Discontinuers vs. Continuers

	Odds Ratios and Incidence Rate Ratios			
	Unadjusted	P-value	Adjusted	P-value
Inpatient Stays				
Number of patients with a stay	1.49	0.203	2.94	0.009 *
Number of stays per patient	1.43	0.402	3.58	<0.001 *
Emergency Room Visits				
Number of patients with a visit	3.77	<0.001 *	5.21	<0.001 *
Number of visits per patient	5.18	<0.001 *	5.73	<0.001 *
Outpatient Visits[1]				
Number of visits per patient	1.21	<0.001 *	1.12	0.001 *

Notes: *P-value <0.05. [1] Patients were required to have at least one outpatient visit in the study period.

Physicians, sampled equally across rheumatologists, dermatologists, and gastroenterologists, selected 2 cohorts that were matched on primary diagnosis: patients who discontinued or switched from the anti-TNF on which they achieved response for non-medical reasons (switchers/discontinuers), and patients who did not discontinue for non-medical reasons (continuers). Switchers/discontinuers were followed for 12 months from the date of discontinuation (index date); continuers were followed for 12 months from the date of an office visit within 2 months of the matched switcher/discontinuer's index date. Generalized linear models were used to compare disease flares, disease control, and use of medical services between cohorts with adjustment for baseline demographics, comorbidities, and resource use.

Results: 377 matched pairs of switcher/discontinuers and continuers were analyzed (N=754). Compared to continuers, switchers/discontinuers had a higher risk of flares and more frequent flares across all severity levels (**Table 1**).

Conclusions: Switching or discontinuation of an anti-TNF therapy for non-medical reasons was associated with significantly worse clinical outcomes and increased healthcare resource use.

P505
Biosimilar but not the same

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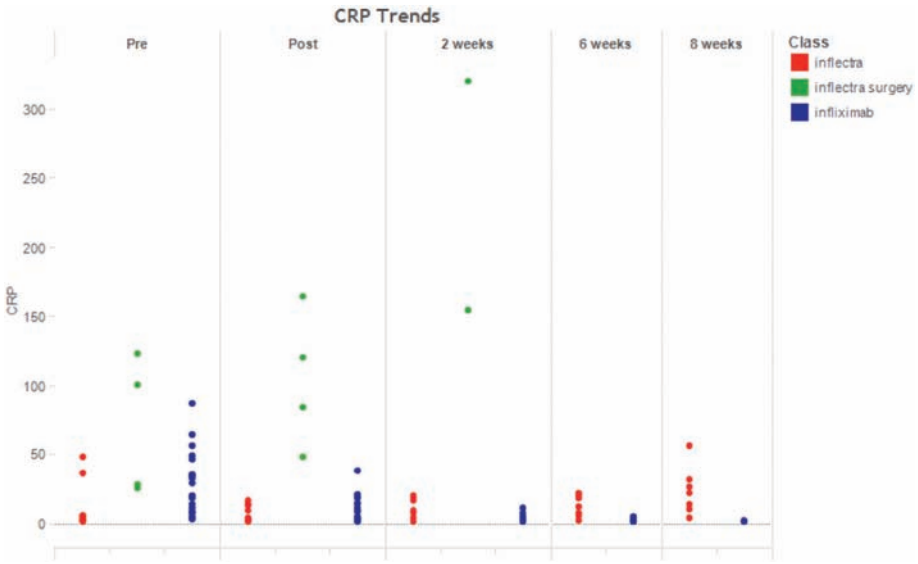
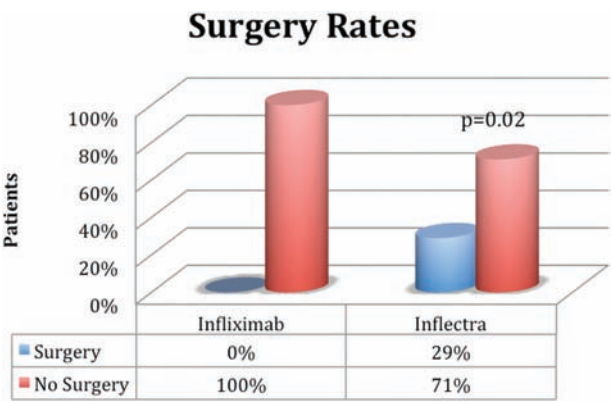
Background: A biosimilar medicine is a biological medicine that is developed to be similar to an existing biological medicine (the 'reference medicine') [1] . The European Medicine Agency allows extrapolation of indications for use of approved biosimilars based on indications for use of the reference product with the need for rigorous pharmacovigilance. Biosimilars have been viewed as potentially



"Rates of surgery in Infliximab and Inflectra groups"



"CRP trends in Infliximab, Inflectra and Inflectra surgical patients groups."

cost saving. [2] Inflectra was introduced in the department for IBD patients requiring commencement of anti-TNF treatment in January 2014. This is the first discription of the use of biosimilars in an IBD population in the Western World.

Methods: In this descriptive study, 14 consecutive patients who were commenced on Inflectra from January to July 2014 are compared to 22 consecutive patients commenced on Infliximab (Remicade) from Dec 2011 to Dec 2013. A direct comparison and statistical analysis was performed investigating surgery rates, readmission rates, use of steroids, disease activity and CRP trends.

Results: Demographics of both patient cohorts were comparable. 29% of patients in Inflectra group required surgery versus 0% in the Infliximab group (p= 0.02).

80% of the inflectra group required hospital readmission versus 5% of the infliximab (remicade) group. (p=0.00004). 60% of patients in the Inflectra group needed steroid augmentation of standard steroid tapering protocol with 50% requiring multiple increases in steroid dose versus 8% of patients in the Infliximab (p-value = 0.0007).Over the course of 8 weeks, 93% of patients in the Inflectra group had an increase in CRP with 7% remaining unchanged whereas 100% of patients in the infliximab group had a decrease in CRP (p=<0.001).

Conclusions: Our results suggest that biosimilars may not be as efficacious as the reference medicine. The results found reflect the ECCO statement position that the use of most biosimilars in IBD will require testing in this particular patient population [3] and cannot be extrapolated from other disease populations.

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P506
Predictors of Health-related Quality of Life in Asian Patients with Inflammatory Bowel Disease: Psychological, Clinical and Demographic factors

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Background: An impaired health-related quality of life(HRQOL) has been demonstrated in patients with inflammatory bowel disease(IBD). The factors associated with decreased HRQOL have not been fully known, specially the psychological factors. In this study, we aim to identify the predictors of HRQOL in a Chinese population of IBD patients.

Methods: We conducted a cross-sectional, prospective study of patients presenting to our tertiary care IBD center. A total of 219 patients with IBD were recruited into the study. HRQOL was measured using the 36-Item Short-Form Health Survey (SF-36) and Inflammatory Bowel Disease Questionnaire (IBDQ). Anxiety and depression were assessed by the Hospital Anxiety and Depression Scale (HADS). Perceived stress and perceived social support were

also assessed by standardized scales. Clinical and demographic data were obtained from our database and the electronic medical records . Univariate analyses and multiple linear regression analysis were performed to identify predictors associated with HRQOL.

Results: 91.3%(200/219) of patients included completed the questionnaires. The prevalence of anxiety and depression in our study population were 24%(48/200) and 16%(32/200). Univariate analyses showed that anxiety symptoms, depression symptoms , perceived stress , perceived social support ,disease activity , previous hospitalizations and relapses, hemoglobin and medical costs were strongly or moderatly correlated with HRQOL. Multivariate regression analysis revealed that both disease activity and anxiety symptoms were strong predictors of impaired HRQOL.

Conclusions: Our study demonstrates that psychological disorder contributes to impaired HRQOL in IBD, independent of the disease activity. Therefore, psychological distress should be considered in our current management of IBD patients and appropriate psychotherapy may improve HRQOL of these individuals.

P507
Long term outcome of children born to IBD mothers: preliminary result from a multicenter retrospective study in the Netherlands

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Background: The long term outcome of children born to mothers with inflammatory bowel disease(IBD) are relatively unexplored. The aim of this study is to analyze the health status of children who were born to mothers with IBD.

Methods: All women diagnosed with IBD prior to their pregnancy that gave birth between 1999 and 2011 were invited. After informed consent from both parents, the general practitioner (GP) was contacted for the following child outcomes: growth, number of infections for which antibiotics were needed, allergies and allergic reactions to vaccinations. Low birth weight was stated as <2500g, preterm birth as gestational age <37 weeks. The EUROCAT guideline was used to classify congenital abnormalities.

Results: In total 935 invitations (in 2 rounds) were sent to women with IBD from 8 Dutch hospitals. The response was 46.8%(438). Until November 2014 362 children from 239 IBD mothers (257(71.0%) CD,93(25.7%)UC and 12(3.3%)IBDU) were included. Median child age at follow up was 6 years(IQR 4-11). In utero 118(32.6%) children were not exposed to any IBD drug, 97(26.8%) to only mesalazine, 79(21.8%) to thiopurine, 38 children(10.5%) to anti- TNF, 20(5.5%) to both anti- TNF and thiopurine and 10(2.8%) were unknown.

There was no difference in anti- TNF exposed and the non- exposed children considering; median gestational age (39 weeks(IQR 38-40)), pre- term births (67(18.5%)), overall birth weight (3268 gram(IQR 2893-3638)), low birth weight (40(11%)) and major congenital abnormalities (8(2.2%)).

Five(1.5%) children showed a primary or secondary growth deficiency. None of these children were exposed to anti- TNF. Apart from one extended rash after vaccination there were no reports of severe vaccination reactions. Overall 88 children had allergies. These allergies were more common in the non anti- TNF exposed children(36.9%) compared to the anti- TNF exposed children(15.7%) (p=0.03). Median number of infections was 1(IQR0-3). There was no difference in infections rate between anti- TNF exposed children compared to non- anti TNF exposed. Furthermore, there was no increased infection rate in thiopurine exposed children or children exposed to both anti- TNF and thiopurine.

Conclusions: In this long term follow-up study in children born to IBD mothers we show no major adverse events, an overall normal growth and development as compared to the Dutch population. Apart from a lower incidence of allergies no difference was observed between in utero anti-TNF exposed and non-exposed children.

P508
Vedolizumab for the Treatment of Fistulising Crohn's Disease: An Exploratory Analysis of Data From GEMINI 2

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Background: Fistulising disease includes symptoms of anal pain, purulent discharge and incontinence, and is associated with high morbidity and impaired quality of life. Vedolizumab (VDZ) is a monoclonal antibody to α4β7 integrin with demonstrated efficacy and safety in the treatment of Crohn's disease (CD). This exploratory analysis evaluated the efficacy of VDZ in the subpopulation of patients with fistulising CD from a phase 3 placebo (PBO)-controlled trial (GEMINI 2, NCT00783692).[1]

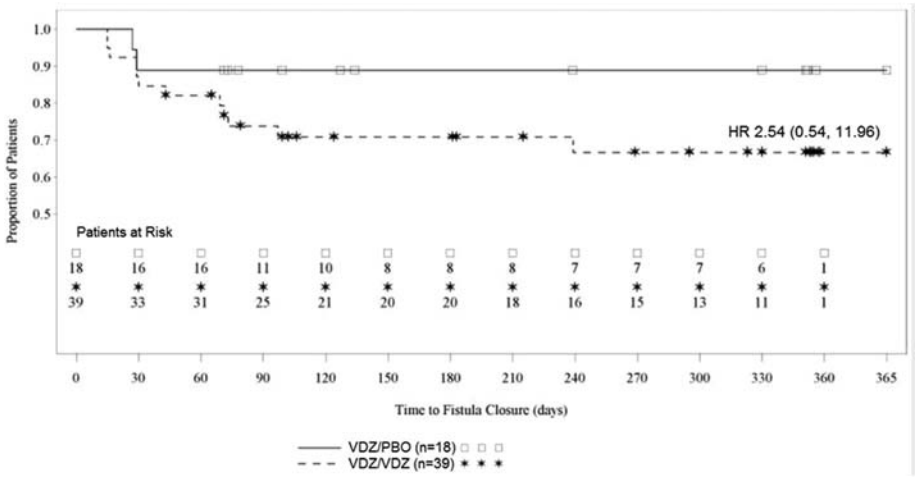
Methods: In GEMINI 2, after 6 weeks (wks) of induction treatment with 2 doses of VDZ, 461 patients achieved a clinical response and received maintenance treatment (intent-to-treat [ITT] population) with PBO or VDZ 300 mg every 8 or 4 wks (Q8W or Q4W). Among patients with fistula at study entry, fistula closure, a prespecified exploratory endpoint, was assessed at each visit (2-6 wk intervals) until wk 52. The percentage of patients achieving fistula closure and mean time to fistula closure were calculated.

Table. Number of patients with ≥ draining fistulae at wk 0 who achieved fistula closure over time (maintenance ITT population)

Week	VDZ/PBO[a] n=18	VDZ/VDZ[b] (Q8W) n=17	VDZ/VDZ[b] (Q4W) n=22	VDZ/VDZ[b] (combined) n=39
	Number of patients achieving fistula closure (%) [95% CI]			
6	4 (22.2) [6.4, 47.6]	3 (17.6) [3.8, 43.4]	3 (13.6) [2.9, 34.9]	6 (15.4) [5.9, 30.5]
14	2 (11.1) [1.4, 34.7]	5 (29.4) [10.3, 56.0]	6 (27.3) [10.7, 50.2]	11 (28.2) [15.0, 44.9]
26	3 (16.7) [3.6, 41.4]	6 (35.3) [14.2, 61.7]	5 (22.7) [7.8, 45.4]	11 (28.2) [15.0, 44.9]
52	2 (11.1) [1.4, 34.7]	7 (41.2) [18.4, 67.1]	5 (22.7) [7.8, 45.4]	12 (30.8) [17.0, 47.6]

Abbreviations: ITT, intent-to-treat; PBO, placebo; Q4W, every 4 wks; Q8W; every 8 wks; VDZ, vedolizumab; wk, week.
[a] Patients in the PBO group received VDZ at wk 0 and wk 2 in the 6-wk induction phase and then PBO in the 46-wk maintenance phase.
[b] Patients in the VDZ group received VDZ at wk 0 and wk 2 in the 6-wk induction phase and continued on VDZ Q8W or Q4W in the 46-wk maintenance phase.

Figure. Mean time to fistula closure in patients with ≥1 draining fistulae at wk 0 (maintenance ITT population)[a]



Results: At study entry, 57 (12%) patients in the maintenance ITT population had ≥1 draining fistulae, with 74% of fistulae located perianally. Among these patients, 44-49% had failed prior anti-tumour necrosis factor therapy and 39-54% had prior surgery for CD. By wk 14, 28% of patients treated with VDZ/VDZ (Q8W + Q4W combined) had achieved fistula closure (vs 11% VDZ/PBO; Table). This treatment difference was maintained up to wk 52. Kaplan-Meier probabilities of fistula closure with VDZ were 29% and 33% at 6 and 12 months, respectively; notably, the number of patients at risk was small (Figure).

Conclusions: In the GEMINI 2 maintenance ITT population, a greater percentage of CD patients with draining fistulae at wk 0 who continued VDZ treatment after induction achieved fistula closure compared with those who were re-randomised to PBO. This effect was maintained through to wk 52. These preliminary findings supporting the role of VDZ in the treatment of fistulising disease warrant further exploration in dedicated prospective studies in this population.

The clinical study was funded by Millennium Pharmaceuticals, Inc. (d/b/a Takeda Pharmaceuticals International Co.). Medical writing assistance was provided by inVentiv Medical Communications and supported by Takeda Pharmaceuticals International, Inc.

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P509

Risk score for Crohn's Disease activity using red cell distribution width, platelet count, erythrocyte sedimentation rate and C-reactive protein

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Background: Recent evidence has shown that Red Cell Distribution Width (RDW) is associated with active inflammatory bowel disease. [1] RDW is cheap and easily available and may be used as a rapid, non-invasive tool in diagnosing disease activity. C-Reactive Protein (CRP) and Erythrocyte Sedimentation rate (ESR) have low sensitivities (54% and 55%) and specificities (71% and 90%) in detecting Crohn's disease (CD) activity. [2] In this study, we have analysed the usefulness of a risk score based on RDW, platelet count, ESR and CRP in assessing disease activity in CD.

Methods: Serum CRP, ESR, platelet count and RDW in CD patients were assessed on the day of colonoscopy and compared with CD activity. A total of 308 endoscopic procedures on 161 CD patients were performed over a 48 month period. 89 patients were male with a median age of 40.2 years (9-85 years). Disease activity was determined according to endoscopic and histologic findings at colonoscopy. A risk score for disease activity was then created by giving 1 point to each elevated marker (CRP, ESR, platelet count >400,000 and RDW > 14.9%).

Results: Histological and endoscopic confirmation of disease activity was present in 191 colonoscopies (62%). RDW, platelet counts, ESR and CRP were all significantly elevated in patients with active CD (independent samples t test p <0.005) when compared with patients with quiescent disease. RDW, platelet counts, ESR and CRP had low sensitivities (43%, 21%, 68% and 44%) and specificities (73%, 93%, 40% and 64%) in detecting disease activity in CD patients.
90% of patients with a score of 4 (n=10) and 89% of patients with a score of 3 (n=37) had histologically active disease at endoscopy. Meanwhile 66.6% of patients with a score of 2 (n=72), 53% of patients with a score of 1 (n=91) and 54% of patients with a score of 0 had active disease at endoscopy. There was a statistically significant difference (p <0.0001) between the mean risk score in histologically quiescent disease (mean 0.9145, n=117) and the mean risk score in histologically active disease (mean 1.461, n=191).
Conclusions: Biomarkers have low sensitivities in detecting active CD. However, a score of 3 or more based on RDW, CRP, ESR and platelet count should raise the suspicion of ongoing inflammation.

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P510
Efficacy and safety of certolizumab pegol in an unselected Crohn's disease population: long-term data of the FACTS III survey

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Background: In Europe Certolizumab pegol (CTZ) is approved for the treatment of Crohn's disease (CD) only in Switzerland. In view of the limited long-term data from pivotal registry trials we aimed to evaluate the efficacy and safety of CTZ in clinical long term practice in Switzerland.
Methods: In the FACTS III (First Approved Certolizumab Therapeutic Experience in Switzerland) phase IV multicenter practice-based patient cohort patients receiving CTZ were prospectively included all over Switzerland in (non-) academic hospitals and private practice.
Results: A total of 104 patients (52 male) were included with first CTZ dose between 11/2007 and 08/2013 with a currently ongoing follow-up of until present between 6 weeks up to 5 years (mean 67.5 weeks, CI 6-208) and baseline-characteristics as follows: mean age: 36.6 years; mean age at diagnosis: 29.4 years (Montreal A1: 8.7%, A2: 68.3%, A3: 20.2%, unknown 2.8%); disease localization L1: 13.5%, L2: 63.5%, L3: 22.1%, unknown: 1.9%; disease behavior B1: 25%, B2: 25%, B3: 47.1%, unknown: 3.9%; smokers: 33.7%; previous surgery: 44%; anti-TNF naïve: 22.1%; previously received IFX, ADA orb both: 28.8%, 1.9% and 46.2%, respectively.
During treatment with CTZ we observed a significant decrease of mean HBI from 8.4 at baseline to 6.1 (p=0.017), 6.1 (p=0.063), 5.4 (p=0.002), 5.1 (p=0.009), 4.5 (p<0.001) and 3 (p<0.001) at week 6,26,52,78,104 and 156, respectively, corresponding to significantly increased rates of clinical remission at these points in time (41.4%, 40.7%, 51.9%, 58.1%, 53.6%, 73.3%; for all p<0.01). In addition, we found a sustained HBI decrease also in week 208 and 260 with mean HBI 5.6 and 5.2, respectively (however no significant difference to baseline due to small sample size), corresponding to a remission rate of 42.9% and 50% .
Looking specifically at anti-TNF naïve, exposed, prior non-response and prior loss of response (LOR) we did not observe any differences in mean HBI during the whole period of CTZ treatment between these four groups of patients. However, at the end of induction (week 6), anti-TNF naïve patients with a mean HBI of 2.6 showed a significantly better response than anti-TNF experienced (6.8, p<0.01), those with prior LOR (7.1, p<0.01) or those with prior non-response (8.5, p<0.01) to anti-TNF.
In contrast to the published data regarding Adalimumab, we did not observe significant differences in mean HBI while on treatment between patients with these different intervals of disease duration (and also at baseline).
Conclusions: CTZ is an effective long-term treatment in CD, including patients with long disease duration, prior treatment with 1-2 anti-TNF agents or previous LOR and non-response, suggesting that - similar to UC - Europe could use a third anti-TNF agent in CD.

P511
Efficacy and safety of granulocyte/monocyte adsorptive apheresis in steroid-dependent Active Ulcerative Colitis with insufficient response or intolerance to immunosuppressants and/or biological therapies (the ART trial): Results at 24 and 48 weeks

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Background: Treatment options in steroid-dependent, chronic-active ulcerative colitis (UC) with insufficient response or intolerance to immunosuppressants and/or biologicals are limited. The ART trial intended to document efficacy and to describe difficult-to-treat UC subpopulations which could benefit from Granulocyte/ Monocyte adsorptive (GMA) apheresis (Adacolumn®).
Methods: This was an uncontrolled, open-label, multicenter trial conducted in the UK, France and Germany. 86 patients (18-75 years) with steroid-dependent active UC (Clinical Activity Index (CAI) ≥ 6; Endoscopic Activity Index (EAI) ≥ 4) and insufficient response or intolerance to immunosuppressants (IS) and/or TNF inhibitors were included. Patients received up to 8 GMA aphereses in a single induction series over up to 8 weeks. Primary endpoint was the remission rate (CAI ≤ 4) at Week 12; secondary efficacy endpoints were clinical response (reduction in CAI of ≥ 3), and steroid-free remission and response rates in the Intention-to-treat (ITT) population. Patients remained enrolled for the duration of the follow-up; concomitant medication changes were recorded. Endpoint analyses up to 48 Weeks used a conservative approach including additional analyses of sustained remission and response, defined as the respective events observed at Weeks 12, and 24, and 48.

Results: As previously reported [1], among 84 patients in ITT, remission and response rates were 39.3% and 55.9% in Week 12. We now report remission rates of 34.5% in Week 24 and 33.3% in Week 48; response was seen in 46.4% and 39.3%, respectively. Out of 30 patients with prior failure of IS and biologicals, 33.3% were in remission in Week 24 and 20% at Week 48. Steroid-free remission at Week 24 was achieved by 19%, and 15.5% at Week 48. Sustained remission or response was seen in 29.8 % of patients at 48 Weeks. Concomitant IS medication was kept stable, steroid dose equivalents were reduced, and QoL improved further. 30 patients (41.7%) experienced at least 1 AE during follow-up; fifteen subjects experienced SAEs. None of the SAEs was related to the treatment. No new safety signals were seen.
Conclusions: We describe a cohort of steroid-dependent moderate to severe active UC patients with ineffectivity or intolerance to IS and/or biologicals treated with GMA apheresis induction therapy. Cinical benefit was seen in over 50% of patients at Week 12, in 46.4% at Week 24, and in 39.3% at Week 48. GMA apheresis may be a safe alternative treatment option in patients with UC failing or intolerant to immunosuppressants and TNF-inhibitors. Further randomized controlled clinical trials seem warranted to identify the place of GMA in the current treatment algorithms of UC.

References:

[1] Dignass, et al., (2014), Efficacy and safety of GMA apheresis in steroid-dependent active UC with insufficient response or intolerance to immunosuppressants and/or biological therapies (the ART trial): Results at 12 weeks , P500, ECCO 2014 Copenhagen

P512
Bowel ultrasound is useful in Crohn's disease monitoring: Analysis from the TRUST study in Germany

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Background: Reliable tools for measuring parameters of disease activity in patients with Crohn's disease (CD) are desirable. The purpose of this study is to characterise ultrasound (US) parameters, which allow individual disease follow-up and thus help to monitor response to therapy. The hypothesis of the TRUST (TRansabdominal Ultrasonography of the bowel in Subjects with Crohn's disease To monitor disease activity) study is that transabdominal US is an easy to use, easily repeatable, and accurate diagnostic tool in the assessment of CD activity and in monitoring the course of the disease, and in the early detection of CD complications.
Methods: TRUST is an ongoing prospective, observational multicentre study in Germany (51 sites) in patients with active CD. The primary objective of this study is the prospective evaluation of bowel wall US in order to assess its value in monitoring CD patients in routine medical practice. Standard follow-up is clinical, using Harvey-Bradshaw Index (HBI).
Results: For 100 of 232 patients with active CD enrolled in TRUST complete follow-up of 12 months was available. The patients' median age was 32 yrs, with a median disease duration of 3.8 yrs. All patients (63% female) displayed acute inflammatory symptoms at baseline, with at least moderate disease activity which required an initiation or escalation of treatment. At the baseline US examination, most patients showed bowel wall thickening (BWT) in the terminal ileum (70% of patients) and sigmoid colon (54%). BWT (measured in mm) decreased significantly at almost all colonic areas after 3 and at all after 12 months. Loss of bowel wall stratification, fibro-fatty proliferation and moderately or markedly increased signals in color Doppler US (Limberg scores of 3 or 4) was shown in approximately half of the patients at baseline. After 12 months, US examination showed significant improvements of the following parameters (p<0,001): BWT (e.g. terminal ileum 70% to 40%, sigmoid colon 54% to 24%), loss of bowel wall stratification (54% vs 24%), and fibro-fatty proliferation (47% vs 19%). Limberg scores also improved significantly (50% vs 12% with scores 3 or 4). Median HBI decreased from 10.5 at baseline to 1 at 12 months.
Conclusions: In this analysis, US examination was useful to monitor disease activity and response to therapy in CD patients. Almost all examined bowel US parameters improved significantly within 12 months from treatment intensification. Improvement of BWT, bowel wall stratification and mesenteric fibro-fatty proliferation might be useful in monitoring early and long term response to treatment. The US changes were accompanied by a significant decrease of clinical disease activity as measured by HBI.

P513
The effect of intravenous iron treament on quality of life in Inflammatory Bowel Disease patients with non-anemic iron deficiency

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Background: Iron deficiency is the most prevalent systemic complication of inflammatory bowel disease (IBD). Herein, we investigated the effect of intravenous iron treatment on quality of life (QoL) in non-anemic IBD patients.
Methods: Eighty-five IBD patients (55 ulcerative colitis, 30 Crohn's disease) who were non-anemic and in remission were recruited for this prospective study. The patients were intravenously administered 500 mg iron sucrose (FeS) in the first week of the study. Hematologic parameters and QoL were evaluated before prior to iron treatment and during the 12th week of treatment. The Inflammatory Bowel Disease Questionnaire (IBDQ) and the Short Form-36 (SF-36) Health Survey (version 2) were used to assess QoL.
Results: Prior to intravenous iron administration, the IBDQ, SF-36 Physical Component Summary and Mental Component Summary scores were 152.3±30.6, 46.7±7.3, and 45.7±9.8, respectively. In the 12th week of iron administration, those scores were 162.3±25.5 (p<0.001), 49.3±6.4 (p<0.001), and 47.6±8.9 (p=0.024), respectively, which were all significantly different from the scores prior to iron administration. The mean changes in the IBDQ scores for ulcerative colitis and Crohn's disease were 8.7% and 3.0% (p=0.029), were 6.4% and 4.7% (p=0.562) for the SF-36 Physical Component Summary, and were 4.6% and 3.2% (p=0.482) for the SF-36 Mental Component Summary, respectively.
Conclusions: Intravenous iron treatment may improve QoL in non-anemic, but iron deficient, IBD patients.

P514
Need for anti-TNF escalation in Inflammatory Bowel Disease - A single center experience

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Background: Anti-TNF therapy has become the standard of care in patients with moderate to severe Ulcerative Colitis(UC) and Crohn's Disease(CD). However, patients who initially respond may lose efficacy over time. Treatment escalation by increasing dosage or shortening intervals between administrations has proven to be effective in regaining response.

Our primary goal was to compare the need and time until anti-TNF escalation in patients with CD and UC. We also evaluated potential predictors of the need for treatment escalation.

Methods: We retrospectively reviewed patients followed in our institution under maintenance therapy with Infliximab (IFX) or Adalimumab (ADA). Patients not responding to induction therapy or with a history of previous failure to another anti-TNF were excluded. Statistical analysis was performed using SPSS v 20.0

Results: 203 patients (175 CD, 28 UC) met our inclusion criteria. IFX was prescribed in 144 patients (122 CD, 22 UC) and ADA in 59 patients (53 CD, 6 UC). Except for a higher prevalence of perianal disease in CD patients under IFX, baseline characteristics were similar between groups. 48/127 (37.8%) CD and 13/28 UC (46.4%) required therapy escalation (p=0.042). This was not associated with the type of anti-TNF used (p=0.350 and p=0.843 respectively for IFX and ADA) or with concurrent immunomodulation (p=0.157). Overall, patients with CD were younger at the time of first infusion (36.4±14.2 years versus 42.9±14.4 years, p=0.032) and time until escalation was shorter in patients with UC (1.0±0.8 years versus 3.3±2.6 years, p=0.003). The cumulative probability of avoiding escalation was higher in CD patients (Breslow exact test, p=0.002; p=0.006 if adjusted for type of anti-TNF). Predictors associated with the need to escalate anti-TNF included a positive C-reactive-protein (p< 0.0001), moderate to severe inflammation at baseline endoscopy (SES-CD > 11, Mayo > 2, p= 0.027) and a drop in hemoglobin levels in patients with anemia at induction (p=0.04).

Conclusions: Treatment failure is a common event in patients under anti-TNF therapy. Dose intensification occurs earlier and more frequently in patients with UC independently of the anti-TNF used. C-reactive-protein, endoscopic scores and hemoglobin levels may be useful in predicting earlier need for escalation.

P515
Basic laboratory parameters of inflammation compared to serum hepcidin level in inflammatory bowel disease (IBD)

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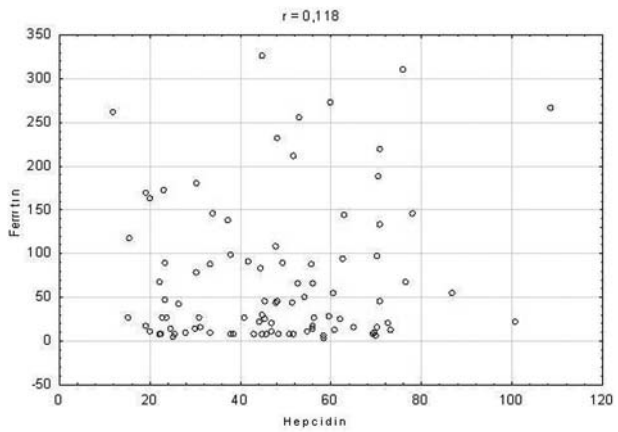

Background: Hepcidin is a small antimicrobial protein produced in the liver and transcriptionally up-regulated by high iron levels as well as inflammation. Hepcidin is known as key mediator of anaemia in inflammation. One of the positive regulator of hepcidin transcription is IL-6. Both hepcidin and IL-6 are not generally assayed in the laboratory. There are a lot of study about anaemia and hepcidin in Crohn's disease (CD) and ulcerative colitis (UC). Information about hepcidin level compared with basic, generally tested inflammatory markers can be useful tool in predicting a type of anaemia and choosing an appropriate way of treatment for patient with IBD.

Methods: We analyzed 97 patient with IBD (51 CD, 46 UC) recruited at the Department of Gastroenterology and Hepatology, Wroclaw Medical University, Poland. Routine laboratory tests included full blood count, erythrocyte sedimentation rate (ERS), C-reactive protein (CRP), fibrinogen and ferritin. Serum hepcidin levels were measured using enzyme-liked immunosorbent assay. Anaemia was defined as hemoglobin <12.0 g/dl and 13.0 g/dl, in women and men respectively.

Results: Anaemia has been established in 40 patients (18 CD, 22 UC). 13 patient had iron deficient anaemia (IDA), 8 anaemia of inflammation (AI) and 19 IDA/AI. Significantly more cases of elevated levels of hepcidin was observed in patients with CD (23 vs. 12). There was no statistically significant difference in the distribution of hepcidin in relation to sex or age. Increased level of CRP was observed in 24 patient with CD and 21 with UC. Half of the patients (26 CD, 24 UC) had an elevated ESR. 31 patients with CD and 23 with UC had fibrinogen above the upper limit of normal. Ferritin level >100ug/l was found in 21 patients (11CD, 10 UC) and in the range of 30-100 ug/l in 22 patient (15 CD, 7UC). Leukocytosis occurred in the same number of patients (8/8). Hepcidin showed a statistically significant positive correlation with CRP (p = 0.0118) and fibrinogen (0.0096) for whole group of IBD patients. After divided into groups, a clear and statistically significant positive correlations of hepcidin with CRP, ESR and fibrinogen were found only in patients with UC. The correlations of hepcidin with ferritin (Fig.1) and WBC were weak and not statistically significant (p>0.34). In regression model for whole group of IBD patients, increased hepcidin level was more likely to occur in case of elevated fibrinogen and CRP, OR =1.1 and OR=1.5 respectively.

Conclusions: Basic, nonspecific markers of inflammation such as CRP and fibrinogen can be useful in assessing the risk of developing anemia associated with elevated hepcidin level.

P516
Immunisation status and factors influencing vaccination decision-making in patients with inflammatory bowel disease

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Background: Patients with inflammatory bowel disease (IBD) are at higher risk of severe course of infections. Immunisations are recommended for this group of patients but the vaccine uptake is very low. However, it has not been yet investigated in the Polish population of IBD patients.

Methods: The aim of the study was to assess the vaccination status in patients with IBD and factors influencing patient opinion about immunisation. An author-designed survey was conducted among IBD patients hospitalised in the Department of Gastroenterology and Hepatology from November 2013 to March 2014. The survey was comprised of the following sections: demographic information, medications used for IBD treatment, vaccination history,

vaccine-preventable disease history and patient attitude toward vaccination. Patients who have not received influenza vaccines were asked to complete a multiple-choice type question about the reasons for non-immunisation. Randomly, patients completed the survey in the presence of physician to verify comprehension of the questions. In order to provide test-retest reliability a group of ten patients completed it twice. The chi-squared test was used to compare categorical variables.
Results: The survey was completed by 143 IBD patients (73 men), 60% with colitis ulcerosa, 40% with Crohn's disease. Mean age was 37 yrs (range 16-91 yrs). Most often patients reported hepatitis B (HBV) vaccination, 64%; then influenza, 35%; and tetanus, 12%; vaccines. There was a very poor uptake of hepatitis A and pneumococcal vaccines: 8% and 3%, respectively. As many as 24% of the patients did not know if they had received any vaccine. In 35% of the subjects at least one influenza vaccination was performed, but only 7% of them were receiving this vaccine annually. The uptake of influenza vaccine depended on the educational level: primary, 13%; secondary, 32%; tertiary, 44%; (p=0.046), while there was no influence of patient place of residence (village vs town, p=0.77). The reasons for influenza vaccine refusal were: no information from physician (51%); unawareness of the recommendations (38%); fear of vaccines side effects (28%); patients' doubts regarding vaccines efficacy (25%); vaccination costs (2%). Predominantly a gastroenterologist was chosen as the most reliable source of vaccines information (72%).
Conclusions: In Poland a vaccine uptake recommended for IBD patients, except for HBV vaccine, is very poor. There is a need to increase awareness among health care providers and their patients concerning immunisation guidelines. Gastroenterologists should be more involved in active vaccine promotion especially regarding pneumococcal and influenza vaccines. Patients with IBD should be equipped with a reliable documentation regarding vaccination.

P517
Efficacy of antisecretory factor in reducing high intestinal output in patients with ileostomy for Crohn's disease

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Background: Crohn's disease (CD) patients (pts) with ileostomy after gut resection can suffer from high-output stoma (HOS) (>1.500 ml/24 h), even in the absence of any inflammatory activity. HOS may cause water and salt depletion, with malnutrition occurring as a late complication, often needing a total parenteral nutrition (TPN). Antisecretory factor (AF) is a protein with anti-secretory and anti-inflammatory effects. High concentrations of AF protein are present in egg yolk and can be administered as egg yolk powder (AF-powder). In addition, endogenous AF stimulation can be induced by intake of specially processed cereals (SPC). A 2-4 wks long period of intake of SPC is necessary for obtaining a significant AF plasma concentration. A diet supplemented with AF has shown to reduce diarrhea in patients with inflammatory bowel disease. The aim of this study was to evaluate the effect of the AF-powder on the intestinal output of CD pts with HOS.
Methods: From January 2014 to July 2014 all CD pts in a remission phase, treated with AF-powder (4 g dissolved in water, 3 times/day for 15 days) associated to SPC (1 gr/kg/day introduced in the fourth day, for 1 month) for HOS, were included in this evaluation. A HOS was considered an ileostomy output >1.500 ml/24 h for at least 7 consecutive days before starting the treatment. Dietary conditions, fluid intake and concomitant therapy did not change during the study period. Clostridium difficile infection was excluded in all pts at the baseline visit.
Results: Ten pts entered the study (6 M; mean age 51.7 yrs, range 30-69 yrs; mean disease duration 24 yrs, range 3-47 yrs; mean weight 57.4 kg, range 43-68 kg; mean height 168 cm, range 158-180 cm). Mean time from ileostomy to study inclusion was 78.5 months (range 1-258 months), and mean ileal resection length 80 cm (range 30-185 cm). Nine pts had been previously treated because of HOS with loperamide, 1 pt with budesonide and 4 pts received TPN. Concomitant therapies included loperamide in 2 pts, TPN in 3 pts, and enteral nutrition in 2 pts. Four pts were receiving adalimumab, 2 pts infliximab, 1 pt mesalazine and 3 pts no therapy for CD. A mean daily intestinal output reduction from 2.160 ml (range 1800-2800 ml) at baseline to 1.650 ml (range 1000-2400 ml) at the end of treatment with AF-powder was observed in 9 out of 10 pts. One pt did not report any improvement. A mean creatinine value decrease from 1.9 mg/dl (range 1.5-2.6 mg/dl) to 1.4 mg/dl (range 1.1-1.7 mg/dl) was observed in 4 out of 6 pts. No adverse events were observed.
Conclusions: To our knowledge this is the first case report of a treatment with AF- powder in CD pts with HOS. This supplement food appears to be effective and deserves further evaluation.

P518
Five year outcomes of Crohn's small bowel strictures treated with double balloon enteroscopic dilatation.

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Background: The management of Crohn's small bowel (SB) strictures remains a difficult problem. Options include medical management, endoscopic strategies and surgical procedures. St Mark's Hospital performs double balloon enteroscopy (DBE) and dilatation. We report the outcomes of this cohort of patients, in whom DBE dilatation was performed for SB strictures with follow-up period of at least 5 years, with the primary endpoint being avoidance of surgical resection.
Methods: All patients with CD, obstructive symptoms and documented SB strictures referred for endoscopic dilatation between January 2007 and February 2009 were included. A retrospective data analysis was performed, including case note review and structured patient interview. The following factors were evaluated: patient demographics; disease extent, location and severity; symptomatology; requirement for further DBEs; requirement for future surgery and complication rate.
Results: A total number of 12 patients were identified with a mean age of 39 years (20- 59 years) and 65% were female. Prior to the procedure, all had been evaluated by cross-sectional imaging and/or endoscopy, with 9/12 undergoing imaging alone. 3/12 had prior resections for small bowel disease with one having short gut syndrome (approx. 70cm remaining). The follow up period was a median of 5.9 years (4.5-7.1).
A median of 2 (range 1-3) DBEs was performed per patient during the six year (median 5.5 - 8) follow up with 3/12 undergoing a single procedure, 8/12 undergoing 2 procedures and 1/12 undergoing 3 procedures. 7/12 patients had DBE via the rectal route with 5/12 per orally. Dilatation was performed in the ileum in 9/12 patients with the rest having duodenal (2/12) or jejunal (1/12) dilatation. 1 patient suffered a viscous perforation, diagnosed within 12 hours of the procedure, necessitating emergency laparotomy and resection with ileostomy. The remaining 11 patients did not suffer any post-procedure complications.
9/12 patients avoided surgical resection, and all 9 required multiple DBEs. The remaining 3/12 patients underwent a single DBE and

subsequently required SB resection (1/12 suffered a perforation and 2/12 did not receive any symptomatic benefit from the dilatation). 5/12 patients gained a symptomatic improvement after dilatation.
The two patients who underwent 3 DBEs have felt well with weight gain and no recurrence of symptoms.
Conclusions: This analysis suggests that, for patients with CD, DBE dilatation of SB strictures can be effective at preventing progression to surgery, and that it may be a reasonable treatment option.

P519
Thiopurines Undertreatment among Inflammatory Bowel Disease Patients Referred for antiTNF Therapy

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Background: The therapeutic effect of thiopurines in inflammatory bowel disease (IBD) is dose-dependent, with optimal dose of 2-2.5mg/kg for azathioprine (AZA). In general, the doctors` adherence to guidelines is often low and the real life `audit` data on thiopurines dose used in IBD are scarce. In majority of countries, thiopurines are used as the first line maintenance therapy of IBD and patients are referred for anti-tumor necrosis factor (antiTNF) therapy in case of side-effects or thiopurines failure. Therefore, the aim of our study was first, to assess the rate of deviation from normal thiopurines dose regimen among IBD patients referred for biological therapy. Second aim was to analyse whether the reasons for low dose thiopurines regimen were justified and properly documented.
Methods: All IBD patients referred for antiTNF therapy at one referral center were included and their medical records were reviewed. The dose of azathioprine at the time of indication for step-up to antiTNF was noted, as well as reasons for the use of low dose of AZA defined as dose lower than 2mg/kg.
Results: In total, 186 IBD patients were eligible, 10 patients were excluded because of lacking data, leaving 176 patients for further analysis - 120 (68%) with Crohn`s disease, 54 (31%) ulcerative colitis, 2 (1%) IBD unclassified; 92 (52%) men; mean age 37 years, range 18-76 years.
Overall, only 28 pts (16%) had adequate dose of azathioprine; 93 (53%) patients had not used AZA previously (8 pts; 5%) or had low dose of AZA (85 pts; 48%) without documented reasons.
Fifty five (32%) patients had discontinued (38 pts; 22%) or undergone dose reduction (17 pts; 10%) of azathioprine because of adverse events. Reasons for discontinuation of treatment were myelotoxicity (7 pts; 18% of all patients who discontinued), hepatotoxicity (6 pts; 16%), pancreatitis (5 pts; 13%), GI symptoms (4; 11%), allergic reactions and arthralgia (5 pts; 13%), one female patient discontinued therapy for cervical carcinoma in situ. For ten patients (26%), the type of adverse reaction was not documented. Reasons for dose reduction were myelotoxicity (5 pts; 29% of all patients who underwent dose reduction), hepatotoxicity (3 pts; 18%), GI symptoms, arthralgia and flu like syndrome (5 pts; 29%) and in four patients (24%) the type of adverse event was not specified.
Conclusions: In a real life clinical practice setting, substantial proportion of IBD patients referred for antiTNF therapy are using low dose azathioprine with only a minority for well documented reasons of biologically-determined intolerance.

P520
Accuracy of rapid fecal calprotectin test in monitoring Inflammatory Bowel Diseases under treatment with TNF-alpha antagonists

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Background: Anti-TNFalpha antibodies are effective in treating IBD (Inflammatory Bowel Diseases) unresponsive to the standard treatments. Information about the role of rapid Fecal calprotectin (FC) in monitoring ambulatory IBD patients under treatment with anti-TNFalpha are lacking. Our aim was to assess the accuracy of rapid FC in monitoring those patients.
Methods: 72 pts (38 males, 34 females, mean age 42.5 years, range 23-57 years), affected by Ulcerative Colitis (UC) (20 pts) or by Crohn's Disease (CD) (52 pts) were treated with anti-TNFalpha antibodies. FC was assessed by a rapid semi-quantitative test. Clinical, FC and endoscopic assessment was performed every 6 months during a 36-month scheduled follow-up.
Results: All UC patients were treated with IFX, while 32 CD patients were treated with IFX and 20 with ADA. With respect to the absence of clinical remission, FC test showed sensitivity of 71.8%, specificity of 65.2%, PPV of 41.8%, and NPV of 86.9%. In UC patients FC test showed a sensitivity of 66.7%, a specificity of 56.1%, a PPV of 18.2%, and a NPV of 92.0%. In CD patients FC test showed sensitivity of 70.6%, specificity of 65.2%, PPV of 50.0%, and NPV of 81.8%.
With respect to the presence of endoscopic lesions FC test showed sensitivity of 73.5%, specificity of 96.0%, PPV of 96.2%, and NPV of 72.7%. In UC patients FC test showed sensitivity of 47.2%, specificity of 84.6%, PPV of 89.5%, and NPV of 36.7%. In CD patients FC test showed sensitivity of 90.1%, specificity of 79.7%, PPV of 71.9%, and NPV of 93.3%.
Conclusions: Diagnostic accuracy of rapid FC seems better in predicting persistence of endoscopic lesions than clinical remission in IBD patients under treatment with anti-TNFalpha.

P521
Correcting iron deficiency anaemia in IBD with oral ferric maltol: Use of proton pump inhibitors does not affect efficacy

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Background: Ferric maltol (ST10) has been shown to correct iron deficiency anaemia (IDA) in a group of IBD subjects intolerant of oral ferrous sulphate. Ferrous iron products work most effectively in an acid environment in the stomach, where the iron remains in an oxidized 2+ form, and raised pH reduces iron absorption. Ferric maltol

	n	UC		n	CD	
		Mean Hb change g/dL (ferric maltol vs placebo, at w12)	Lower 97.5% CI *		Mean Hb change g/dL (ferric maltol vs placebo, at w12)	Lower 97.5% CI *
All subjects ITT	58	2.45	1.68	70	1.98	1.66
Taking PPI	14%	2.43	1.51	24%	1.65	0.89
No PPI	86%	2.50	1.61	76%	2.14	1.70

has been shown to be stable and soluble at a wide range of pH. Use of proton pump inhibitors (PPI) raises gastric pH and has been linked to reduced effectiveness of oral iron. Ferric maltol has been shown in a randomised study (AEGIS) to be effective in raising Hb in IBD subjects with IDA. The aim of this subgroup analysis was to examine Hb change following ferric maltol treatment in patients taking PPIs.

Methods: In a previously reported double blind randomised controlled trial (AEGIS) of 128 IBD subjects with IDA, and intolerant of ferrous sulphate (Hb 9.5 - 12.0g/dL female, 9.5-13.0g/dL male; and ferritin <30µg/L), were randomised to receive oral 30mg ferric maltol twice a day for 12 weeks or identical placebo. The primary endpoint of the initial study was change in Hb compared to baseline, at week 12. PPI intake was recorded at baseline. The subgroups (PPI vs no PPI) were analysed by UC or CD for Hb change at week 12 compared to baseline, using the intent to treat population.

Results: 128 subjects were randomised 1:1 and all included in the ITT population. Mean age was approximately 40 years in both UC and CD groups and 64% female. Overall Hb increased by 2.25g/dL in the ferric maltol group compared to 0g/dL in the placebo-group at week 12 (p<0.0001). PPI use was 14% in UC- and 24% in CD-patients. We did not observe a significant difference in Hb increase in the PPI vs no-PPI subgroups (see table; mean Hb change and lower 97.5% confidence interval).

Conclusions: Increase in Hb in IBD subjects with IDA following 12 weeks of ferric maltol treatment did not appear to be affected by concomitant PPI use in UC subjects. However there was a greater difference in the CD group. The numbers in each subgroup are modest and further studies are needed to confirm these findings. So far these data support the appropriate use of ferric maltol irrespective of PPI treatment.

P522
Factors reducing bone mineral density in patients with inflammatory bowel disease

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Background: One of the extraintestinal manifestations of inflammatory bowel disease (IBD) is a reduction in bone mineral density (BMD) - osteoporosis and osteopenia. It is known that the basis of reduction of BMD in patients with ulcerative colitis (UC) and Crohn's disease (CD) are clinical features of IBD, malabsorption of vitamins, as well as long-term use of drugs, in particular corticosteroids. The aim of our study was to identify the factors reducing the level of BMD in patients with IBD.

Methods: 159 patients with IBD were included into the study, UC was 92 (57,9%) patients, CD - 67 (42,1%) patients. The average age of patients was 36,4 ± 4,1 years, in patients with UC - 32,6 ± 2,8 years, CD - 37,2 ± 3,1 years. By gender, men patients with IBD were 72 (45,3%), women - 87 (54,7%) patients.

BMD was measured by using minidozed digital X-ray diagnostic instrument "Diascan". Interpretation of the results was performed using T-test. Normal bone density was determined at the level of T-kriteriya ≥ -1, osteopenia - in the range of -2.5 <T-score <-1, osteoporosis was defined as T-kriteriya ≤ -2,5.

Results: Normal BMD observed in 33 (20.8%) of patients with IBD, UC - 17 (51.6%), CD - 16 (48.9%). Decrease in BMD was detected in 126 (79.2%) patients, of whom 62 (49%) - osteopenia, 64 (51%) - osteoporosis.

Assessment of depending level of BMD and patient gender showed that women slightly more common normal BMD and osteopenia (61%), and men - osteoporosis (55%).

Analysis of the effect of treatment on the reduction of BMD in IBD patients showed that patients treated with steroids for over a year, had a significant decrease in BMD compared to patients at least a year of therapy (60% vs 35%, OR 2.8). The dose steroids also had a decrease in BMD value: patients receiving prednisone at a dose of 30mg, also had a significant decrease in BMD compared to patients treatment with prednisone at least 30mg (54% vs 27%, OR 3.2).

Conclusions: Decrease in BMD was observed in the vast amount (79%) of patients with IBD. Was found a higher prevalence of osteoporosis among men (55%). Duration of use of steroids and their high dosage over an extended time significantly affects the level of BMD patients (p<0,05).

P523
Efficacy of cyclosporine therapy in intestinal Behçet's disease

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Background: Behçet's disease (BD) is a systemic inflammatory disease caused by abnormal responses of both innate and acquired immunity. Intestinal ulcers of BD tend to perforate easily and be refractory to immunosuppressive therapies including biologics. Cyclosporine A (CsA) is a calcineurin inhibitor which inhibits IL-2 expression in Th1. Although the efficacy of CsA therapy to BD uveitis has been proven, the efficacy to intestinal BD remains unclear. This study is aim to evaluate the efficacy of induction and maintenance therapy by CsA in the patients with active intestinal BD.

Methods: Ten patients with moderately to severely active intestinal BD were treated by peroral or intravenous CsA for 2 weeks. The dose of CsA was adjusted to achieve the CsA trough plasma concentration of 100-150ng/ml in peroral group and of 500ng/ml in intravenous group. The disease activity was assessed by Disease Activity Index for Intestinal Behçet's Disease (DAIBD) and endoscopic findings. A clinical response was defined as a decrease at least 20 points of DAIBD from the baseline. After induction therapy,

patients continued to take oral CsA as maintenance therapy. The endpoint of maintenance therapy was defined as disease recurrence, addition of other treatment or withdrawal of CsA by adverse events. Non-recurrence rate was analyzed by Kaplan-Meier estimate.

Results: In induction therapy, mean dosage of CsA was 4.2mg/kg body weight/day in oral group and 2.9mg/kg body weight/day in intravenous group. Two weeks after CsA induction therapy, mean DAIBD score was decreased from 92.5 to 43.0 and a response rate was 70.0% (60.0% in oral CsA group and 80.0% in intravenous CsA group). Even in patients with failure to biologics therapies, a response rate was high (80.0%). The endoscopic findings of all of 6 patients, who could examine in both baseline and week 2, showed partially to significantly improvement. In maintenance therapy, mean dosage of peroral CsA was 4.1 mg/kg body weight/day. Non-recurrence rate of CsA maintenance therapy was 67.5% in 26 weeks, 33.8% in 52 weeks, and 22.5% in 78 weeks. Adverse events associated with CsA therapy were pyomyositis, nephropathy, hyperkalemia, tremor, and hypertrichosis.

Conclusions: CsA induction therapy is effective to active intestinal BD which is refractory to the conventional therapies including biologics. Yet, the efficacy and the safety of CsA maintenance therapy remain controversial. Further controlled study is needed.

P524
Could histological lesions predict reactivation in ulcerative colitis patients with mucosal healing?

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Background: Mucosal healing (MH) is a potential target in the treatment of patients with ulcerative colitis (UC), reducing the need for surgery and the risk of colorectal cancer. MH lowers the risk of disease reactivation, but some patients relapse in spite of the presence of MH. It is reasonable to think that the microscopic disease activity beyond MH could explain these cases. Our aim is to assess how many patients with MH have a microscopic disease activity and what kind of lesions are associated with mid-term reactivation (after 6 and 12 months).

Methods: We retrospectively enrolled UC patients showing MH, expressed as Mayo 0 at colonoscopy, and undergone multiple biopsies during the same exam. We reviewed the corresponding histological lesions evaluating the presence of the typical histological lesions associated with UC, such as acute or chronic inflammatory infiltrate, basal plasmacytosis, basal lymphoid aggregates, stromal changes, lamina propria eosinophils, crypt branching, crypt distortion, crypt atrophy/depletion, cryptitis, crypt abscesses, surface irregularity, mucin depletion, erosions and Paneth cell metaplasia. We evaluated the number of clinical reactivation 6 and 12 months after baseline colonoscopy.

Results: Among 50 enrolled patients, only 3 showed no histological lesions. The most common lesion was chronic inflammatory infiltrate (82%) followed by basal lymphoid aggregates (58%), acute inflammatory infiltrate (42%) and crypt distortion (28%). After 6 and 12 months, 19% and 30% of patients relapsed, respectively. The most prevalent lesion in patients relapsing after 6 months was chronic inflammatory infiltrate (100% of relapsers vs 70% of non-relapser), followed by acute inflammatory infiltrate (71% vs 37%,), basal lymphoid aggregates (57% vs 50%,), basal plasmacytosis (43% vs 17%,) and lamina propria eosinophils (43% vs 17%,). After 12 months, chronic inflammatory infiltrate was found in 82% of relapsers vs 81% of non-relapsers , basal lymphoid aggregates in 73% vs 46% and acute inflammatory infiltrate in 45% vs 42% , respectively.

Conclusions: A microscopic disease activity persists in the major part of patients with MH. Some lesions are associated with disease reactivation. Further studies are required to assess if these microscopic features can predict mid- and long-term reactivation.

P525
Evolution of IBD-related costs over two years of follow up: increase of anti-TNF α therapy related costs with a decline of hospitalization costs

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Background: With the introduction and increasing use of anti-TNF ɣ therapy in IBD a shift of costs has been observed with medication costs replacing hospitalization and surgery as the greatest source of healthcare expenditure. We explored the impact of the use of anti-TNF ɣ therapy on IBD-related costs from a societal perspective over two years of follow-up.

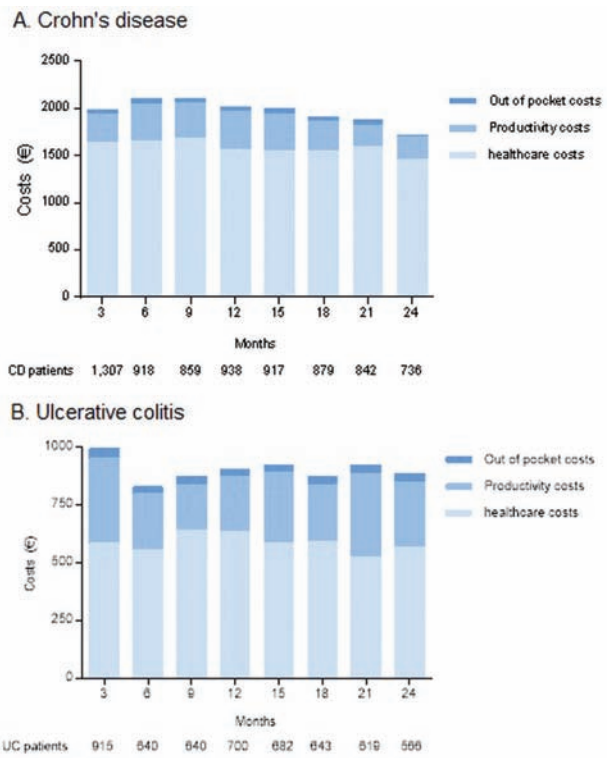
Methods: A total of 1,307 Crohn's disease (CD) patients and 915 ulcerative colitis (UC) patients was prospectively followed for two years by three-monthly web-based questionnaires (the COIN study). Changes of healthcare costs, productivity costs and out-of-pocket costs over time were assessed using mixed model analysis. Multivariable logistic regression analysis was used to examine the impact of baseline demographics and clinical characteristics on increase of costs over time.

Results: A total of 737 CD patients (40% males, mean age 48 years (SD 13 years)) and 566 UC patients (53% males, mean age 50 yaers (SD 13 years)) were followed for two years. Total costs were stable over two years of follow-up, with annual total costs of € 8,317 in CD and € 4,114 in UC.

Although healthcare costs did not change over time, the proportion of anti-TNFa therapy-related costs increased over two years from 64% to 72% in CD (p<0.01) and from 31% to 39% in UC (p < 0.01). In contrast, the proportion of hospitalization costs decreased from 19% to 13% in CD (p<0.01), and 22% to 15% in UC (p < 0.01).

Penetrating disease course was associated with increase of healthcare costs (adjusted odds ratio (adj. OR) 1.95 (95% CI 1.02–3.37) in CD. In UC only age < 40 years was associated with an increase of healthcare costs (adj. OR 4.72 (95% CI 1.61–13.86).

Conclusions: Total IBD-related costs do not change over time. However, the proportion of anti-TNF α related healthcare costs increased over two years of follow-up, at the expense of hospitalization costs. Factors associated with increased healthcare costs were penetrating disease course in CD and age < 40 in UC.



"Figure 1. Healthcare costs, productivity costs and out of pocket costs over two years of follow up"

P526
Impact of postinduction infliximab trough level and disease activity on primary response in Crohn's Disease

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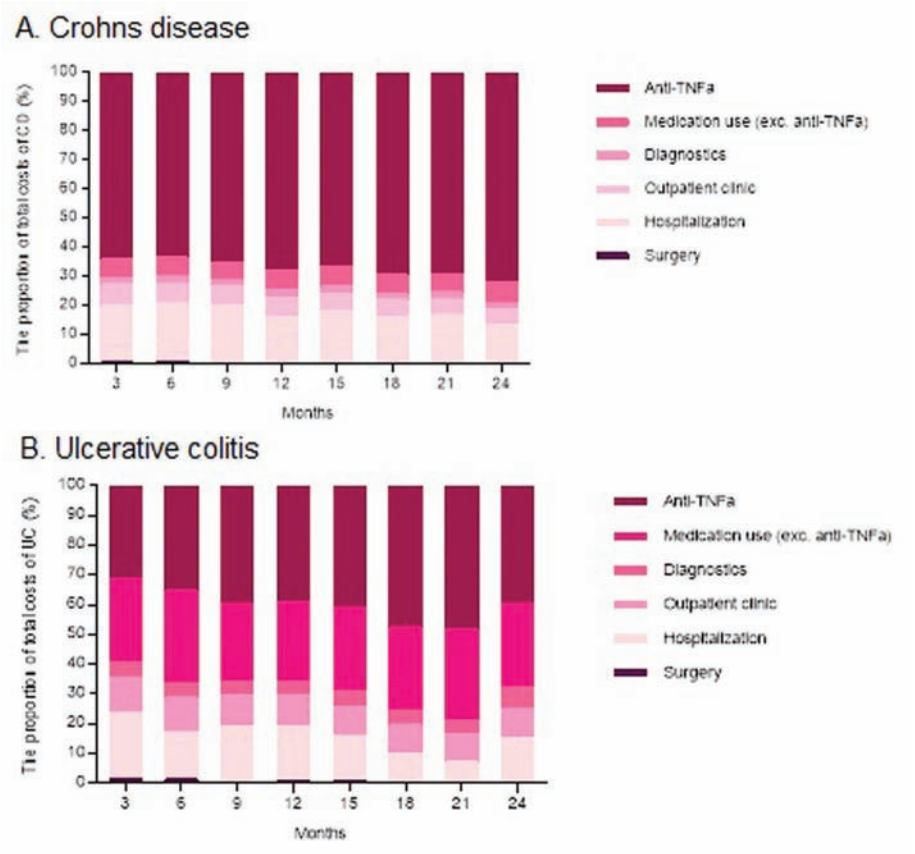

"Figure 2. The proportion of healthcare costs over two years of follow up"

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Background: Primary non-response to infliximab (IFX) induction therapy occurs in 10-20% of cases in clinical series. Few data have been reported on the clinical impact of low serum IFX trough levels after the induction treatment and their relation with clinical response, disease activity or the development of immunogenicity.

Methods: There are two primary aims of this study: 1. To assess the clinical relevance of a low serum IFX level during induction therapy. 2. To identify possible risk factors associated with reduced serum levels of IFX.

We included 36 Crohn´s disease patients with moderate to severe disease under infliximab induction treatment. Patients were treated

with IFX 5mg/kg at 0,2 and 6 weeks as induction dose, followed by 5mg/kg every 8w. Blood samples were drawn at standardized time points before and after induction therapy (at 0,6,14 and 30w) just before IFX

treatment. Serum IFX trough levels and anti-Infliximab antibodies (ATI) were measured using an enzyme-linked immunosorbent

assay (ELISA). Disease activity was assessed at the same time points by means of the Harvey-Bradshaw Index (HBI; remission< 3, mild-moderate disease 4-14, and severe disease >15) and CRP/calprotectin levels.

Results: After IFX induction therapy, the median serum IFX trough level was significantly higher in patients in clinical remission (IFX: 7,62ug/ml) than in patients with active disease (IFX 0,032 ug/ml P< 0,01).

Receiver operating characteristic curve analysis indicated a cut-off value of 3ug/ml at week 6. The positive predictive value of high

postinduction IFX trough level (IFX >3 ug/ml at 6w) for predicting good response and sustained remission after IFX induction was >90%

ATI levels were detected in 26% of IFX treated patients and were significantly related to low trough levels and infusional IFX

reactions. Low postinduction IFX trough levels were related to primary failure in 80% of patients. The cumulative number of patients

with low IFX trough levels were significantly higher in patients with severe disease activity and ATI detection

Conclusions: 1. Low post-induction IFX trough levesl are associated with primary failure.

2. Optimal predictors of postinduction clinical remission to IFX were week 6 trough level>3ug/ml and a low disease activity before treatment.

P527
Characterization of variables determining satisfaction with life in Crohn's Disease patients

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Background: Satisfaction with Life is a vital personality resource impacting the individual's ability to cope with life stressors including chronic disease. Yet, among Crohn's Disease (CD) patients the protective health-promoting effects of this factor is incompletely understood. Our aim was to assess the associations between Satisfaction with Life in CD patients and clinical and demographic factors, psychological symptoms and family support.

Methods: Consecutive patients consenting to participate in an ongoing socio-economic study of CD in the Israeli adult patient population completed the following self-administered socio-psychological questionnaires: Satisfaction with Life Scale (SWLS), Brief Symptom Inventory (BSI, measures psychological stress), Carver's Brief COPE Inventory (COPE, measures coping skills) and MacMaster Family Assessment Device (FAD). Demographics, clinical data, Harvey-Bradshaw Index (HBI) of disease activity and Irvine's SIBDQ were obtained simultaneously.

Results: The cohort comprised 148 men (40.4%) and 219 women (59.6%), mean age ± SD: 35.7 ± 13.4 and 40.3 ± 15.1 years respectively ($p < 0.01$). There were no significant differences of disease duration (men 10.5 ± 8.8 and women 12.5 ± 9.4 years), Harvey-Bradshaw Index (6.5 ± 5.4 and 6.5 ± 5.6), SIBDQ (48.2 ± 14.8 and 46.6 ± 13.5) and years of education (14.2 ± 3.0 and 14.5 ± 2.7). SWLS mean scores were moderate and similar in men (21.0 ± 7.9) and women (22.8 ± 7.4). FAD mean scores (6 domains) were similar in men (1.80 ± 0.53) and women (1.78 ± 0.58). BSI in all 9 domains indicated low anxiety levels, with mean score in men 0.99 ± 0.94, and women 0.95 ± 0.87. COPE demonstrated that women used significantly more active coping, self-distraction, emotional support, instrumental support and venting than men (all at least $p < 0.03$), while substance use was greater in men than women ($p < 0.01$). In a best fit model with R squared = 0.514, the following factors (beta) were found to be significant predictors of Satisfaction with Life: economic status (0.229), COPE positive reframing (0.136), COPE substance use (-0.101), BSI depression (-0.453) and FAD (-0.192). Age at disease onset and HBI were not significant predictors.

Conclusions: Satisfaction with Life in CD patients is determined by the interplay of economic status and a variety of psychological parameters, but not disease severity. These findings show an important role for psychological treatment and family support in the overall management of CD patients.

P528
Efficacy of vedolizumab with concomitant corticosteroid or immunomodulator use in patients with Crohn's disease in GEMINI 2

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Background: Crohn's disease (CD) is often treated with corticosteroids (CS) or immunomodulators (IMM). The efficacy and safety of vedolizumab (VDZ), an anti-α4β7 integrin monoclonal antibody for the treatment of CD, were investigated in the GEMINI 2 trial (NCT00783692).[1] Here, the efficacy of VDZ therapy in subgroups of patients (pts) in GEMINI 2 who were on stable doses of CS or IMM or both at baseline (and experiencing a symptom flare-up) are investigated with post hoc analyses. The safety of concomitant CS or IMM use has been presented previously.[2]

Methods: In the 6-week (wk) induction phase of GEMINI 2, pts were treated with double-blind (DB) placebo (PBO) or VDZ (induction intent-to-treat [ITT] population) or open-label (OL) VDZ. VDZ responders were re-randomised to DB PBO or VDZ every 8 or 4 wks (Q8W or Q4W) in the 46-wk maintenance phase (maintenance ITT population). CS use was tapered on or after wk 6 in VDZ responders. In the United States, IMM use was discontinued at study entry for OL VDZ-treated pts and at wk 6 for pts on DB VDZ. Clinical efficacy outcomes for VDZ were evaluated by concomitant medication use at study entry.

Results: At baseline (wk 0), 30%, 17%, and 17% of pts were taking CS, IMM, or CS and IMM, respectively. A trend favouring VDZ was observed for most outcomes. With CS or CS and IMM use at baseline, numerically higher percentages of VDZ-treated pts achieved clinical remission (Figure) and enhanced clinical response at wks 6 and 52 and CS-free remission at wk 52 compared with PBO. However, efficacy endpoints for VDZ-treated pts with concomitant IMM use only did not differ numerically from those on PBO.

Conclusions: The clinical efficacy of VDZ induction or maintenance therapy in GEMINI 2 was similar with or without the use of CS or both CS and IMM at baseline. The interpretation of these data is limited by the small sample size and discontinuation of CS and IMM during maintenance treatment. Because the study was not designed to specifically address outcomes with concomitant medication, conclusions are preliminary. The apparent synergy between VDZ and either CS or IMM needs to be further explored in prospective studies.

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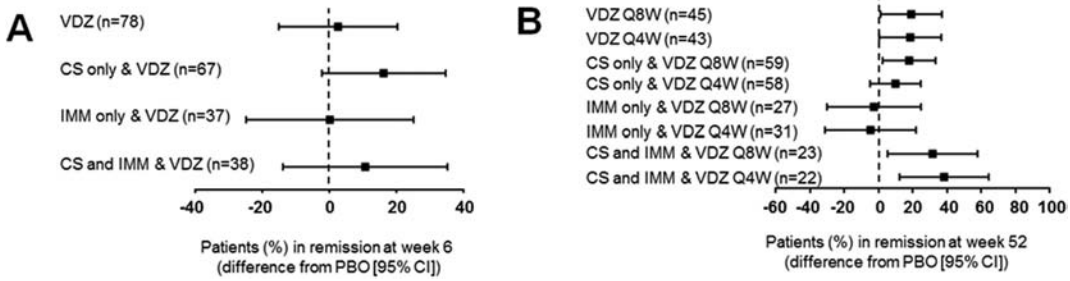

P529
Maintenance of clinical remission in Crohn's disease patients after discontinuation of antiTNF agents: Results from a single centre cohort

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Background: To maintain therapy with antiTNF in patients in clinical remission is a debated issue. Aim of our study was to assess maintenance of remission in a cohort of Crohn's disease(CD)patients who discontinued antiTNF because of clinical benefit and to identify predictive factors of relapse. A secondary objective included the assessment of retreatment with antiTNF for relapsers

Methods: Consecutive CD patients followed in a referral centre for IBD who received infliximab(IFX)or adalimumab(ADA),for at least 12 months and discontinued the drug because in clinical remission were included. All patients had ileocolonoscopy performed before and after treatment. Variables evaluated are listed in table 1.

Results: Among 516 patients treated with antiTNF from 1999 to 2011 in our Centre, 58 patients were included. 47 received IFX and 11 ADA. Median duration of treatment was 19 months (range 13.6-26.2).Median number of IFX infusions was 11(range 9-15),median number of ADA administrations was 47(range 37-73). 66% of patients were on combo therapy with immunosuppressants(ISS). Mucosal healing was achieved in 39 patients(67%).After antiTNF discontinuation 84% of patients were maintained with ISS. Kaplan-Meier curves showed a cumulative probability of a disease free course at 1 year of 69%. 2 years after antiTNF discontinuation 48% of patients relapsed;probability of relapse was 65% after 5 years. No variables were associated with the probability of maintaining clinical remission in univariate analysis. Thirty out of 58 patients were retreated with antiTNF: 63% achieved remission, 26% experienced loss of response. Acute infusion reactions were reported by 3 patients(10%)

Conclusions: In our cohort of CD patients treated with antiTNF at least for 1 year, who discontinued the treatment because in clinical remission, the probability to maintain clinical benefit at 2 years was 52%. The rate of relapse was higher in the first 2 years from withdrawal. Mucosa healing did not predict sustained clinical remission. Retreatment with antiTNF for relapsers was well tolerated and effective in the majority of patients. So,discontinuation of antiTNF therapy does not seem to be a successful strategy in half of patients. Multicentric prospective studies on predictive factors of risk are needed to identify persons with a higher probability of relapse

Demographic and clinical variables	Treatment related variables
Gender	Duration of treatment
Age	Change in dose or time of administration
Duration of disease	Concomitant treatment
Disease Location	Treatment at discontinuation of antiTNF
Perianal disease	Endoscopy result
Previous surgery	

P530
Is microscopic colitis a rare disease in Southern Europe? A prevalence population-based study in Terrassa (Spain)

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Background: Few studies have assessed the prevalence of microscopic colitis (MC). Two studies conducted in the USA and Sweden have reported prevalence rates of 219 and 123x105 inhabitants, respectively. In Spain there is only one study showing a prevalence of 48x105 inhabitants. In Europe a rare disease is that affecting less than 1 in 2000 people, so the figures described in Spain fall into this definition. The natural history and the need for long-term maintenance treatment in MC are not well known.Objective: 1. To evaluate the prevalence of MC in the catchment area of Terrassa (Barcelona, Spain); 2. To assess the need for long-term maintenance specific treatment.

Methods: Methods: Cases were obtained from the pathology department registry of the HUMT. The belonging to the catchment area, the current residence in the area and to be alive at 31-August-2014 were confirmed for each case. The prevalence rate by age and sex using as a reference the general population in the catchment area was calculated. Current active drugs for MC in every patient (excluding those diagnosed in the last year) were also recorded.

Results: Between January 1993 and August 2014, 410 MC patients were diagnosed. Of these, 201 patients (96 CC and LC 105) were alive and living in the area (75% women; 68 ± 1 years). The prevalence of MC was 94.3x105 inhabitants (95% CI, 80.3-110), being 45.6 and 48.6 for CC and LC. In the group aged 15-44 years, there were 8 MC, with a prevalence of 11x105 (women, 19.9; men, 2.7; $p<0.05$). In the group aged 45-64 years there were 56 MC, with a prevalence of 130.7x105 (women, 186.5; men, 74.8; $p=0.001$). In the group aged 65 years or older there were 96 MC, with a prevalence of 372.6x105 (women, 487; men, 223.5; $p<0.001$). 24% of the patients were receiving maintenance treatment for MC: 13.2% budesonide, 6.6% mesalazine, 1% cholestyramine, 0.5% methotrexate, 1.6% anti-TNF, and 1% other drugs after a mean follow-up of 7.8 ± 0.38 years from diagnosis.

Conclusions: Conclusions: The prevalence rate of MC in our geographical area is greater than 50x105 inhabitants, not fulfilling the

definition of rare disease. However, both CC and LC separately accomplish this criterion. There is a clear increase in prevalence rate according to older age and female gender. Only one quarter of patients require long-term maintenance treatment and only a minority of them require biological drugs / immunosuppressants for severe diarrhoea unresponsive to budesonide.

P531
Intravenous corticosteroid dosing in paediatric acute severe Ulcerative Colitis (ASC): A multicenter propensity score study

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Background: Data to support dosing of intravenous corticosteroids (IVCS) in pediatric acute severe ulcerative colitis (ASC) are lacking and extrapolated from adult literature. We aimed to explore the optimal dosing of IVCS in pediatric ASC using a robust statistical method on the largest pediatric cohort of ASC to date.

Methods: 283 children treated with IVCS for UC were included from the retrospective and prospective OSCI studies and newly reviewed patients from Jerusalem and Liverpool. Patients were followed for 1 year (46% males, age 12.1 ± 3.9 years, disease duration 2 (IQR 0-14) months, baseline PUCAI 69 ± 13 points). Confounding by indication was addressed by matching high and low IVCS dose patients according to the propensity score (PS) method, using 3 cutoff doses (1mg/kg methylprednisolone to 40mg/day, 1.25mg/kg to 50mg/day and 2mg/kg to 80mg/day).

Results: The median IVCS dose in the entire cohort was 1.0 mg/kg (IQR 0.8-1.4) and 44 mg/day (32-60). 218 children were matched in the 1.25mg/kg cutoff, 94 children were matched in the 1mg/kg cutoff and 86 children were matched in the 2mg/kg cutoff. No differences were found in 25 pre-treatment baseline variables in the three cutoffs, implying successful matching. There were no statistical differences in all outcomes of the two lower cutoffs (including need for salvage therapy during admission and by 1 years, admission duration, day-5 PUCAI< 35 points and day 5 CRP, ESR and albumin; all P >0.05). In the high cutoff, the higher doses were somewhat better but this benefit reversed after excluding one center in a sensitivity analysis that used routinely very high doses and reported better outcomes. In a PS-weighted regression model on the entire cohort, high doses were not associated with better outcome (all P>0.1).

Conclusions: Our data support current guidelines of dosing IVCS in the range of 1-1.5mg/kg/day to a maximum of 40-60mg/day.

P532
Quality of Care in Family Planning and Pregnancy - an Online Survey among 475 Female Patients with Inflammatory Bowel Disease

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Background: Inflammatory Bowel Disease (IBD) often affects young patients. Especially for young patients, family planning and pregnancy are highly relevant matters. Accordingly, when discussing pregnancy and family planning, questions regarding specific risks for mother, pregnancy and children are very important. It was the subject of this survey, to evaluate the satisfaction of IBD patients with the doctors' advice on this topic.

Methods: A questionnaire on the patients' satisfaction with the quality of care specifically regarding family planning and pregnancy was made available through the an online survey system. 475 female patients from Germany, Austria and Switzerland were recruited using communication channels of patient self help organisations (DCCV, ÖMCCV, SMCCV). The results are expressed as mean ± SD (Likert scale from 1-10 with "10" corresponding to "very satisfied"/"agree very much" and "1" to "very dissatisfied/disagree very much").

Results: 197 patients (46%) reported, that IBD had a significant impact on their family planning (Likert scale>7). In general, the patients were satisfied with their physicians' counselling (7.4 ± 2.2). Also, in terms of counselling regarding drug therapy in general, the patients were mostly satisfied (6.6 ± 2.5, p <0.001 vs. treatment in general). In contrast, the patients were significantly less satisfied with the counselling regarding the desire for children and pregnancy (5.2 ± 3.1, p<0.0001) and regarding medication during pregnancy (5.5 ± 3.1, p<0.0001). Patients without children were even more dissatisfied with the counselling regarding family planning (4.8 ± 2.9, p=0.001 vs. patients with children). The package information leaflets were often considered unsettling (6.2 ± 2.9).

Conclusions: The results underline the importance of careful information on chances and risks regarding pregnancy, the health of the children and the disease activity. The relatively high satisfaction with medical care in general shows that the patients do not experience a general communication deficit in their physician-patient relationship. Still, the results underline the need to address specific problems regarding family planning and pregnancy. An intensified focus on these specific problems might improve the quality of care in patients with IBD. Although a causal assessment of the deficits in the quality of care is difficult using the presented data, possible approaches to address these specific needs might include clarifications in package information leaflets and an improved training of physicians with regard to these aspects of IBD.

P533
Assessment of disease-related therapeutic protein drug-drug interaction (TP-DDI) for etrolizumab in patients with moderately to severely active ulcerative colitis (UC)

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Background: UC is an inflammatory bowel disease (IBD) representing a chronic inflammatory condition of the colon associated with a dysregulated mucosal immune system. Etrolizumab is a humanized IgG1 monoclonal antibody (mAb) that specifically binds the beta(β)7 subunit of alpha(α)4β7 and αEβ7 integrins. The efficacy and safety of etrolizumab has been evaluated in patients with moderate to severely active UC in a Phase 2 trial (EUCALYPTUS). The objective of this analysis was to evaluate the TP-DDI risk for etrolizumab, a mAb not directly targeting cytokines, in patients with moderately to severely active UC.

Methods: This TP-DDI assessment focused on the effect on cytochrome P450 3A (CYP3A), since among the few commonly used medications in IBD that involve CYP metabolic pathways, most are CYP3A substrates. First, the IBD disease effect on CYP-mediated drug metabolism was evaluated by comparing literature pharmacokinetic (PK) data of CYP3A substrate drugs from patients with IBD (UC or Crohn's disease) with that of healthy participants. Second, the etrolizumab effect on CYP3A4 messenger RNA (mRNA) expression level (via quantitative polymerase chain reaction) was evaluated in the colonic biopsy samples collected before and after etrolizumab or placebo treatment in patients with UC from EUCALYPTUS.

Results: Review of the literature data showed similar drug exposure and PK parameters between patients with IBD and healthy participants for prednisolone, budesonide, and cyclosporine. These drugs are substrates of CYP3A and conventionally used as treatment options for patients with IBD. These literature data suggest a low risk of an IBD-related disease-drug interaction for CYP3A substrates. Treatment with etrolizumab did not result in a consistent change in colonic CYP3A4 mRNA expression compared with patients receiving placebo. Additionally, etrolizumab did not show significant treatment effect on C-reactive protein at the targeted therapeutic dose level in patients with UC from the EUCALYPTUS study.

Conclusions: The results from these assessments indicate a low TP-DDI risk for etrolizumab in patients with UC, and in particular, a low impact on the colonic CYP3A4 enzyme.

P534
Efficacy of probiotic treatment with Bifidobacterium longum 536 for induction of remission in active ulcerative colitis: a randomized, double-blinded, placebo-controlled multicenter trial

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Background: Probiotic treatment in patients with ulcerative colitis (UC) has been focused on improving the intestinal microbial balance and cytokine profile. We have previously reported that upregulation of T-bet and tight junction molecules by Bifidobacterium longum 536 (BB536) improves colonic inflammation in patients with UC. Therefore, to investigate the efficacy of BB536 supplementation for induction of remission in patients with active UC, we conducted a randomized, double-blinded, placebo-controlled multicenter trial.

Methods: A total of 56 consecutive patients with mild-to-moderate UC (27 male, 29 female; mean age 44 ± 14) were enrolled in the study. Eight patients of these (14%) were affected with pancolitis and 31 (56%) had left-sided colitis; 17 (30%) had proctitis. Patients were randomly treated with 2-3 × 1011 freeze-dried viable BB536 (28 patients) or placebo (28 patients) for 8 weeks.

Results: Twenty-four patients in the BB536 group and 23 patients in the placebo group completed the study (86% and 82%, respectively). In 7 of the remaining 9 patients, other treatments were needed because of exacerbation. One patient from the BB536 group withdrew from the study because of a mild side effect, and 1 patient from the placebo group withdrew from the study on entry. In total, 63% of patients receiving BB536 showed clinical remission (UC disease activity index (UCDAI), ≤ 2) at week 8 compared to 52% of those receiving placebo (p = 0.395). There was a significant decrease in UCDAI scores from 3.5 ± 1.9 at baseline to 2.5 ± 1.7 at week 8 in the BB536 group (p = 0.034), whereas there was no significant decrease in these scores in the placebo group. Regarding endoscopic improvement, there were significant decrease in the EI score at week 8 in the BB536 group and placebo group (Wilcoxon t-test). None of the patients in the BB536 group experienced a worsening of EI score during the follow-up, whereas two patients in the placebo group showed a worsening. One patient (1.8%) in the BB536 group reported a mild side effect (dry cough), but no other serious adverse reactions were observed.

Conclusions: Supplementation with BB536 was well-tolerated and reduced UCDAI and EI scores after 8 weeks in Japanese patients with mild-to-moderately active UC.

P535
Transition in adolescents with IBD: study of a measuring instrument for transfer readiness

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Background: Transition of adolescent IBD patients to adult health care is often troublesome. Transitional programs are designed to provide a successful transfer. Self-efficacy is important in the process of transition and reflects the level of independence that an adolescent thinks and says he has in dealing with his disease. In 2008, we developed an IBD-specific questionnaire measuring IBD-knowledge and self-efficacy, called "IBD-yourself". The presented follow-up study aims to evaluate the success of transition in IBD patients and to assess the predictive value of "IBD-yourself" for successful transition and transfer to adult care.

Methods: This follow-up study was performed in the study population from 2008. In 2008, 50 adolescent IBD patients attending our IBD transition clinic were recruited to complete the "IBD-yourself". In 2013, when all patients had been transferred to an adult gastroenterologist, these patients were asked to participate in this study. First, an index scoring system was developed reflecting the outcome of transition based on a) adherence to visits to the outpatient clinic b) adherence to therapy and c) qualitative evaluation of transition by the patient. Total scores reflected successful -, moderately successful- or failed transition. Secondly, the relationship between "IBD-yourself" and success of transition was studied by comparing the domains of the "IBD-yourself" to the outcome of transition. Additionally, confounding factors (demographic and disease factors) were studied in relation to success of transition.

Results: Informed consent was obtained in 36 out of 50 patients. Transition was successful in 24 (66.7%), moderately successful in 11 (30.6%) and failed in 1 patient. Comparing success of transition to the "IBD-yourself" showed that adolescents with successful transition had significantly higher scores only on the domains "actual behavior medication use" and "actual behavior outpatient clinic". Ethnicity, age at diagnosis and transfer, IBD type, transfer to a regional hospital or the Erasmus MC or presence of a transfer letter were of no importance for success of transition. Clinical remission at time of transfer was associated with successful transition. Boys had higher rates of successful transition, while higher educational level and divorced parents appeared to have a negative impact on success of transition.

Conclusions: In this study we have developed a scoring system reflecting the outcome of transition. The "IBD-yourself" questionnaire did not seem predictive of successful transition. We showed that 67% of the adolescents had a successful transition after attending our IBD transition clinic.

P536
Long term efficacy and safety for Sequential Rescue Treatments in patents with steroid refractory Ulcerative Colitis - Two years follow up data

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Background: Although medical management of moderate to severe steroid refractory ulcerative colitis (UC) still remains a challenge, medical interventions with sequential rescue therapies in recent years showed encouraging results. Even though sequential use of rescue treatments is potentially risky, many patients like to have additional rescue therapies to avoid colectomy.

AIM: To evaluate remission, response and adverse event rates in the cohort treated with one or sequential rescue therapy over two-year period.

Methods: The outcome after two years follow up of the cohort of 108 patients with steroid-refractory moderate to severe ulcerative colitis treated with a single or sequential rescue treatments with Infliximab (5mg/kg intravenously at week 0, 2, 6 and then every 8 weeks), Cyclosporine (iv CsA 2mg/kg/daily and then oral CsA 5mg/kg/daily) or Tacrolimus (0.05mg/kg divided in 2 doses, aiming for serum trough levels of 7-12 ng/mL) was retrospectively evaluated. The primary endpoint was 2 year response and remission rate; the secondary endpoint was the late adverse event (AE) rate in 2nd year of follow up.

Results: Out of 108 patients in the primary cohort, 98 patients (90%) were followed for at least 2 years; 69/76 patients treated with single, 23/26 patients with double and all 6 patients on triple rescue treatment. 10 patients were lost to follow up. 2 years after the induction with single or sequential rescue therapies 73% (72/98) still have response. Corticosteroid free remission rate in the whole cohort slightly decreased from 39 % (42/108) after first year to 29% (28/98) [p=0.118 OR 1.59 CI 0.89 - 2.86]. In the selected group of patients treated with sequential treatments (double or triple) steroid free remission rate insignificantly decreased from 22% (7/32) to 17% (5/29) (p= 0.649 OR 1.35 CI 0.38-4.83). The AE rate in the 2nd year of follow up was 14% (14/98). No significant difference of the AE rates between the patients treated with single -10% (7/69) or sequential rescue treatments -24% (7/29) (p=0.071 OR 2.81 CI 0.88 - 8.95) was identified.

Conclusions: According to our results, sequential rescue therapies regime showed prolonged response with mild frequency of the late AEs in the group of patients with steroid refractory UC, 2 years after the induction rescue therapies. Still, further follow up and adverse effects analysis will be necessary for the estimation of the real impact of sequential rescue therapies in UC.

P537
The effect of anti TNF induction therapy on body composition parameters in inflammatory bowel disease

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Background: Nutritional status and particularly sarcopenia may influence disease outcome in chronic disorders. Our aim was to assess the changes in body composition during the initiation phase of anti-TNF-alpha therapy in inflammatory bowel disease (IBD).

Methods: 40 IBD outpatients (33 Crohn's disease [CD], 7 ulcerative colitis [UC]) were included into our study. 24 patients received adalimumab (ADA: 160/80mg at weeks 0/2, then 40mg every other week) and 16 patients were treated with infliximab (IFX 5 mg/kg at week 0, 2, 6 and then in every 8 weeks). Bioelectrical impedance analysis (BIA) was performed and body composition was measured by the InBody 720 body analyzer right before starting biological therapy. The measurement was repeated 3 months later. Body composition indexes were derived from the computed values (fat-free mass index [FFMI], skeletal muscle index [SMI] and body fat mass index [BFMI]) of BIA.

Results: According to our findings baseline BMI and muscle parameters increased significantly during the observed period (BMI: 23.81 ± 7.19 kg/m2 vs. 24.52 ± 7.34kg/m2, p<0.001; FFMI: 17.64 ± 3.00 kg/m2 vs. 18.14 ± 3.08 kg/m2, p<0.001; SMI: 9.81 ± 1.83 kg/m2 vs. 10.05 ± 1.90 kg/m2; p=0.003; body cell mass: 34.04 ± 7.97 vs. 35.11 ± 8.24; p<0.001 at week 0 vs. week 12, resp). However no significant changes were detected in body fat parameters (BFMI: 6.21 ± 5.20 kg/m2 vs. 6.44 ± 5.27 kg/m2; Body Fat Percent: 23.24 ± 11.34 vs. 23.56 ± 11.71; Visceral Fat Area: 109.01 ± 68.57 vs. 107.11 ± 73.58; resp.). There was no significant difference between the effects of ADA vs. IFX treatment on body composition parameters (deltaFFMI: 0.55 ± 0.82 vs. 0.43 ± 0.69; deltaSMI:0.51 ± 07.78 vs. 0.11 ± 0.42; deltaBFMI: 0.23 ± 0.85 vs. 0.21 ± 1.01; resp.). Greater improvement was observed regarding muscle parameters in CD than UC patients (deltaFFMI: 0.61 ± 0.74 vs. -0.04 ± 0.69, p=0.038; deltaSMI: 0.34 ± 0.44 vs. -0.24 ± 0.33, p=0.002). There was no significant difference in the extent of changes in body composition parameters whether the patients were on corticosteroids (n=15) or not (n=25) at week 0 (deltaFFMI:0.44 ± 0.84 vs 0.59 ± 0.72; deltaSMI:0.17 ± 0.48 vs 0.31 ± 0.47; deltaBFMI:0.366 ± 1.12 vs. 0.09 ± 0.71 on and without steroid, resp.)

Conclusions: Comparing baseline and week 12 data we observed significant improvement in BMI and in body composition muscle parameters. Risk of sarcopenia defined by FFMI and SMI decreased during the anti-TNF induction therapy, while fat parameters have not changed significantly. Our findings suggest that induction anti-TNF therapy has beneficial effect on nutritional status and body composition regardless leaving the steroid therapy. We observed no difference between IFX and ADA treatment in the effect on body composition.

P538
Pooled safety analysis of long-term, once-daily multimatrix mesalazine use

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Background: Mesalazine, the recommended first-line treatment for mild-to-moderate ulcerative colitis (UC), has also been examined for prevention of recurrent diverticulitis (DV). In this study, safety data from 6 clinical trials evaluating long-term multimatrix mesalazine use (2.4-4.8 g/d for up to 24 mo) in patients (pts) with UC or a history of DV were analyzed.

Methods: Results from 2 trials examining mesalazine for prevention of recurrent DV (NCT00545740, NCT00545103) and 4 trials examining mesalazine for maintenance of UC remission (NCT00151944, NCT00151892, NCT00446849, NCT01124149) were pooled. Pts in the DV trials had prior acute DV that resolved without surgery and were administered 1.2, 2.4, or 4.8 g/d mesalazine for 24 mo. Pts in the UC trials had quiescent symptoms or complete or partial remission (defined using a combination of qualifying symptom and endoscopy scores), and were given 2.4 g/d mesalazine for 6 to 12 mo; in some trials, remission was initially achieved via 8 wks of acute treatment with 4.8 g/d mesalazine. Safety was analyzed in the following groups: pts in all trials, pts on high-dose (4.8 g/d) mesalazine from the DV trials, and only UC pts.

Results: Across all 6 trials, ≥1 dose of mesalazine was given to 2,859 pts (880 from DV trials, with 299 on 4.8 g/d; 1,979 from UC trials), and 1,542 (54%) reported treatment emergent adverse events (TEAEs). TEAEs leading to discontinuation were observed in 9% of pts. The most common TEAEs were abdominal pain (5%), headache (5%), diarrhoea (4%), UC (4%), nasopharyngitis (4%), and urinary tract infection (3%). Maximum severity of TEAEs was mild in 23% of pts, moderate in 24%, and severe in 7%. Serious TEAEs were reported by 5%; the most common was UC (1%). Treatment-related AEs included diarrhoea (2%), abdominal pain (1%), UC (1%), and headache (1%). For high-dose pts in the DV trials, 71% (211/299) experienced TEAEs; the most common were abdominal pain (11%), diarrhoea (10%), headache (9%), back pain (6%), and urinary tract infection (6%). In this subgroup, treatment-related AEs included diarrhoea (3%), headache (2%), nausea (2%), and abdominal pain (2%). For pts in the UC trials only, 45% (897/1,979) experienced TEAEs; the most common were UC (6%), headache (4%), ineffective drug (4%), and nasopharyngitis (3%). For UC pts, treatment-related AEs included UC (2%), headache (1%), diarrhoea (1%), and abdominal pain (1%).

Conclusions: At doses up to 4.8 g/d, multimatrix mesalazine was well-tolerated for up to 24 mo. Most TEAEs were mild or moderate in severity. Differences in treatment duration (24 mo vs 6-12 mo) and dosing (4.8 vs 2.4 g/d) may, in part, contribute to the higher incidence of TEAEs observed in the high-dose DV subgroup compared with UC pts.

P539
Outcome of acute severe ulcerative colitis in patients previously exposed to immunosoppressive therapy

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Background: Overall mortality of ulcerative Colitis (UC) is comparable to that of general population, but the acute severe flare of UC (ASUC) remains a life-threatening condition. Intravenous steroid course still represents the standard treatment, while cyclosporine (cys) and infliximab (IFX) can be used with similar efficacy in case of failure. Since few data are available for patients with previous immunosuppressive (IMS) therapy, we aimed in this study to evaluate the outcome of ASUC in our referral centre, with particular attention paid to patients previously exposed to IMS drugs.

Methods: We retrospectively collected data from 86 ASUC cases (32 females and 54 males, mean age 44.1 yrs, mean duration of disease 6,5 yrs), according to Truelove and Witt's criteria, consecutively admitted to our Gastroenterology Unit from January 2008 to September 2014. According to ECCO's Guidelines all ASUC patients were treated with a short course of iv. steroid and in case of failure they were treated with a rescue therapy with Cys or IFX if colectomy was not deemed necessary by the surgeon. All statistical analyses were done by the SPSS software. A P value less than 0.05 was considered statistically significant.

Results: 72 (83,7%) patients had an extensive colitis while only 8 (9,3%) were at first diagnosis. 39 patients were never treated with IMS (group A), while the remaining 47 had previous therapy, alone or in combination, with AZA (n=37), Cys (n=11) or IFX (n=27) (Group B). Patients of group B were significantly younger (40,9 yrs vs 47,9 yrs; p=0,05) and with a longer disease duration (8,5 yrs vs 4,8 yrs; p=0.02). 29 patients responded to steroids (33,7%), 15 underwent colectomy (17,4%) and 42 (48,8%) were switched to rescue therapy (14 Cys, 28 IFX), which failed in 4 patients requiring colectomy. The early (within 1 month) colectomy rate was 22,1, with a trend towards a lower response rate to steroids (25,5% vs 43,6%; p=0,10) and an higher need for colectomy (29,8% vs 12,8%; p=0,07), in group B compared to group A. During the follow-up period (19,5 months, range 1-72) further 10 patients underwent colectomy (5 for each group). The colectomy rate at the end of follow-up was 25.6% in Group A and 40.4% in group B (p=0.17) (33,7% in the entire cohort). The Kaplan Meyer probability to avoid surgery was 71,9% and 65,5% at 1 yrs and 71,9% and 55,4% at 2 yrs (p=0,30), for group A and B, respectively.

Conclusions: Patients with previous IMS therapy have a trend towards lower response to steroid treatment compared to IMS naïve patients, but the response rate to rescue therapy remains satisfactory, with similar need for colectomy.

P540
Efficacy and safety of infliximab's biosimilar (REMSIMA) for IBD

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Background: The biosimilar to infliximab, Remsima have been recently shown to be equivalent to infliximab in efficacy and safety in rheumatologic diseases. However, there are no data for patients with inflammatory bowel disease (IBD). We aimed to assess the efficacy and safety of Remsima in Korean patients with IBD.
Methods: This was a retrospective multicenter study including IBD patients who received at least one Remsima infusion. Both anti-TNF naïve patients and patients who switch from Remicade or Humira to Remsima were included. Short- term clinical outcomes and adverse events of Remsima were evaluated.
Results: A total of 55 Crohn's disease (CD) patients (23 anti-TNF naïve patients and 32 patients who switch to Remsima) and 51 ulcerative colitis (UC) patients (41 anti-TNF naïve patients and 10 patients who switch to Remsima) were included. In anti-TNF naïve CD patients, the rates of clinical response and remission were 91% and 78% at week 8. In anti-TNF naïve UC patients, the rates of clinical response, clinical remission, and mucosal healing were 87%, 31%, and 54% at week 8. Three patients (2.8%) discontinued Remsima because of an adverse event. The efficacy of Remsima was maintained in 86% of patients with CD and in 67% of patients with UC after switching from Remicade.
Conclusions: Remsima showed an excellent short-term clinical response and a good safety in both moderate to severe CD and UC. Further prospective studies with long-term follow up are needed to confirm the efficacy of Remsima.

P541
Long-term colectomy rates in patients with Ulcerative Colitis treated with Infliximab: A single Canadian tertiary care centre's experience

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Background: In the era prior to the introduction of biologic agents for the treatment of Ulcerative Colitis, rates of colectomy were estimated to be 20%(1). More recent evidence suggests that the risk of surgery at 1, 5, and 10 years after diagnosis was 4.9%, 11.6% and 15.6% respectively(2). Infliximab has shown to decrease early colectomy rates in Ulcerative Colitis(3), however its effects on long-term colectomy rates are unclear.
Infliximab for the treatment of Ulcerative Colitis was approved in Canada in 2005. Data up to 2010 have reported a colectomy rate of 9% in the post-Infliximab era(4). However the majority of this data was collected between 2008 and 2010 and data beyond this in Canada has been limited.
Our aim was to assess the long-term rates of colectomy at our institution in patients treated with Infliximab for Ulcerative Colitis.
Methods: Medical records of patients with a diagnosis of Ulcerative Colitis on Infliximab were retrospectively reviewed. Inclusion criteria consisted of Infliximab initiation between January 2005 and January 2012. Charts were reviewed to January 2014 for study outcomes. 18 of 22 gastroenterologists practicing at McMaster University provided consent to review patients charts. 76 patient charts were eligible for review, although 10 patients were excluded.
Baseline demographic information was collected in addition to pre and post-Infliximab data. Our primary outcome was a colectomy. Although primarily descriptive data was obtained, eligible information was statistically analyzed using a t-test.
Results: Of the 66 eligible patients, 31 were female and 35 male. The mean age at diagnosis was 27.2 (95 % CI 23.73-30.60). The mean number of months from diagnosis to the initiation of Infliximab and the mean duration of Infliximab treatment was 66.6 (95% CI 47.14-85.99) and 46.2 (95% CI 39.85 to 52.58) respectively. A total of 9 patients required a colectomy, however only 7 (colectomy rate 10.6%) were for refractory ulcerative colitis. The mean number of months from the initiation of Infliximab to colectomy was 10.7 (95% CI 4.14 to 17.29). The mean duration of disease prior to starting Infliximab between the colectomy and non-colectomy groups were 9.4 and 72.2 months respectively (p=0.046). The mean number of hospitalizations prior to and on Infliximab were 1.1 and 0.4 respectively (p<0.001).
Conclusions: Our findings suggest comparable long-term rates of colectomy to the current literature. An aggressive phenotype may explain the failure of Infliximab and the need for a colectomy earlier in the course of disease. Unfortunately the small number of patients in our study limit our ability to make any strong inferences although our data is reassuring on the long-term effectiveness of Infliximab in Ulcerative Colitis.

P542
Care of women with gastrointestinal conditions during family planning and pregnancy

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Background: Gastrointestinal (GI) diseases affect women of reproductive age and can impact pregnancy outcomes. There is a need to understand how patients (pts) are managed by their physicians. We investigated the treatment pathway and care of women with GI conditions who become pregnant.
Methods: Two online surveys were conducted - one in gastroenterologists (Gastros) and one in pts - in the US, UK, Germany and Mexico. Gastros were questioned on the last 3 pts with Crohn's Disease (CD) or Ulcerative Colitis (UC) who they have consulted whilst being pregnant or considering becoming pregnant. Pt survey included women with Inflammatory Bowel Disease (IBD) who had been pregnant in the past 2 years. Pts were questioned on their interactions with Gastros and obstetrics/gynaecology physicians (OBGYN).
Results: 20 Gastros and 56 IBD pts completed the physician and pt surveys respectively. Gastros were aware of the pt's intention to become pregnant in 55% of pts. When planning their pregnancy, 41% of pts consulted with their Gastros and 50% with their OBGYN. On learning they were pregnant, 36% of pts consulted with their Gastros and 71% with their OBGYN. For Gastros, the majority of initial visits occurred prior to pregnancy (65%). During pregnancy Gastros saw 28% of pts once a month or more, 58% every trimester and 13% only once during pregnancy. 83% of pts reported that Gastros were very influential on how they managed their pregnancy. For OBGYN, this figure was 88%. The majority of pts rated the reliability of information on managing disease from both Gastros and OBGYN as very reliable. Gastros initiated a treatment plan related to management of CD/UC and pregnancy for 57%

Table: Changes in treatment for women with CD or UC who were pregnant or considering becoming pregnant

	Proportions of pts on medications before and after Gastros made medication changes based on pregnancy considerations (pts, n=16)	
	Before change n (%) pts	**After change n (%) pts**
Steroids	7 (44)	1 (6)
Biologics	6 (38)	8 (50)
NSAIDs	5 (31)	2 (13)
DMARDs	4 (25)	2 (13)
Other treatment	2 (13)	4 (25)
No treatment	0 (0)	2 (13)
Response to question: Thinking about your last three patients who have consulted you whilst being pregnant or considering becoming pregnant, what treatment change did you make during pregnancy? Please indicate the product before and after the switch.		

of pts. 27% of Gastros made treatment changes in anticipation of or during pregnancy. 68% of pts reported they had a treatment plan in place prior to pregnancy. When considering changes in treatment during pregnancy, Gastros decreased steroid, DMARD and NSAID use but increased use of biologics (Table).

Conclusions: Gastros are highly involved in the treatment of pts who become pregnant or who plan to do so, and have considerable influence over the management of their condition. However, only half put a treatment plan in place related to management of CD/UC or pregnancy. Pts reported that they had a high level of interaction with both Gastros and OBGYN before and during pregnancy. This highlights the need to ensure that engagement between physicians and pts remains high and that pt concerns are alleviated throughout their pregnancy.

P543
Assessment of Lactose Intolerance in Ulcerative Colitis Patients on Remission

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Background: Lactose intolerance is a syndrome of symptoms caused by lactase deficiency, a condition that affects approximately 60% of the world's population. The symptoms of lactose intolerance are similar to those of inflammatory bowel disease, and hence patients with inflammatory bowel disease are known to be prone to make restriction of milk and dairy products in their diet. This study aims to determine the frequency of lactose intolerance and daily calcium intake from dairy products in ulcerative colitis patients on remission.

Methods: Eighty six ulcerative colitis patients who were on remission and had been followed up by our outpatient clinic were included in this study, and 92 healthy volunteers served as controls. Remission was assessed according to Clinical Activity Index. Patients and control subjects received 25 mg lactose following 8 hours of fasting and hydrogen breath test was performed with intermittent measurements. Intolerance was defined as >20 ppm increase in breath hydrogen concentration over baseline. Demographic characteristics of the patients and symptoms emerged during the test were recorded. A survey about patients' consumption rates of dairy products was filled and daily calcium intake was measured by a dietician.

Results: Mean age of the patients and the control subjects were 46.25 ± 12.44 and 44.79 ± 11.03 years, respectively. Fifty two of the patients (60.5%) and 49 of the healthy volunteers (53.3%) were male. There was no difference between the patients and the control subjects in terms of age and gender.

Lactose intolerance was significantly lower in patients compared to control subjects (p=0.01) with the intolerance being detected in 7 of the patients (8.1%) and 20 of the control subjects (21.7%). Twenty two of the patients (25.6%) and 20 of the healthy volunteers (21.7%) had gastrointestinal complaints related to hydrogen breath test but the difference was not statistically significant. None of the subjects in the patient and control groups developed systemic symptoms during the test.

Mean calcium intake from dairy products in patients (372.08 ± 279.73 mg/day) and control subjects (402.60 ± 249.47 mg/day) did not differ significantly.

Conclusions: To our knowledge, this is the first study in literature to report that patients with ulcerative colitis experience lactose intolerance less frequently than healthy volunteers, and the underlying pathophysiologic mechanisms of this observation need to be clarified. Besides, our data show that the daily calcium intake from dairy products in these patients lower slightly, though statistically insignificantly which may be in part due to the informing of the patients during regular follow-up.

P544
Factors associated with drug non-adherence in an Indian IBD patient cohort: It's not always the cost

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Background: Drug adherence plays an important role in the efficacy of medical management of IBD. Non-adherence to treatment is associated with an increased risk of relapse with consequent morbidity. The barriers to adherence in the developing world have not been evaluated but cost has been implicated. The aim of this study was to evaluate the prevalence of medication non-adherence and identify associated significant demographic, clinical and psychosocial factors in a cohort of IBD patients from India.

Methods: 463 consecutive IBD patients, (278 with UC and 185 with CD), mean age 38.6yrs were interviewed by a self-administered questionnaire in the IBD clinic of a large tertiary referral centre. Demographic, clinical, physician and psychosocial related data was recorded. Adherence (A) was assessed using the validated Morisky Medication Adherence Scales (MMAS); non-adherence (NA) was defined MMAS score >3. Statistical analysis was done using

Chi-square, T-test and Mann-Whitney U tests. Multivariate logistic regression was performed to identify independent variables that correlated with non-adherence. Measurement of risk associated with NA using odds ratios (OR) was calculated along with 95% CI.

Results: The overall rate of self reported non-adherence was 51% (53% UC and 49% CD). There was no statistically significant difference between A and NA groups in relation to age, gender, marital status, education, employment, disease duration and geographical location. Logistic regression analysis revealed age>50yrs (OR 0.45; 95%CI 0.22-0.93) was associated with NA. Patients in remission (OR 1.73; 95%CI 1.08-2.77) and who were married (OR 2.20; 95%CI 1.15-4.20) were likely to be A to treatment. Large number of concomitant medication use (OR 0.47; 95%CI 0.25-0.88) and non-availability (OR 0.43; 95%CI 0.23-0.80) increased risk of non-adherence. Patients who perceived that IBD medication was expensive (OR 2.03; 95%CI 1.36-3.03) and it protects disease from worsening (OR 1.79; 95%CI 1.10-2.89) were likely to be adherent. Physician re-enforcement of importance of drug adherence increased adherence (OR 2.50; 95%CI 1.20-5.18). Patients who felt that medication disrupts their life (OR 0.34; 95%CI 0.14-0.81) and causes mental disturbance (OR 0.47; 95%CI 0.25-0.87), were at risk of non-adherence. Medication adherence was associated with improved Quality of life score (mean QoL score was 5.0 in A and 4.7 in NA groups, p=0.001).

Conclusions: Non adherence is common in Indian IBD patients. Adherence was associated with disease remission and improved QoL. Cost of medication does not appear to be the major factor for non adherence. The identified predictive factors should be explored to improve adherence to therapy of IBD and improve patient outcomes.

P545
An Open-label Prospective Randomized Multicentre Study of Daily Granulocyte and Monocyte Adsorptive Apheresis as Compared with Intensive Treatment in Patients with Active Ulcerative Colitis

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Background: Among patients with ulcerative colitis (UC), those who respond to therapeutic granulocyte and monocyte adsorptive apheresis (GMA) with an Adacolumn have avoided pharmacologics and express favourable views on GMA for its good safety profile. This study was to better understand the optimum dosage of GMA in terms of treatment frequency, and the number of sessions for remission induction in UC patients.

Methods: This was an open-label randomized multicentre clinical trial using daily and intensive GMA with the Adacolumn in a small number of UC patients (prospective trial setting). Twelve patients whoyhad a clinical activity index (CAI) score of > 6 according to Lichtiger were included. Patients were randomly assigned to daily or intensive GMA in 1:1 ratio. Intensive GMA was performed at two sessions per week, while daily GMA was done at five sessions per week in the first and the second weeks. Treatment efficacy was assessed in the third week. Primary endpoint was clinical remission (CAI ≤4) at week 3. Secondary endpoint was clinical response (decrease in CAI by ≥ 5) at week 3 together with safety. Additionally, endoscopic findings before and after GMA therapy, faecal calprotectin (fCal), faecal lactoferin (fLac) and haematologic variables were evaluated.

Results: Clinical remission was achieved in 4 of 6 patients (66.7%) in each group, while clinical response was achieved by 4 of 6 patients (66.7%) in the intensive GMA and 5 of 6 patients (83.3%) in daily GMA. Further, Matt's endoscopic grade 4 fell to 3 in 1 patient in the intensive GMA and in 2 patients in the daily GMA. C-reactive protein (CRP), fCal, fLac, and white blood cell counts showed improvement post GMA, but did not reach statistical significance level. Mild transient fever and headache were seen in one patient in the daily GMA group.

Conclusions: In this prospective trial, the study end paint (week 3) was not long enough to see the full potential of GMA on mucosal healing, fCal, and fLac. Likewise, no significant difference in efficacy was found between daily and intensive GMA due to small number of patients. The most significant finding of this study could be the treatment safety because daily GMA over a two week period was well tolerated and was without any serious safety concern. Accordingly, we believe that our trial strategy warrants to be undertaken in large cohorts of patients with inflammatory bowel disease.

P546
Impact of mucosal healing on the clinical course in a cohort of paediatric patients affected by Crohn's Disease

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Background: Crohn's disease (CD) is a chronic relapsing inflammatory condition of the gut that primarily affects young individuals, often leading to significant impairment of quality of life. The major objective of medical therapies in CD is the modification of the clinical course of the disease. Mucosal healing (MH) has recently arisen as a therapeutic goal able to predict sustained clinical remission.

Our aim was to evaluate the clinical outcome, after 2 years of follow-up (FU), of a cohort of pediatric CD patients according to the achievement of MH during maintenance therapy with anti-TNFalpha antibodies.

Methods: Pediatric CD pts starting infliximab (IFX) or adalimumab (ADA) from January 2009 were enrolled. All pts were naïve to biological therapies. An endoscopy was performed before starting biologics and after 12 months to evaluate MH. Clinical and endoscopic disease activity were assessed by Pediatric Crohn's Disease Activity Index (PCDAI) and Simple Endoscopic Score (SES CD) at time 0 (T0) and at the time of the endoscopic FU. A further 1-year clinical FU was performed to evaluate differences in relapse rates, surgical rates and corticosteroid (CS) need according to the achievement of MH at endoscopic FU

Results: Thirty-seven patients were enrolled. At two years, 26 of 30 patients in maintenance treatment with anti-TNFalpha were in clinical remission, 4 were not; and the remaining 7 (22%) had stopped therapy for either surgery (4 pts) or loss of response (3 pts). All of the patients that had achieved a complete MH and 75% of those that had achieved a partial MH were in clinical remission at this further FU. Two pts that had obtained a complete MH and 4 of those that had obtained a partial MH needed a course of CS.

Kaplan Meier survival curves showed no statistical difference at two years from therapy introduction dividing patients according to treatment (ADA vs IFX) for risk of disease relapse

Conclusions: In pediatric Crohn's disease, biologics are effective in inducing clinical remission and in achieving MH. The achievement

of MH appears able to predict a better clinical outcome at least in the short term. Larger studies will highlight the effect of MH on the long-term disease evolution.

P547
Phlegmonous Crohn's disease: A review of outcomes at a tertiary centre

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Background: Penetrating Crohn's disease (CD) can be complicated by sealed-off perforation resulting in the development of an phlegmon (inflammatory mass). The optimal management strategy and long-term outcomes of phlegmons in CD remains unknown.

Methods: Patients with CD and confirmed phlegmons on MRI/CT between January 2009 and December 2013 were identified retrospectively. Radiographic evidence of co-existing strictures, abscess, fistula and/or perforation was recorded. Medical records were reviewed and demographic data, CD phenotype, CD therapy prior to and following presentation, requirement for abscess drainage or surgical resection, and clinical status at most recent follow-up were recorded. Clinical remission was defined as a Harvey -Bradshaw index of <5. Repeat imaging was evaluated to assess phlegmon resolution.

Results: 17 patients (8 male) were identified with median follow up of 40 months (range 33-61 months). 4 had ileal and 13 had ileocolonic CD. 13 had co-existing strictures, 6 had co-existing abscess, and 5 had co-existing enteroenteric fistula. 6 patients were receiving a thiopurine at presentation with phlegmon. 16 patients reported significant abdominal pain with 9 requiring admission. In 5 of these, imaging studies confirmed perforation. 2 patients required short-term parenteral nutrition and 6 were managed with exclusive liquid diet.

8 patients were treated primarily with medical management (2 with prolonged courses of antibiotics, 6 with thiopurine and corticosteroids, and subsequently 3 escalated to an anti-TNF agent) and this led to phlegmon resolution in 5 patients, and clinical remission in 3 patients. 3 patients have subsequently required surgery, and 1 persists with low grade obstructive symptoms treated conservatively.

9 patients were managed with primary surgery. All received a thiopurine as post-operative prophylaxis, of whom 4 escalated to an anti-TNF agent for significant post-operative recurrence. Repeat surgical resection or abscess drainage was not required subsequently.

3 of 5 patients presenting with perforation and phlegmon at presentation were treated surgically, 2 of 5 patients with enteroenteric fistula and phlegmon at presentation were treated surgically, and 4 of 6 patients with abscess and phlegmon at presentation were treated surgically. All 6 patients on thiopurine at presentation required surgery.

Conclusions: Phlegmonous disease remains challenging to treat. Medical and surgical management are both viable options, however phlegmon resolution was more likely in the surgically treated group. Medically treated patients remain at risk of need for future surgery. Surgically treated patients require aggressive medical treatment postoperatively, to limit recurrence of CD.

P548
Early intervention of infliximab prevent reoperation for the recurrence of Crohn's disease

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Background: We aimed to evaluate the prognostic factors, including early use of infliximab for first surgery and reoperation following first surgery in CD patients in Japan.

Methods: The clinical records of 115 patients who were diagnosed as having CD at Kawasaki Medical School Hospital between January 1987 and July 2012 were retrospectively investigated. The cumulative rate of bowel resection for CD-related intestinal manifestations following onset until first surgery and the cumulative rate of reoperation following first to second surgery were estimated using the Kaplan-Meier method and the related to each factor were statistically analized using the log-rank test. The background factors that influenced the cumulative rate of bowel resection following onset until first surgery and the cumulative rate of reoperation following first to second surgery were evaluated using univariate and multivaliate analyses.

Results: Of these 115 patients, 81 were men, the mean age of onset was 26.2 years, the mean disease duration was 9.69 years, patients who received intravenous infliximab (5 mg/kg) at an 8-week interval within 1 year following onset were 12, patient who received azathioprine within 1 year following onset was 1, ileocolitis-type CD were 68, and 48 patients underwent one or more surgeries. The 3-, 5-, and 10-year cumulative rate of bowel resection following onset were 10.5%, 25.9%, and 39.4%, respectively. On multivariate analysis, the cumulative rate of bowel resection following onset in CD patients was significantly associated with ileocolitis-type CD (hazard ratio [HR], 2.39; p = 0.004) and male sex (HR, 2.23; p = 0.05). Of 48 patients who underwent bowel resection ,19 patients underwent reoperation, the mean age of onset was 25.8 years, the mean disease duration was 8.32 years, patients who received intravenous infliximab (5 mg/kg) at an 8-week interval within 1 year following first surgery (infliximab group) were 22, patients who didn't receive intravenous infliximab within 1 year following first operation (non infliximab group) were 26, patients who received azathioprine within 1 year following first surgery were 10, and ileocolitis-type CD were 33. The 3-, 5-, and 10-year cumulative rate of reoperation following first to second surgery were 10.7%, 20.7%, and 40.9%, respectively. The 5-year cumulative rate of reoperation decreased significantly in infliximab group compared to in non infliximab group (10.6% vs. 28.6%, p = 0.026).

Conclusions: The sex and extent of the disease may be a prognostic factor of bowel resection due to CD-related intestinal manifestations. Early intervention of infliximab is likely to prevent reoperation for the recurrence of Crohn's disease.

P549
Short and long term therapeutic Efficacy of Oral Nutritional Therapy in pediatric Crohn's Disease ; A Single Center Experience

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Background: Exclusive enteral nutrition (EEN) is as effective as corticosteroids at inducing remission and have direct impact on improving nutritional complications. However data on maintaining disease remission and resumption of normal growth with partial enteral nutrition (PEN) are scare.

The present retrospective analysis aims to demonstrate the short- and long-term therapeutic efficacy of oral nutritional therapy (ONT) in children upon disease activity and growth parameters.

Methods: Patients newly diagnosed with moderate to severe CD in December 2004 to February 2013 who were managed with exclusive oral elemental nutrition therapy to induce remission at Asan Medical Center Children`s Hospital and followed up more than years with partial ONT were enrolled. Data were retrospectively collected from patients' medical records including basic demographics, clinical, laboratory findings.

Results: Twenty four of the 25 patients (96%) achieved clinical remission, with a median time to remission of 29 days. In children responding to ONT, mean Pediatric CD Activity Index (PCDAI) decreasing from 37.35 ± 14.01 to 5.44 ± 5.23 after 6 weeks and 3.24 ± 3.45 after 1 year. Five patients discontinued exclusive ONT within 6 weeks and 8 patients withdrawals partial ONT after 6 weeks due to unplatable enteral formula. Between presentation and 12 months after ONT, there was a significant increase in standardized z -scores for weight for height and Body Mass Index (BMI). The cumulative probability of relapse was 66 % at 1 year and 50 % at 2 years, respectively. If we excluded the patients (n=8) who had poor compliance to nutrition therapy, the cumulative probability of relapse was 82 % at 1 year and 70 % at 2 years, respectively.

Conclusions: EEN and PEN can be the effective treatment for inducing and maintain remission without relapse. A randomized controlled trial would be beneficial in helping to clarify these provisional findings further.

P550
Long - term efficacy of Tacrolimus in Inflammatory Bowel Disease: a retrospective pilot study

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Background: Crohn's disease and ulcerative colitis are lifelong conditions marked by multiple periods of inflammatory activity and remission. A significant number of patients suffer a steroid-refractory or dependent disease and require maintenance immunosuppression. The available options in this situation are thiopurines, methotrexate and biologics. However, intolerance and loss of response are not uncommon. Tacrolimus is a macrolide calcineurin inhibitor that is commonly used to prevent kidney and liver transplant rejection. It inhibits the production of interleukin-2 and T lymphocyte activation. There is sparse evidence about the efficacy of Tacrolimus in Inflammatory Bowel Disease (IBD), almost retrospective and uncontrolled. Due to the lack of available data and the potential for drug toxicity, the use of Tacrolimus in the management of refractory IBD is controversial.

Methods: This is a retrospective multicentre study conducted in three Spanish IBD Units. The local ethics committee approved the study protocol. A total of 15 patients were included in the study. All the information was obtained from the medical report of each institution. In order to assess the efficacy of Tacrolimus, clinical, analytical and endoscopic variables were included.

Results: A total of 8 patients with Crohn's disease and 7 with ulcerative colitis were included. Most of them suffered from a long-standing disease and were refractory to immunosuppressive therapy. All of them have previously received azathioprine and 69 % biologics. The most common indications for starting Tacrolimus were steroid - dependence and fistulising disease. The drug was maintained at least 12 months in 9 patients (69%). The mean follow up time since the start of the drug was 43.5 ± 21.3 months. Mean drug levels were between 5 - 10 ng/mL. The median PCR levels at baseline were 6.5 mg/dL [2.5 - 12.3]. Complete clinical remission was observed in 5 patients (38 %) and partial clinical response in 4 patients (30 %). Five patients developed adverse events (38 %), none of them were severe. The drug was withdrawn in ten patients during the follow up, mainly due to loss of response and in three subjects because of an adverse event.

Conclusions: This clinical - practice study found steroid - dependence and fistulising disease as the most common indications for the use of Tacrolimus. The treatment showed a relative good clinical efficacy with a reasonable safety profile. This study suggests that Tacrolimus may be included as an option in patients refractory or intolerant to previous therapy, but more data is required to establish the exact role of Tacrolimus in the treatment algorithm of IBD.

P551
Hospital readmissions in patients with inflammatory bowel disease: A UK single centre experience

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Background: The prevalence of inflammatory bowel disease (IBD) is increasing worldwide. Meanwhile, evolving definitions of disease control and outcome measures coupled with the rising direct and indirect cost of IBD therapy underpin the need to examine health care utilization and processes mitigating the economic impact whilst delivering value improvement in IBD care. Hospital inpatient admissions are increasing in the UK with an estimated annual cost of all cause 28-days readmissions of £2.2 billion each year to the National Health Service [1]. IBD accounts for approximately 108,000 hospitalizations in the UK each year [2]. We aimed to assess the readmission rate and associated predictive risk factors in our IBD cohort.

Methods: Patient readmissions within 28-days of an index admission, resulting from an exacerbation of IBD, to our inpatient gastroenterology service were identified using local hospital databases from April 2011 to October 2013. We retrospectively reviewed and carried out a descriptive analysis of patient demographics, baseline IBD and index admission factors, and reasons for readmission.

Results: We identified 157 patients, 57.6% female and 42.4% male, admitted at a mean age of 44 years with Crohn's disease (47.1%, n=113), Ulcerative colitis (46.3%) or indeterminate colitis (6.6%). The readmission rate within 28-days of index

admission was 21% (n=33). These occurred following a mean average of 16 days, due to dehydration/anaemia (27.3%), surgery or surgical complications (12.2%), pain control (6.1%), sepsis (6.1%), obstruction (6.1%), venous thromboembolism (3.0%) or other/unknown (39.2%). Readmissions occurred more commonly in younger patients (t-test, p<0.05), who had less severe endoscopic and microscopic baseline IBD disease (X^2=5.194, p<0.05, n=112), shorter length of stay during index admission (t-test, p<0.02, n=99) and who were discharged with less opioid analgesia (X^2=9.669, p<0.005, n=114).

Conclusions: CONCLUSION IBD readmission rates are higher than general readmission rates for myriad reasons that remain complex and challenging [2]. Identifying and addressing avoidable risk factors has the potential to empower and deliver optimal and high standard care and better outcomes with the ability to improve and reassess cost-efficacy in the context of a full cycle of care.

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P552
Prognosis of patients with Ulcerative Colitis in remission after thiopurines withdrawal

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Background: The ideal length of treatment with thiopurines in ulcerative colitis (UC) patients in sustained remission remains unknown. It is widely accepted that the withdrawal of these drugs is associated with a worse outcome of the disease. The aim of this study is to analyze the clinical outcome after this withdrawal and to identify possible predictors of clinically significant relapse (CSR).

Methods: A multi-centre, observational and retrospective study was designed. 102 patients with UC that discontinued thiopurines (after a period of at least 6 months of treatment) in a situation of sustained free-steroids clinical remission were included. All the patients were followed-up until last revision or until CSR (defined as the occurrence of signs and symptoms of UC that required the administration of a rescue treatment).

Results: The mean duration of the disease in all patients was 13 +/- 0.61 years, the mean time from diagnosis to the start of thiopurines was 48.14 +/- 5.51 months and the mean duration of total treatment with thiopurines was 60.87 +/- 4.89 months. After thiopurines were withdrawn, overall CSR was recorded in 32.35% of the patients. The cumulative percentage was 18.88% in the first year, 36.48% in the third year and 43.04% in the fifth year after withdrawal. In the univariate analysis, the total duration of treatment with thiopurines (p=0.0097) and time of free-steroids clinical remission before the suspension (p=0.0216) reached statistical significance. On multivariate analysis, predictors of recurrence were the time from diagnosis of UC until thiopurines were administered for the first time (HR 1.01, CI 95% 1.01-1.02, p=0.0397), a longer treatment with thiopurines (HR 0,15, IC 95% 0,03-0,66, p=0,0125), a situation of biological remission at the time of withdrawal (HR 0,004, IC 95% 0,0001-0,14, p=0,0021), the number of clinical relapses during treatment with thiopurines (HR 1.3, 95% CI 1.01-1.66, p=0.0298) and pancolitis (HR 5.01, 95% CI 1.95-26.43, p=0.0277).

Conclusions: The withdrawal of thiopurines in UC patients, although in sustained remission, is related to an increased risk of disease recurrence. Clinical variables such as the extent of the disease, the total duration of treatment or time of free-steroids clinical remission have been identified as factors to be considered before stopping these drugs. Further larger, controlled, randomized and prospective studies with long follow-up periods are required to research and clarify this issue.

P553
An Evaluation Study of Lactobacillus Brevis CD2 in Orofacial Granuolomatosis

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Background: A small proportion of patients with Crohn's disease develop orofacial granulomatosis (OFG), a rare, chronic disfiguring condition of unknown aetiology affecting the oral mucosa and perioral region. Previous studies have suggested that alterations in the oral microbiota may be involved in the pathogenesis of OFG. CD2 is a novel probiotic containing Lactobacillus brevis which has anti-inflammatory properties, primarily via reduced arginine availability. Previous studies have shown that CD2 reduces oral inflammation in chemotherapy-induced oral mucositis, Behcet's disease and recurrent aphthous stomatitis. Our aim was to evaluate the tolerability and efficacy of CD2 lozenges in reducing oral inflammation in patients with active OFG.

Methods: This was a single-centre prospective open-label observational study. Patients were recruited from a specialist OFG clinic between February and August 2014. Patients with active OFG received an eight week course of CD2 lozenges taken four times per day. Patients were reviewed before and after treatment and disease activity assessed by Oral disease activity score (ODAS),Visual analogue scale (VAS) of oral soreness and Global physician assessment (GPA).

Results: 28 patients were recruited with 4 patients withdrawing (3 non-compliance, 1 of which had severe learning difficulties; 1 re-classified as aphthous stomatitis). 7 patients failed follow-up leaving 17 patients (9 males) available for final analysis. The median age was 35 years (range 18-70 years) with 5/17 patients diagnosed with concurrent intestinal Crohn's disease. Before treatment, the median ODAS was 12 (range 2-36), median VAS was 50% (range 0-90%),

with 9/17 patients classified as having mild disease, 2/17 moderate and 6/17 severe. Post treatment, the median ODAS was 12 (range 1-34), median VAS was 20% (range 0-70%), with 9/14 patients had mild disease, 7/14 moderate and 1/14 severe.

The reduction in the mean ODAS at 2 months was 6.1 (18.8-12.7). The mean improvement in oral soreness measured by VAS was 25.3%. There were no adverse events, however one patient discontinued treatment due to severe diarrhoea which resolved upon CD2 cessation.

Conclusions: CD2 appears to be safe, well-tolerated and of benefit in reducing oral inflammation and oral soreness in active OFG. Based on these results, a larger double-blind prospective study is recommended. The treatment shows promise as an adjunct to dietary therapy and an alternative to systemic immunosuppression.

P554
Comparative efficacy of biologics in the treatment of moderately to severely active ulcerative colitis (UC): A systematic review and network meta-analysis

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Background: This study aimed to assess the comparative efficacy and safety of biologics in adult patients with moderately to severely active UC, stratified by prior exposure to anti-TNF inhibitors.

Methods: MEDLINE, Embase, The Cochrane Library, and ClinicalTrials.gov were systematically searched using a predefined search strategy, without language restrictions, for studies of approved biologics for UC (adalimumab, golimumab, infliximab, vedolizumab) published before February 2014. Two reviewers independently assessed studies for inclusion using a 2-step process; data on study design, patient characteristics, and outcomes were extracted from 8 RCTs (GEMINI I, ULTRA-1, ULTRA-2, ACT-1, ACT-2, PURSUIT-SC, PURSUIT-M, Suzuki et al., 2014 [1]) that met the inclusion criteria and were suitable for network meta-analysis (NMA). The NMA was conducted for key endpoints at induction and maintenance, where data were available, in R and OpenBUGS using Bayesian fixed effects mixed treatment comparisons. Assumptions were made to account for differences in maintenance study design.

Results: Seven studies were included in the analysis of induction treatment for anti-TNF-naïve patients. All biologics were more effective than placebo in terms of response, remission, and mucosal healing, but rankograms suggested no significant differences between the included biologics. These results were consistent with recent reports [2]. Five studies were included in the analysis of maintenance treatment for anti-TNF-naïve patients. Vedolizumab every 8 weeks (Q8W) resulted in improved results versus comparators for all outcomes at week 52 and was associated with a significantly higher rate of durable clinical response than all comparators (Table 1). In patients who had previously received anti-TNFs, only vedolizumab and adalimumab could be compared. At induction, no significant differences in efficacy were observed between the 2 biologics. During maintenance treatment, vedolizumab resulted in improved rates of durable response and remission and significantly improved rates of mucosal healing compared with adalimumab (Table 1).

Conclusions: This study adds to the current understanding of the comparative efficacy and safety of biologic treatment for UC, encompassing outcomes and populations not included in previous studies. All biologic treatments are effective in the treatment of UC, with vedolizumab demonstrating benefits compared with all comparators irrespective of prior anti-TNF exposure in the maintenance setting.

Table 1: Odds ratio and 95%CI for vedolizumab Q8W vs. placebo and approved comparators in the anti-TNF-naïve and anti-TNF-experienced/failure maintenance population

	Odds Ratio (95% CI) for vedolizumab Q8W vs. listed comparator			
Subpopulation (endpoint at week 52)	**Placebo**	**Adalimumab 40mg eow**	**Golimumab 100mg**	**Infliximab 5mg/kg**
Anti-TNF naive				
Durable clinical response	5.27* (2.68-11)	3.96* (1.67-9.84)	2.33* (1.04-5.41)	3.18* (1.14-9.2)
Clinical remission	3.63* (1.75-7.72)	1.81 (0.74-4.9)	2.03 (0.84-5.05)	2.93* (1.03-8.28)
Discontinuation due to AEs	0.31 (0.06-1.13)	0.14* (0.02-0.67)	0.21* (0.03-0.99)	0.34 (0.05-1.69)
Mucosal healing	4.79* (2.33-9.93)	3.21* (1.33-7.35)	NA	2.43 (0.87-6.66)
CSF remission	2.57 (0.92-7.57)	12 (0.23-5.97)	NA	1.66 (0.39-6.99)
Anti-TNF experienced/failure				
Durable clinical response	4.89* (1.74-16.0)	2.04 (0.44-9.01)	NA	NA
Clinical remission	12.0* (3.14-78.0)	3.4 (0.4-33.0)	NA	NA
Discontinuation due to AEs	NA	NA	NA	NA
Mucosal healing	9.09* (2.74-40.0)	6.72* (1.36-41.0)	NA	NA
CSF remission	NA	NA	NA	NA

AE = adverse event; CI = confidence interval; CSF = corticosteroid free; eow = every other week; NA = not applicable; Q8W = every 8 weeks.

*Significant vs. comparator ($P < 0.05$).

Durable clinical response was defined as response at both start and end of maintenance. Remission was defined as a complete Mayo score of ≤ 2 points and no individual subscore > 1 point. Clinical remission data were analyzed at end of maintenance. Mucosal healing was defined as Mayo endoscopic subscore of ≤ 1 point. CSF remission was defined as Crohn's Disease Activity Index ≤ 150 points plus no corticosteroid use.

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P555
Adherence to medical therapy and follow up in IBD patients

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Background: In inflammatory bowel disease (IBD) care non-adherence to out-patient visits can be detrimental for various reasons including the lack of monitoring drug-related side effects, disease progression and complications. The actual focus on adherence is mainly addressed to evaluate optimal therapy assumption.

Methods: Patients selected from our IBD database not referring for regular follow-up visits in the last 24 months have been compared to patients regularly attending the clinic in a ratio 2:1. A structured questionnaire has been administered during a telephone call by the nurse in order to assess: disease activity (Modified Truelove Witts Severity Index - MTWSI in UC, Harvey Bradshaw Index - HBI in CD) and adherence to medical therapy (Morisky-8 scale: < 6 = low adherence, 6-7 = moderate adherence, 8 = high adherence). Statistical analysis included standard error at 95% and odds ratio.

Results: 455 patients have been enrolled: 382 (54% UC and 46% CD) accepted to answer all the questions, 132 regularly attending patients (75 males - mean age 41.6 yrs ±13) and 250 non-attending patients (137 males, mean age 47.8 yrs± 15.5). Sixty patients did not answer the phone and 13 did not want to answer the questions. Non-adherent patients were more frequently females (OR=1.40 IC=0.83-2.36), age > 55 yrs (OR=4.06 IC =1.77-9.27), with UC (OR=1.71, IC=1.00-2.91) and with disease duration less than 12 months (OR= 2.52, IC 0.88-7.16). The Morisky score was significantly lower in non-adherent than in adherent patients (p= 0.003). Higher risk of non-adherence was found in patients with a Morisky score lower than 6 (OR 3.46 -IC=1.89-6.33) or equal to 8 (OR = 5.75- IR 2.53-13.06), in females (p=0.000), in younger patients (p=0.007) and in CD vs UC (p=0.003). The 30% of non-adherence patients after call by the nurse they accepted to return to out-patient visits.

Conclusions: The majority of the patients did accept positively the telephone call. Patients not-attending regular follow up visits are at high risk of non-adherence to medical therapy as well.

Females, patients older than 55 years, patients with UC and a short disease duration are at higher risk of out-patient non-adherence. Efforts need to be addressed to improve global adherence, included regular attendance of follow up visits. Reinforcement and motivation by the IBD nurse may help to increase patients' empowerment.

P556
A randomized, multicentre, clinical trial to compare prednisone plus granulocyte and monocyte apheresis (GMA) versus prednisone alone for inducing steroid-free remission in patients with steroid dependent Ulcerative Colitis (UC)

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Background: Steroid-dependency occurs in up to 30% of UC patients responding to systemic corticosteroids. Thiopurines and anti-TNF drugs have demonstrated efficacy in inducing steroid-free remission but up to 50% of patients are intolerant or fail to respond to these drugs.

Methods: This was a randomized, multicentre, open trial promoted by the Spanish Working Group on IBD (GETECCU), that compared 7 weekly sessions of GMA plus oral prednisone (40mg/day and tapering) to prednisone alone in patients with mild-to-moderate active UC (Mayo score 4-10) were steroid-dependent (inability to withdraw corticosteroids in 3 months or relapse within the first 3 months after discontinuation). Patients were stratified by concomitant use of thiopurines at inclusion, and the same 9-week prednisone tapering schedule was pre-established in both study groups. The primary end-point was steroid-free remission (as defined by a Mayo score equal or less than 2 with no individual subscore higher than 1) at week 24, with no reintroduction of corticosteroids during the study period.

Results: One hundred and twenty-three patients were included (63 GMA group, 62 prednisone alone). 27% of patients concomitantly used thiopurines and 55% were taking steroids during the screening period. In the ITT analysis, steroid-free remission at week 24 was achieved in 13% of the GMA group vs. 6% in the control group (P=0.11). No differneces were found in the per protocol analysis. However, time to relapse was significantly longer in the GMA group (HR 1.7 [1.16-2.48], P=0.005). In the subpopulation of thiopurine-naïve patients, steroid-free remission rates were significantly higher in the GMA group (13% vs. 0%, P=0.03). Steroid-related adverse events were significantly less among patients in the GMA group (6% vs. 20%, P<0.05).

Conclusions: The addition of 7 weekly sessions of GMA to a conventional course of oral prednisone in patients with active steroid-dependent UC does not increase steroid-free remission although it significantly delays clinical relapse.

P557
Improved mucosal healing during scheduled adalimumab maintenance therapy in patients with Crohn's disease initiated following surgical resection of active lesions

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Background: Crohn's disease (CD) is a chronic relapsing-remitting inflammatory bowel disorder with variable disease expressions, giving rise to multiple complications. CD can affect any part of the digestive track from the mouth to the perianal region. Adalimumab(ADA) is an anti-tumour necrosis factor (TNF) antibody, which has shown efficacy in patients with CD. Further, given its efficacy in active CD, ADA has been reported to be effective as maintenance therapy to post-operative recurrence. However, examinations of endoscopic images indicate that during maintenance ADA, complete mucosal healing is not achieved and that disease activity continues including the formation of intestinal strictures.

Methods: With the afore background in mind, we thought that ADA maintenance therapy might produce an improved efficacy if administered immediately following surgical removal of active CD lesions (we called this 'Re-set ADA therapy'). This study was prospective, single center, open-label analysis. A total of 48 patients were included, the conventional therapy group (conventional, n=15), the routine ADA group (Routine ADA, n=6) and the Re-set ADA group (Re-set ADA, n=27). In the conventional group at low-risk for post-operative recurrence (POR), patients received metronidazole, 5-ASA, enteral nutrition or azathiopurine to induce remission of CD relapse following surgery. In the Routine ADA group, patients received ADA to induce remission of CD relapse following surgery to eliminate all colonoscopically detectable active CD lesions and then received scheduled maintenance. Similarly, in the Re-set ADA group at high risk for POR, patients received scheduled maintenance ADA immediately following surgery to eliminate active CD lesions. Several groups were followed for 1 year during which patients disease profiles including mucosal healing were monitored.

Results: During 1 years of follow up, remission maintenance rates were 33.3%, respectively in the conventional group. The corresponding maintenance remission rates in the Routine ADA group were 33.3%, and in the Re-set ADA group 70.3%. Likewise, complete mucosal healing (rutgeerts score i0) rate at 1 year was 0% in the conventional group, 0% in the Routine ADA and 54.5% in the Re-set ADA group, reflecting vastly better maintenance efficacy rates in the Re-set ADA group as compared with the conventional group or Routine ADA group. (p=0.00153, p=0.090)

Conclusions: In the clinical settings described above, scheduled maintenance ADA therapy appeared to produce improved efficacy outcomes when initiated immediately after resections of active CD lesions. More notably, the efficacy of ADA to induce mucosal healing was better in the Re-set treatment setting vs the conventional therapy or routine setting.

P558
Twice-daily budesonide rectal foam induces complete mucosal healing in Japanese patients with mild to moderate ulcerative colitis: Results of multicenter, randomized, double-blind, placebo-controlled trial

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Background: Budesonide rectal foam is widely used as effective, easy to use, well tolerated corticosteroid rectal preparation for ulcerative colitis (UC) in Europe. We evaluated the efficacy and safety of budesonide rectal foam in Japanese UC patients.

Methods: This study was multicenter, randomized, double-blind, placebo-controlled trial.165 patients with active, mild to moderate UC were randomized to three groups that were given budesonide foam (2mg/25mL) once or twice daily or placebo for 6 week. Primary endpoint was remission at 6 week (Rectal bleeding subscore=0, endoscopic subscore< =1 and stool frequency subscore=0 or decrease >=1).

Results: At week 6, the percentages of remission in once or twice daily budesonide foam group were 50.9% (95% CI 38.1 to 63.6), 48.2% (95% CI 35.7 to 61.0), respectively, compared with 20.4% (95% CI 11.8 to 32.9) in placebo group (P=.0015, P=.0029). The percentages of complete mucosal healing (endoscopic subscore=0) in once or twice daily budesonide foam group were 23.6% (95% CI 14.4 to 36.3), 46.4% (95% CI 34.0 to 59.3), respectively, compared with 5.6% (95% CI 1.9 to 15.1) in placebo group (P=.0159, P<.0001). No serious adverse event occurred in all groups. Blood cortisol decrease (<4ug/dL) occurred in 21.8% and 46.4% of once and twice daily budesonide foam groups, but all of them returned to normal level after treatment.

Conclusions: Budesonide rectal foam was effective to induce remission in Japanese patients without any serious problems. Especially, twice daily administration was highly effective to achieve complete mucosal healing.

P559
Improving Health Care of Patients with Inflammatory Bowel Diseases (IBD) by Fostering Networking of Physicians - it´s not that easy!

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Background: IBD-patients (pts) suffer from a wide range of somatic and psychosocial problems. They are in need of comprehensive, interdisciplinary and cross-sectoral health care. In- and outpatient gastroenterologists in a region of Northern Germany tried to optimize their quality of care by network activities.

The impact on patient related outcomes (PROs) was evaluated. We report the 6-months interim analysis of this 12-months prospective study.

Methods: In the beginning of 2014 349 outpatients with IBD were included in a prospective controlled cohort study. 15 gastroenterologists included 189 pts in the intervention-region (IG: intervention group) and another 18 gastroenterologists from the rest of Germany included 160 pts in the control group (CG). At baseline, 6 and 12 months pts completed a questionnaire assessing 22 somatic and psychosocial problems, medical data on the course of the disease were gathered by the gastroenterologists. Primary outcomes were health related quality of life (HRQoL: EQ-VAS) and social participation restrictions (IMET), secondary outcomes were disease activity (GIBDI) and work productivity (WPAI). Pts in the intervention group (IG) promptly received written feedback of their problem-profile together with individualized recommendations for appropriate treatment. Further interventions in the IG were the introduction of interdisciplinary IBD-case conferences and the offer of a patient training in small groups.

Results: 310 (IG: 160; CG: 150) of 349 IBD-pts (UC: 47.6%; CD: 52.4%) participated in the 6-months follow-up. Baseline characteristics were broadly similar (age: 43 years; 60% female; 63% in remission; 67% in full- or part time employment). Only minor differences between IG and CG for age, school education and medication could be found. No significant differences between IG and CG were seen at 6-months follow-up with respect to the primary outcomes: neither for HRQoL (EQ-VAS: changes from 73.3 to 74.2 in IG; from 70.6 to 72.7 in CG; p=0.267) nor for social participation restrictions or further secondary outcomes. In contrast, the feedback of the physicians in the IG were more favorable at the 6-months follow-up. 67% of the physicians participated in IBD-case conferences, the benefit of networking has been ranked with 7 on a scale from 0 (no benefit) - 10 (best benefit).

Conclusions: The 6-months interim analysis could not show any significant improvements in the primary outcome parameters (HRQoL and IMET) in the IG vs. CG. Nevertheless, the participating physicians described clearly positive effects for their daily work. We are looking forward to the 12-months follow up, hoping for beneficial effects in the patient´s experience in the long run, too.

P560
Patients and gastroenterologists' perceptions of treatments in Inflammatory Bowel Disease: Do doctors and patients speak the same language?

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Background: Perceptions of risks and benefits of therapies may differ between gastroenterologists (GIs) (as treatment providers) and inflammatory bowel disease (IBD) patients, (as treatment consumers). Very few studies have focused on the patients' point of view on medication and prioritization of outcomes. The aim of this study was to explore and compare Swiss GIs' and patients' perceptions of appropriateness (i.e., balance of risks and benefits) of treatments for IBD.

Methods: This study used qualitative methods. Four vignette cases were drawn from typical clinical situations and formed the basis of three focus group discussions, managed by a psycho-sociologist, between either GIs (n=7), ulcerative colitis patients (UC-p, n=8) or Crohn's disease patients (CD-p, n=6). The contents of the three focus group discussions were compared using qualitative content analysis.

Results: UC-p agreed more often with GIs' treatment choices than CD-p. Most agreement was found around 5-ASA therapy, considered as the most convenient and safest drug to take. For CD-p, 5-ASA was often considered to be a placebo. For UC-p, topical 5-ASA was seen as a temporary solution, neither comfortable nor practical when professionally active; longer-term treatment with oral 5-ASA was preferred to azathioprine by both physicians and patients. Both also perceived azathioprine as the treatment for which the risks versus benefits is the highest; concerning anti-TNFs, the main risk perceived by patients was related to a potential loss of response. Divergences between GIs' and patients' opinions were observed on two main issues: 1) stop of treatment: UC-p did not easily concur with stopping the treatments, which differed from the GIs' expectation of patients' perception; on the contrary, CD-p were more prone to consider stopping treatment than GIs; 2) perception of outcomes: physicians aimed at obtaining a histological remission, and had a focus on long-term objective goals. In contrast, patients' expectations were of shorter term and focused on clinical remission. Patients' expectations of follow-up mainly concerned stress management and nutritional advice, in addition to a need for more information on the effects of treatments.

Conclusions: In the majority of cases, patients and GIs agreed on perception of IBD treatments. However, GIs seemed more concerned about objective and scientific measures of remission whereas IBD patients focused on quality of life and social outcomes when it came to evaluating a therapy. Better communication about those different goals and expectations may improve patients' adherence to therapy as well as physician-patient relationship, leading to better satisfaction with general healthcare.

P561
Time course and clinical implications of development of binding and neutralizing antibodies against adalimumab in patients with inflammatory bowel disease

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Background: Antibodies (Abs) against adalimumab (ADL) have been associated with low ADL trough levels and treatment failure in inflammatory bowel disease (IBD). This study investigated the temporal characteristics of anti-ADL Ab formation including course of changes during ongoing ADL therapy in IBD.

Methods: Single-center cohort study including all IBD patients assessed for anti-ADL Abs by fluid-phase radioimmunoassay (RIA).(1) In those cases where anti-ADL Abs became undetectable at repeated assessments by RIA then: A) the positive anti-ADL

Abs samples were reassessed in independent analyses by RIA and quantified as titers (cpm relative to normal human serum); B) the negative anti-ADL Ab samples were assessed by a solid phase enzyme immunoassay (EIA) less prone to drug interference; C) all anti-ADL Ab positive and negative samples were assessed for both anti-ADL Abs and ADL by a functional cell based reporter gene assay (RGA).(1)

Results: Anti-ADL Abs were evaluated in 133 serum samples obtained from 72 patients (Crohn's disease n=53, ulcerative colitis n=19). Of these, 17 patients (24%) were positive for anti-ADL Abs after a median of 194 days, IQR 66-361. Most patients (13/17: 76%) developed anti-ADL Abs within first year of ADL therapy. The proportion of patients who had developed anti-ADL Abs after one year on ADL was 22% assessed by Kaplan-Meier analysis. This proportion remained stable at 32% from 21 months until end of follow-up after 6 years. Anti-ADL Abs generally persisted at repeat assessments during continued ADL therapy (n=8). Rare fluctuations of anti-ADL Ab-detection (n=3) were caused by methodological biases, e.g. false positive detection of non-functional non-persistent anti-ADL Abs in binding assay (RIA), or false negative anti-ADL Ab measurements both by binding (RIA) and functional assay (RGA) likely due to drug interference. Anti-ADL Abs appeared pharmacologically active as judged by a median ADL concentration below limit of detection vs. 7.4 µg/ml in anti-ADL Ab negative samples (p<0.0001). Anti-ADL Abs associated with loss of treatment response (OR estimated 67, p<0.0001), and shorter treatment duration (p<0.0001).

Conclusions: Antibodies against ADL usually appear in the circulation within the first year of therapy, and associate with diminished ADL detection and treatment failure. As anti-ADL Abs furthermore tend to persist at repeat assessments during continued ADL therapy, ADL cessation is generally to be recommended once anti-ADL Abs have been detected. On the other hand, test results should always be interpreted in a clinical context as methodological biases may generate false positive or false negative anti-ADL Ab detections.

(1) Steenholdt et al. Ther Drug Monit (2013)

P562
Clinical outcomes of surgery versus endoscopic balloon dilatation for stricturing Crohn's disease

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Background: Endoscopic balloon dilatation (EBD) and surgery are commonly practiced in stricturing Crohn's disease (CD). Nonetheless, there are still scant data directly comparing these two strategies. The aim of this study was to compare the short and long term outcome of EBD versus surgical resection in symptomatic Crohn's strictures at one tertiary center.

Methods: This was a retrospective cohort study. The outcomes of all patients referred to EBD were compared to patients referred to surgery due to stricturing disease between the years 2006-2013. Patients undergoing surgery for non-CD stricturing disease were excluded.

Results: Seventy nine patients were identified, 40 in the surgical group and 39 in the EBD group who underwent an overall of 72 dilatation procedures. The mean age was 42.81 ± 13.91 years and 38.52 ± 12.24 years in the EBD and the surgical group, respectively. Median duration of follow-up after the index procedure was 2.7 years (IQR, 3.7-1.2) and 3.5 years (IQR,5.6-1.2) for EBD and surgery, respectively (p=0.33). The patients' characteristics regarding disease location, perianal disease and immunosuppressive treatment during follow-up were similar. Disease duration was significantly longer in the endoscopically-treated patients (16.4 vs12 years; p=0.05). The stricture's location was not significantly different between the EBD and surgery group (Ileum: 68.2% versus 85.7%, p=0.51; Colon: 31.6 % versus 12%, p=0.1). The average stricture length was significantly shorter in the endoscopic dilated group compared to the strictures in the operated group (4.21 ± 2.13 cm versus 7.47 ± 4.84cm, p<0.05). Anastomotic strictures were more prevalent in the EBD group (30% versus 7.5%, p=0.01). The proportion of patients that required any re-intervention during follow-up was significantly lower in the surgical group in comparison to the EBD group (OR=5.62; 95% CI 1.66 19.01; p=0.005). The need for surgery/re-surgery during follow-up was also significantly lower in the surgically-treated group (OR 3.53; CI 1.01-12.29; p=0.047). Re-intervention-free survival and surgery-free survival were both significantly shorter in the endoscopically-treated group in a Kaplan-Mayer analysis. The major complication rate in the endoscpically and surgically-treated groups were similar and were 7.6% and 5%, respectively (p=0.7).

Conclusions: In our cohort of patients with fibrostenotic CD, a direct comparison shows that the long term outcome after surgery was more favorable compared with EBD.

P563
Vedolizumab exposure in pregnancy: Outcomes from clinical studies in inflammatory bowel disease

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Table: Number and outcome of patient/healthy volunteer pregnancies and partner pregnancies in clinical studies with vedolizumab

Pregnancy Outcome	Treatment						Total
Pregnant Patients/Volunteers	Placebo (n=3)			Vedolizumab (n=24)			
	Healthy	UC	CD	Healthy	UC	CD	(n=27)
Live birth	0	1	0	0	4	6	11
Congenital anomaly	0	0	0	1	0	0	1
Elective termination	0	0	0	0	2	3	5
Spontaneous abortion	1	0	1	0	2	2	6
Undocumented[a]	0	0	0	0	1	3	4
	Placebo (n=4)			Vedolizumab (n=16)			Total
Pregnant Partners	Healthy	UC	CD	Healthy	UC	CD	(n=20)
Live birth	0	2	1	0	6	3	12
Elective termination	0	0	1	0	1	1	3
Spontaneous abortion	0	0	0	0	1	1	2
Undocumented[a]	0	0	0	0	1	2	3

Abbreviations: CD, Crohn's disease; UC, ulcerative colitis.

[a] Includes pregnancies that were ongoing at last patient contact and pregnant partners who withdrew consent.

Includes studies NCT01981616, C13001, NCT00619489, NCT00783718 [GEMINI 1], NCT00783692 [GEMINI 2], and NCT00790933 [GEMINI LTS data up to 27 June 2013].

Background: Vedolizumab (VDZ) is a gut-selective immunoglobulin G_1 monoclonal antibody to α4β7 integrin with demonstrated efficacy and safety in the treatment of Crohn's disease (CD) and ulcerative colitis (UC) in adults. Placental transfer of VDZ is anticipated to be similar to all other immunoglobulin G_1 therapeutic antibodies and increases in a linear fashion as pregnancy progresses, with the largest amount transferred during the third trimester. There are no controlled studies with VDZ in pregnant women. Here we report the effect of VDZ on pregnancy outcomes for female study participants and partners of male patients exposed in clinical studies.
Methods: Data from the VDZ clinical development programme up to 27 June 2013 were reviewed. According to the study protocols, female participants who became pregnant were to discontinue the study. The outcomes of pregnancies for female participants who became pregnant during the study and male patients with pregnant partners were summarised descriptively.
Results: The number of pregnancies reported were 27 in females (25 in patients with UC or CD, 2 in healthy volunteers) and 20 pregnancies in the partners of male patients in 6 clinical studies (placebo and VDZ were administered in 2 single dose studies and 2 multiple dose 1-year studies; VDZ was also administered in 2 long-term, open-label, multiple dose studies of 78 weeks and 4 years [ongoing]; Table). Of the 24 VDZ-treated females, 11 resulted in live births (2 premature). A congenital anomaly of agenesis of the corpus callosum was reported in the healthy volunteer with an obstetric history of 2 spontaneous abortions and 1 ectopic pregnancy who had received a single dose of VDZ 79 days prior to the estimated date of conception. Among the 16 VDZ-exposed partner pregnancies, there were 9 live births, 2 spontaneous abortions, 2 elective terminations, and 3 undocumented outcomes at the last follow-up.
Conclusions: Although female participants were discontinued if they became pregnant during the study, data from the VDZ clinical development programme provide some insight into pregnancy outcomes of VDZ-treated patients. An observational pregnancy registry enrolling patients with UC or CD on VDZ is currently in development to observe and evaluate the long-term safety of VDZ in pregnancy.
The clinical study was funded by Millennium Pharmaceuticals, Inc. (d/b/a Takeda Pharmaceuticals International Co.). Medical writing assistance was provided by inVentiv Medical Communications and supported by Takeda Pharmaceuticals International, Inc.

P564
Changes of fecal calprotectin concentrations after adalimumab induction therapy in patients with moderate-to-severe Crohn's disease

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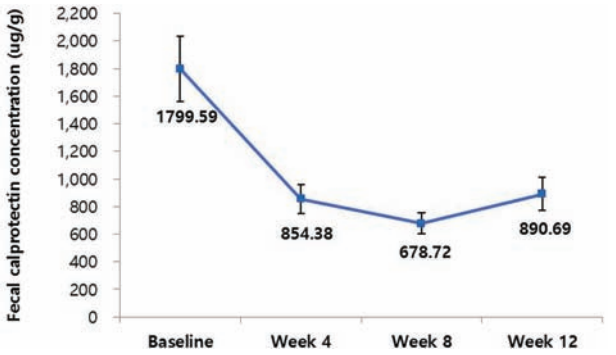

"Change of fecal calprotectin concentration from baseline to week 4, 8, and 12."

Background: In the era of biologics, mucosal healing (MH) has been proposed as a treatment goal for Crohn's disease (CD) because of its association with favorable long-term disease outcomes. Fecal calprotectin (FC), a neutrophil-derived protein, is a sensitive marker of intestinal inflammation and correlates closely with endoscopic disease activity. We examined the changes of FC concentrations in patients with moderate to severe CD receiving adalimumab induction therapy.
Methods: This was a prospective, multicenter, observational study. Moderately to severely active luminal CD patients with baseline FC≥150 μg/g were treated with adalimumab and followed up every 4 weeks for 12 weeks. Crohn's disease activity index (CDAI) and fecal calprotectin were measured at baseline, 4, 8, and 12 weeks. Fecal samples for calprotectin were shipped to central laboratory for a quantitative analysis using ELISA. Primary endpoint was the percentage of patients with FC concentration<150 μg/g after completion of adalimumab induction treatment at week 4.
Results: A total of 93 patients were enrolled in this study. Patients showed male predominance (M:F=2.1:1) and mean age was 30.7 ± 8.9 years. CDAI score decreased from 288.2 ± 60.2 at baseline to 129.9 ± 74.9 at week 4, and 66% of patients achieved clinical remission (CDAI <150) at that time point. Accordingly, FC concentration fell from 1799.6 ± 2275.3 μg/g at baseline to 854.4 ± 1002.1 μg/g at week 4 (percent change -34.6 ± 59.9, P<0.0001).
However, only 16% of patients showed FC<150 μg/g at week 4. The proportions were increased up to 21.9% and 18.8% at 8 and 12 week, respectively.
Conclusions: FC concentrations are significantly decreased with adalimumab treatment, implicating improvement of intestinal inflammation. However, FC remained high level in considerable patients with symptomatic improvement. Long-term follow up study is needed to explore the clinical significance of subclinical inflammation in adalimumab-treated CD.

P565
The Increased Prevalence of Non-Alcoholic Fatty Liver Disease in Inflammatory Bowel Disease Patients is not Related To Inflammatory Load

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Background: Aim of the study was to compare the prevalence of non-alcoholic fatty liver disease (NAFLD) between patients with IBD and IBS and determine its predictors among IBD patients.
Methods: In this cross-sectional study IBD and IBS patients' charts were reviewed in a retrospective manner. 276 IBD patients (172 UC and 104 CD) and 161 age and sex adjusted IBS patients were compared regarding the prevalence of NAFLD using abdominal USG. Age at disease onset, at USG, sex, disease duration, location, and behavior, alcohol-steroid use, and complete blood count, blood levels of fasting lipids, glucose, and acute phase reactants and body mass index (BMI) at the time of USG were noted.
Results: None of the subjects had alcohol use more than 20 g/d. The IBD patients' mean age±SD at USG was 44.39 ± 14.14 yr.(52% being female), and of IBS patients 44.11 ± 13.73 yr.(54% being female). Patients in both groups had similar BMI values. The prevalence of NAFLD among IBD patients was significantly higher compared to those with IBS [(36.2% vs. 25.5%, respectively; χ^2 =5.393, p=0.02); OR: 1.663 (95%CI: 1.08 -2.56)]. There were 100 patients with NAFLD in 276 IBD (33.1% in UC, 41.3% in CD; NS) patients. IBD patients with NAFLD had significantly higher albumin, TG, LDL, glucose, hct, MCV, BMI values and significantly lower ESR compared to those without NAFLD. Besides these disease location, extension, behavior, steroid use, and CRP levels at the time of USG did not show any significant difference (Table 1). Cox-regression analysis disclosed higher glucose (p=0.003) and lower ESR (p=0.042) to be the only independent predictors of NAFLD.
Conclusions: In this cross-sectional study the prevalence of NAFLD is higher among IBD compared to age-and sex adjusted IBS patients with similar BMI values. The fact that IBD-NAFLD patients had significantly higher levels of albumin, TG, LDL, glucose, hct, MCV, BMI values and significantly lower ESR compared to those without NAFLD points to nutritional facts rather than inflammatory load in the development of NAFLD in IBD.

	IBD patients with NAFLD n=100	IBD patients without NAFLD n=176	p
Age at USG	47.43±13.00	42.67±14.50	**0.007**
Sex (Female – Male) %	44% - 56%	56% - 44%	**0.05**
Disease duration (mo.)	63.46±62.71	45.96±52.59	**0.014**
Albumin (g/dL)	4.19±0.52	4.00±0.58	**0.008**
Triglyceride (mg/dL)	140.72±98.27	104.83±56.70	**0.000**
LDL (mg/dL)	182.42±49.06	106.77±30.27	**0.000**
Glucose (mg/dL)	97.88±21.06	93.03±17.83	**0.043**
Hct (%)	39.50±3.95	37.11±4.81	**0.000**
MCV	85.39±5.49	82.12±8.15	**0.000**
BMI at the time of USG	25.91±4.11	23.04±4.01	**0.000**
ESR/1h	20.37±14.67	26.28±20.02	**0.008**

"Table 1. Comparison of IBD patients with or without NAFLD."

P566
Efficacy and safety of vedolizumab with advancing age in patients with ulcerative colitis: Results from the GEMINI 1 study

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Background: The efficacy and safety of vedolizumab (VDZ), a gut-selective monoclonal antibody to α4β7 integrin for the treatment of patients (pts) with ulcerative colitis (UC), have been demonstrated. Here we report post hoc analyses of data from the placebo (PBO)-controlled GEMINI 1 study (NCT00783718) [1] that evaluated the effects of VDZ with advancing age in pts with UC.
Methods: In GEMINI 1, pts received double-blind (DB) VDZ or PBO (induction intent-to-treat [ITT] population) or open-label VDZ at weeks (wks) 0 and 2. At wk 6 (end of induction), VDZ responders were re-randomised to receive DB VDZ every 8 or 4 wks (Q8W or Q4W) or PBO up to wk 52 (maintenance ITT population). Efficacy endpoints and adverse events (AEs) were analysed by baseline (wk 0) age category (<35, 35 to 55, and >55 years [yrs]).
Results: At baseline, 139 (37%), 185 (49%), and 50 (13%) pts in the induction ITT population and 155 (42%), 161 (43%), and 57 (15%) pts in the maintenance ITT population were aged <35, 35 to 55, and >55 yrs, respectively. The primary clinical efficacy endpoint for induction treatment in GEMINI 1 was clinical response (≥3-point reduction in complete Mayo score, ≥30% change from baseline and ≥1-point decrease in rectal bleeding subscore [RBS] or absolute RBS of ≤1) at wk 6 and was achieved by 44 (51%), 50 (47%), and 12 (38%) VDZ-treated pts aged <35, 35 to 55, and >55 yrs, respectively. At wk 52, 34 (34%) pts aged <35, 58 (53%) aged 35 to 55, and 15 (42%) aged >55 yrs achieved clinical remission (complete Mayo score of ≤2 points and no individual subscore >1 point). Rates of AEs were similar between VDZ and PBO and were also similar across the ages (Table). Three malignancies were reported (aged 32 ITT VDZ Q8W: colon cancer; aged 40 ITT PBO: transitional cell carcinoma; aged 73 ITT PBO: colon cancer). One death occurred during the study: acute cardiac death of a 66-yr-old man with a history of ischemic heart disease who had received 1 dose of VDZ.
Conclusions: These data suggest that the safety and efficacy of VDZ in pts with UC were generally similar across the age categories analysed. Data interpretation is limited by the small pt population aged >55 yrs. These findings should be further evaluated in prospective studies.
The clinical study was funded by Millennium Pharmaceuticals, Inc. (d/b/a Takeda Pharmaceuticals International Co.). Medical writing assistance was provided by inVentiv Medical Communications and supported by Takeda Pharmaceuticals International, Inc

Table:Adverse events in patients with UC by baseline age category (GEMINI 1)

	Age <35 years		Age 35-55 years		Age >55 years	
	PBO/PBO[a] (n=53)	VDZ/VDZ[b] (n=246)	PBO/PBO[a] (n=78)	VDZ/VDZ[b] (n=286)	PBO/PBO[a] (n=18)	VDZ/VDZ[b] (n=88)
Event	**Number of Patients (%)**					
Any AE	40 (75)	196 (80)	61 (78)	228 (80)	13 (72)	73 (83)
Any SAE	7 (13)	31 (13)	9 (12)	39 (14)	1 (6)	7 (8)
Infections and infestations (SOC)	18 (34)	108 (44)	22 (28)	118 (41)	6 (33)	37 (42)

Abbreviations: AE, adverse event; PBO, placebo; SAE, serious adverse event; SOC, system organ class; UC, ulcerative colitis; VDZ, vedolizumab.

[a] Patients received PBO induction and maintenance therapy.

[b] Patients received VDZ induction and maintenance therapy.

References:

[1] Feagan BG, (2013), Vedolizumab as induction and maintenance therapy for ulcerative colitis, N Engl J Med, 699-710

P567
The long-term efficacy of concomitant enteral nutritional therapy during maintenance infliximab in patients with Crohn's disease: a prospective observational trial

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Background: Several controlled studies have reported that enteral nutrition (EN) with elemental diet (ED) was effective for maintenance of clinical remission in patients with quiescent Crohn's disease (CD). However, most studies on EN have been done before the era of biological therapy and therefore, the long-term efficacy of EN on clinical outcomes during biological maintenance therapy in CD patients has not yet been investigated. This prospective study was undertaken to assess the long-term efficacy of EN on the maintenance rate of clinical remission in patients with quiescent CD receiving infliximab maintenance therapy.
Methods: Eighty patients who achieved clinical remission with infliximab induction therapy received infliximab as maintenance therapy (5 mg/kg, every 8 weeks). Forty-two patients who were known to show good compliance with EN were assigned to an EN-group, and 38 with poor compliance were assigned to a non-EN group. Patients in the EN group received concomitant EN with ED at 1200-1500 mL/day (1200-1500 kcal/day) by using an infusion pump during night time and a low fat diet (20-30 g/day) during daytime, while patients in the non-EN group received neither nutritional therapy nor food restriction. All 80 patients were followed for 3 years. CD activity index (CDAI) was assessed every 8 weeks and CDAI < 150 was defined as clinical remission.
Results: During the 3 years observation time, the mean CDAI was not significantly different between the two groups. During the study period, 20 patients in the EN group ceased EN therapy because they had maintained complete remission. Seventeen (85%) of the 20 patients who ceased EN therapy maintained clinical remission during the study period. On an intention-to-treat basis, 24 patients (57%) in the EN group and 21 patients (55%) in the non-EN group remained in clinical remission during the 3 years observation (not significant). The cumulative proportion of patients in clinical remission was not significantly different between the two groups.
Conclusions: In this long-term study, concomitant EN during infliximab maintenance therapy did not appear to significantly increase the maintenance rate of clinical remission.

P568
Alterations of Intestinal Microbiota in Ulcerative Colitis Patients Treated with Sequential Antibiotic Combination and Faecal Microbiota Transplantation

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Background: Currently, the aetiology of ulcerative colitis (UC) is not understood well. Increasing evidence suggests that the intestinal microbiota is an important component of UC aetiology. Based on this knowledge, faecal microbiota transplantation (FMT), also known as faecal bacteriotherapy is emerging as a new therapeutic approach to restore normal function in the intestinal microbiota. In recent years, we have been interested to improve the efficacy of FMT in UC patients (Am J Gastroenterol 2010;105:1820-9). We have undertaken FMT with the aim of reconstituting an intestinal microbial environment that promotes remission in UC patients.
Methods: An antibiotic combination therapy with oral amoxicillin 1500mg/day, fosfomycin 3000mg/day and metronidazole 750mg/day followed by FMT was undertaken. The antibiotic combination was administered to UC patients for two weeks prior to FMT. A family member was selected as donor, and then blood and faecal samples were screened for pathogens according to "Amsterdam protocol for FMT" (Gastroentrology 2013;145:946-953). The donor faecal suspension was transplanted to the patient's caecum as a single application via a colonoscope. Faecal microbiota of the donors and the patients after or before treatment (6 samples from each group, total 24 samples) were processed by sequencing and analysis of the 16S rRNA gene using a Next-generation sequencer MIseq (Illmina). Up to 8,277,985 reads (average 306,592 reads per sample) were obtained, and 17 bacterial phyla 27 strains were identified.
Results: A 100% stacked bar chart was prepared. After a two-week-antibiotics therapy, the proportion of phylum Bacteroidetes significantly decreased from 29.2 ± 19.3% before treatment to 1.0 ± 1.2% ($P<0.01$), while the proportion of phylum Proteobacteria significantly increased from 9.1% ± 11.7% to 78.6 ± 20.2% ($P<0.001$). In half of the post-FMT patients, the proportion of phylum Bacteroidetes increased up to the level of donor (average 42.4 ± 10.9%). Further, along with the recovery of the Bacteroidetes strains after FMT, a trend toward an improvement in patients' clinical symptoms score was noted.
Conclusions: FMT carries a promise for a natural and toxicity free intervention to replenishing the large intestine with therapeutically relevant strains of bacteria, and achieve disease remission. To our

knowledge, this is the first clinical study of a sequential therapy involving FMT following a combination of antibiotics. We hope that the strategy we have applied may serve as the basis for further progress in understanding how alterations of the intestinal microbiota may become an effective therapeutic strategy for UC patients.

P569
Systemic and peritoneal inflammatory response after laparoscopic vs open emergency colectomy for acute severe ulcerative colitis

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Background: In comparisons of laparoscopic and open surgery, significantly better protection of the systemic immune system was shown with laparoscopic cholecystectomy and Nissen fundoplication than with the conventional approach. These findings have not been investigated in patients with acute severe ulcerative colitis (UC) who require emergency colectomy. This study was to evaluate differences in both the systemic and peritoneal immune response after laparoscopic and open emergency colectomy in patients with acute severe UC.

Methods: Thirty patients underwent hand-assisted laparoscopic colectomy and 30 patients open colectomy. All patients underwent total colectomy with closure of the rectal stump and construction of an end-ileostomy. Interleukin (IL)-1β, IL-6 and tumour necrosis factor (TNF)-α in plasma and peritoneal fluid from a drainage tube were measured on postoperative days 0, 1, 3 and 7. Leukocyte and platelet counts, and C-reactive protein (CRP) levels were also measured perioperatively. Further, incidence of septic complications such as leak, fistula, intra-abdominal abscess or wound infection was investigated.

Results: Between the two groups, patients were matched with respect to age, sex, UC duration, severity, extent, and medications at surgery. Septic complications occurred in 3 patients in each group. IL-1β, IL-6 and TNF-α levels in plasma and peritoneal fluid were not significantly different between the two groups during the entire study period. Similarly, leukocyte and platelet counts, and CRP levels were not significantly different between the two groups during the study period.

Conclusions: Based on the assays of IL-1β, IL-6 and TNF-α levels in the plasma and the peritoneal fluid, this study did not show any significant differences in the systemic and peritoneal immune response after laparoscopic vs open emergency colectomy in patients with acute severe UC. Likewise, surgical approaches did not affect the incidence of septic complications. This study shows that laparoscopic approach can be safely performed for patients with acute severe UC who required emergency colectomy.

P570
The Young Adult's Perception of Life with Inflammatory Bowel Disease and a Stoma: A qualitative examination

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Background: While the experiences of young adults with Inflammatory Bowel Disease (IBD) and a resultant stoma have been investigated in the USA, there is a paucity of such qualitative research in Europe. In Ireland, the voices of this patient cohort have remained remarkably silent.

1. Control	Patient controlled by dictations of IBD
	Efforts made by patient to regain control
	Control of decision to proceed with surgery
2. Secrecy	Delay in diagnosis due to concealment of symptoms
	Awareness of family and friends of IBD and resultant stoma
	Equating success of surgery with invisibility of stoma
	Frankness of consultants
3. Patient Education and Support Services	Experiences with stoma aftercare services
	Self-education
	Experiences with Consultant Surgeons and Gastroenterologists
	Patient support groups
4. Living with Challenging Emotions	Embarrassment
	Fear
	Insecurity
	Frustration/Anger
5. Acceptance and Regrowth	Initial shock
	Regaining independence
	Eventual acceptance

The purpose of this study was to achieve an understanding of the lived experience as depicted by young adults with IBD and a stoma.

Methods: A qualitative approach was adopted comprising a single, detailed semi-structured interview with each of the 5 participants aged 20-30 years. Purposive sampling was employed. Those with a histological diagnosis of IBD and a consequential stoma within the last 12 months were recruited via a letter of invitation. Verbatim transcripts of these interviews and associated field notes were analysed using Interpretative Phenomenological Analysis. Ethical approval was attained prior to study commencement.

Results: Five superordinate themes emerged from the analysis as outlined in table 1: (1) Control, (2) Secrecy, (3) Patient education and support services, (4) Difficult emotions, (5) Acceptance and growth. A universal struggle to preserve autonomy of bodily function, emotions and healthcare decisions existed among participants. Patients embraced the predictability of their stoma relative to the restraints imposed on them by their erratic pre-operative bowel habit. Participants also reiterated the importance of patient education in order to avoid uncertainty and distress for some patients.

Conclusions: This study provides a greater understanding of the education and support requirements of this patient cohort and highlights existing deficits in our healthcare system. Furthermore, we gain a unique insight into the obstacles, fears and emotions of this patient cohort. This resource is invaluable and may serve to guide us when planning resources for patients faced with stoma formation

P571
Long-term operation rate and related prognostic factors in patients with Crohn's Disease treated by infliximab maintenance treatment

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Background: Maintenance treatment by anti-tumour necrosis factor (anti-TNF) antibody has enabled achieving long-term remission in patients with Crohn's disease (CD). However, the factors that allow patients to avoid operative intervention remain unclear. The aim of this study was to investigate the long-term operation rate and related prognostic factors in patients with CD treated by infliximab maintenance treatment.

Methods: Retrospective data was collected from luminal CD patients treated with 5 mg/kg of infliximab for >14 weeks between May 2002 and August 2012 at the IBD Center, Sapporo Kosei General Hospital. The cumulative operation rates following the first infliximab administration was estimated using the Kaplan-Meier method. Further, prognostic factors related to the cumulative operation rates were evaluated using a log rank test and a multivariate Cox regression analysis.
Results: A total of 276 patients were included in this study. Of these, 72 were females with a mean age of 31.2 years and mean disease duration of 7.5 years. The mean C-reactive protein (CRP) level at the first infliximab administration was 2.18 mg/dl. One hundred fifty-two patients had ileocolitis, 68 had ileitis and 56 had colitis. Additiomally, 111 patients had stricturing disease, 36 had intra-abdominal fistulas and 114 had perianal disease; 82 patients were smokers. Concomitant treatment with immunomodulators (azathioprine or 6-mercaptopurine), 5-aminosalicylic acid, elemental diet therapy and prednisolone was administered in 197, 245, 194 and 28 patients, respectively. Before initiating infliximab therapy, 89 patients had had at least 1 surgery, and no patients had prior use of other anti-TNF agents. The 3-, 5- and 7-year cumulative operation rates were 10%, 16% and 23%, respectively. In univariate analysis, the stricturing disease (P = 0.036) and the higher CRP level at the first infliximab administration (>1.00 mg/dl; P = 0.034) were significant prognostic factors for the higher cumulative operation rates. Conversely, concomitant treatment with immunomodulators significantly decreased the cumulative operation rate (P = 0.032). In a multivariate Cox regression analysis, the CRP level at the first infliximab administration (>1.00 mg/dl) and concomitant treatment with immunomodulators were identified as independent predictors for the cumulative operation rates.
Conclusions: Approximately 80% patients receiving infliximab maintenance treatment will not require an operation for up to 7 years. It was demonstrated that combination therapy of infliximab and immunomodulators decreased operative risk. Conversely, stricturing disease and higher CRP level at the first infliximab administration may be prognostic factors for a poor long-term operation rate.

P572
Paradoxical articular manifestations in inflammatory bowel diseases patients treated by anti-TNF

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Background: Articular manifestations are the most common extra-intestinal manifestations associated to inflammatory bowel diseases (IBD). They are named "paradoxical" when they occur during treatment, notably anti-TNF drugs, that are expected to prevent or at least treat them. The aim of this study was to assess the frequency, the characteristics and the associated factors of paradoxical articular manifestations during anti-TNF treatment for IBD.
Methods: In this prospective single-center study, a rheumatological examination was systematically proposed to all IBD patients treated with infliximab (IFX) or adalimumab (ADA) to assess the prevalence of articular manifestations and distinguish those related to IBD treatment of those associated with IBD. Paradoxical manifestations were defined by the occurrence of articular manifestations (excluding induced-lupus and hypersensitivity reaction) during anti-TNF therapy in a patient in IBD intestinal remission. Dosage of biological inflammatory (CBC, CRP), immunological markers (immunoglobulins, anti-nuclear antibody (Ab), anti-DNA Ab, anti-CCP Ab, complement factor, rheumatoid factor, ASCA) and HLA-B27 allele and through serum IFX/anti-IFX Ab were systematically performed.
Results: Between May 2013 to April 2014, 79 patients with Crohn's disease (CD) and 20 ulcerative colitis (UC) treated with IFX (n=80) or ADA (n=19) were included. Immunosuppressants (azathioprine/methotrexate) were associated in 12% of cases. Articular manifestations were observed in 50 (62%) patients treated by IFX and 12 (63%) patients treated by ADA. Twelve percent (n=12) were considered associated to IBD and 16% (n=16) associated to anti-TNF therapy. Among patients with articular manifestations associated to anti-TNF therapy, we identified 12% (n=12) of paradoxical effects, 2% (n=2) of induced lupus and 2% (n=2) of hypersensitivity reaction. Among the 12 patients with paradoxical effects during IFX (n=9) or ADA (n=3) therapy, 11 were treated for CD and presented peripheral arthritis; 3 patients presented a spondyloarthropathy. Paradoxical cutaneous manifestations were associated in 25% of cases. The median duration of anti-TNF therapy was 47 months (Q1=30-Q3=77). No patient has discontinued anti-TNF because of the articular manifestations. Three patients were treated with methotrexate. No clinical or biological factors were associated with the occurence of paradoxical manifestations.
Conclusions: Paradoxical articular manifestations in IBD patients treated by anti-TNF are common, affecting more than 10% of patients. These events are generally mild and not followed by the discontinuation of anti-TNF drugs.

P573
eHealth optimises documentation and enables live access to IBD Multi Disciplinary Team outcomes

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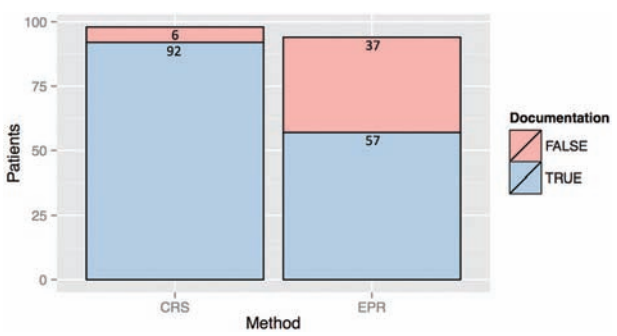
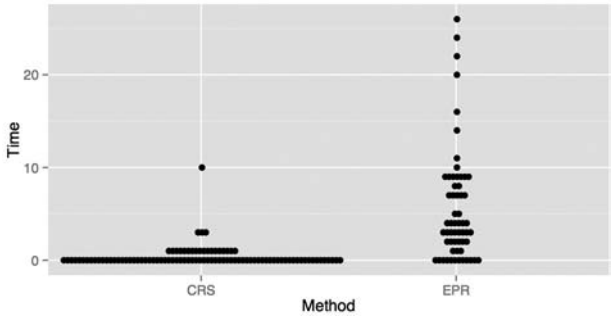
Background: At the Royal London Hospital (Barts Health NHS Trust), weekly multidisciplinary (MDT) meetings are held to discuss patients with complex inflammatory bowel disease (IBD). A recent report has highlighted the role of electronic record keeping in improving effectiveness of MDT meetings [1].
Documentation of IBD MDT outcomes has historically relied on a three-step process:
1) Individual IBD Consultant taking written notes on their own patients' MDT outcomes.



"IBD MDT outcome documentation rates pre (EPR) and post (CRS) intervention."



"Dot plot comparing time (in days) required for individual MDT outcome to be available pre (EPR) and post (CRS) intervention"

2) Subsequent letter dictation, sent to GP and patient by secretary.
3) Letter scanned into "semi-electronic" patient record "EPR" file-store by administrative staff.
We streamlined this process and assessed the effectiveness of a single-step intervention (documentation of MDT outcomes straight into Trust-wide electronic patient health records "CRS", also visible live to primary care GPs) in:
a) Improving MDT documentation rates.
b) Providing same day access to MDT outcomes to healthcare professionals.
Methods: We retrospectively reviewed electronic hospital records of all patients discussed 2 months prior (n=94) and 2 months post (n=98) our intervention. Comparison of pre and post intervention findings (R statistics package) was performed.
Results: 192 patients were discussed (94/192 pre and 98/192 post intervention) over a period of four months. Following live CRS electronic documentation, 92/98 (94%) patients had a formally recorded IBD outcome compared to 57/94 (61%) previously, a significant 33% improvement (p=3.3e-08, chi-squared test).
Median time to data entry was 0 days post intervention (Interquartile Range 0) compared to 4 days (Interquartile Range 1.5–9) prior (p=2.2e-16, Mann Whitney U test).
Conclusions: Patients with IBD often rely on acute services and staff (emergency & acute medicine, rotating gastroenterology trainees) that manage unfamiliar inpatient and outpatient complex cases immediately after a MDT discussion, often during night shifts and busy clinics. Live electronic data input improves completion rates and provides same day MDT outcomes, optimising access to healthcare professionals involved in the care of patients with IBD. Electronic notes are entered in letter format (GPs can view live data), with hard copies generated and sent to patients.
We are now expanding our model to other MDTs (e.g. Cardiology) with similar needs.

References:

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P574
The efficacy of azathioprine and tumour necrosis factor antagonists in preventing Crohn's Disease recurrence after ileal resection: a tertiary center real-life experience

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Background: About one-third of Crohn's disease (CD) patients will undergo abdominal surgery within the first 5 years after diagnosis. However, more than 70% of these patients will develop endoscopic recurrence by the end of the first year after surgery. Both azathioprine and anti-tumor necrosis factor agents (anti-TNFs) have shown efficacy in preventing post-operative recurrence of CD, but there are limited data comparing different preventive strategies in real-life.
Methods: 103 CD patients, followed-up in a tertiary IBD Center, that underwent ileal resection with ileocolonic anastomosis between January 2007 and October 2014, were enrolled. All subjects were given preventive therapy after a median time of 1 month (range 0.2-9.2) with anti-TNFs (infliximab or adalimumab), thiopurines (azathioprine/6-MP) or mesalazine (controls), according to the risk of early recurrence. The primary outcome was to assess the rate of endoscopic recurrence (defined by Rutgeerts score (Rs) >2) within a maximum of 24 months (median 8.2 months). Statistical analysis included logistic regression with univariate analysis for risk factors and Fisher exact test for variance. All differences were considered statistically significant for $p<0.05$.
Results: Among the study population, 24 patients (23.3%) received anti TNF (16 infliximab; 8 adalimumab), 43 (41.7%) received thiopurines, 36 (34.9%) received a mean dose of mesalazine 3 g/day. The presence of 2 or more risk factors (smoking, prior intestinal surgery, penetrating disease behavior, perianal disease) was not associated with a higher risk of endoscopic recurrence (OR 1.53; 95% CI 0.99 to 237; p=0.05), but multivariate analysis showed that only the active smokers were more likely to have endoscopic recurrence (OR 3.09; CI 95% 1.14 to 8.34; p=0.02). Endoscopic recurrence rate was significantly lower in subjects receiving anti-TNFs and thiopurines compared to mesalazine (33.3% vs 66.6%, p=0.017; 41.8% vs 66.6%, p 0.04, respectively). Finally, anti-TNFs and thiopurines were not effective in the prevention of severe recurrence (defined by Rs 3-4). Escalation therapy was performed in 18 patients (28% from mesalazine to anti-TNFs (group A); 22% increased the dose of anti-TNFs (group B); 33% from mesalazine to thiopurines (group C); 17% from thiopurines to anti-TNFs (group D). 50% of them had an improvement of endoscopic recurrence (60%, 25%, 50%, and 33%, respectively), after a median time of 16 months.
Conclusions: Both anti-TNFs and thiopurines were effective in the prevention of endoscopic recurrence compared to mesalazine. No differences were found between anti-TNFs and thiopurines. Escalation therapy improved mucosal lesions in 50% of patients.

P575
The use of mesenchymal stromal cells in order to achieve deep (biological) remission of Ulcerative Colitis

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Background: Currently, the concept of remission ulcerative colitis (UC) should be defined as a condition in which there is no biological and histological signs of inflammation - «remission beyond symptoms». Biological remission UC involves the absence of symptoms,

healing of intestinal mucosa, as well as normalization of serum and fecal biomarkers active inflammation.
Objective: To study the effect of mesenchymal stromal cells (MSCs) of bone marrow to achieve biological remission in patients with ulcerative colitis.
Methods: 68 patients with UC were divided into two groups. The first group of patients (n=36) received standard anti-inflammatory therapy with 5-aminosalicylic acid (5-ASA) and glucocorticosteroids (GCS) + MSCs. Age - 19 to 58 years old (ME-29). The second group of patients (n=32) received the standard anti-inflammatory therapy with 5-ASA and corticosteroids. Age of this group 20 to 62 years (ME-28). Immunobiological treatment efficacy were assessed by the level of CRP and fecal calprotectin (FCP). Histopathology evaluation was performed on the index Geboes. Evaluate the effectiveness of therapy was performed at 2, 6 and 12 months. Baseline CRP in acute disease in the 1-st group was 28,6 ± 2,4 mg/l, in the 2-nd - 28,0 ± 3,0 mg/l (p=0.363). Baseline FCP in the 1-st group was 730 ± 23,4 mcg/g, in the 2-nd - 810 ± 30,1 mcg/g (p=0.086). Index Geboes in the 1-st group was 4,2 ± 0,2 points in the 2-nd - 4,1 ± 0,3 points (p=0.107).
Results: After 2 months, the level of CRP in patients in group 1 was 10,6 ± 1,1 mg/l, in the 2-nd - 11,0 ± 1,1 mg/l (p=0.139). The level of the FCP in patients in the 1st group was 110 ± 12,0 mcg/g, in the 2-nd - 120 ± 12,0 mcg/g (p=0.001). Index Geboes in 1-st group was 0,9 ± 0,1 points, in the 2-nd - 1,1 ± 0,1 points (p<0.001).
After 6 months, the level of CRP in patients in 1-st group was 6,5 ± 0,6 mg/l, in the 2-nd - 8,9 ± 0,1 mg/l (p<0.001). The level of the FCP in patients of 1-st group was 80 ± 5,0 mcg/g, in the 2-nd - 95 ± 0,5mcg/g (p<0.001). Index Geboes in 1-st group was 0,9 ± 0,1 points, in the 2-nd - 1,0 ± 0,1 points (p<0.001).
After 12 months, the level of CRP in patients in 1-st group was 8,6 ± 1,2 mg/l, in the 2-nd - 9,4 ± 1,0 mg/l (p=0.004). The level of the FCP in patients of 1-st group was 75 ± 5 mcg/g, in the 2-nd - 80 ± 5 mcg/g (p<0.001). Index Geboes in 1-st group was 0,6 ± 0,1 points, in the 2-nd - 1,0 ± 0,1 points (p<0.001).
Conclusions: Inclusion of MSCs in a comprehensive anti-inflammatory therapy UC contributes to a deeper immunobiological and histological remission UC.

P576
Therapeutic effects of mouse bone marrow-derived clonal mesenchymal stem cells in a mouse model of inflammatory bowel disease

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Background: Mouse bone marrow-derived clonal mesenchymal stem cells (mcMSCs), originated from a single cell by a subfractionation culturing method, are recognized as new paradigm for cell-based therapy.
Methods: Dextran sulfate sodium (DSS)-induced colitis was induced in C57BL/6 male mice by administrating 2.5 % DSS in a drinking water for 6 days. 4 × 105 cells mcMSCs were injected through tail vein on days 1, 3 and 5, respectively.
Results: mcMSCs significantly reduced the DAI score, including weight loss, stool consistency, and intestinal bleeding, and significantly increased survival rates (p<0.01). The pathological scores were significantly improved with mcMSC (p<0.0001), especially mucosal regenerations accompanied with lesser apoptosis were significant beneficiary actions imposedby mcMSCs(p<0.001). The levels of inflammatory cytokines, including TNF-a, IFN-g, IL-1b, IL-6, and IL-17accompanied with NF-kB repression, were all significantly decreased in mcMSC treated group compared to the control group(p<0.01), and macrophage and neutrophil influx were significantly reduced (p<0.05).
Conclusions: mcMSCs showed significant therapeutic effects in experimental colitis through anti-inflammatory and restorative activities, are applicable as a potential source of cell-based therapy in IBD.

P577
Chemoprevention by mesalamine for colorectal cancer in UC-patients: a meta-analysis

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Background: Mesalamine, a 5-ASA preparation, is used in the treatment of mild ulcerative colitis (UC). It is known to have an anti-inflammatory effect. Multiple studies ascribed chemopreventive properties to this drug throughout the years. This meta-analysis aims to determine the chemopreventive effect of mesalamine (and other 5-ASA preparations) on colorectal neoplasia in patients with UC.
Methods: To determine whether the risk of developing colorectal cancer (CRC) is indeed lower in UC patients using mesalamine, a search for literature on this subject was performed on PubMed and Web of Science up to October 2014. To ensure suitability of the found publications, reviews, in vitro studies and studies on animal models were excluded.
Results: After screening 274 publications, 27 were selected for full-text review. Among these, 8 trials were found eligible and were included in the meta-analysis. It showed an odds ratio of 0.36 (95% CI; 0.21-0.62). Moreover, two meta-analyses were conducted to determine the influence of potential bias. These showed only minor difference as compared to the first meta-analysis.
Conclusions: Mesalamine significantly reduces the risk of CRC in patients with UC and can be considered chemopreventive. The results of this study may be used as an indication for long-term prescription of mesalamine for a chemopreventive purpose.

P578
Assessment of satisfaction with healthcare in patients with inflammatory bowel disease: An Online Korean Association for the Study of Intestinal Disease (KASID) Survey

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Background: Inflammatory bowel diseases (IBD) is chronic relapsing condition with unpredictable course and unclear etiology impacting on patient's quality of life. Patient satisfaction with healthcare services provided for IBD is essential to improve treatment adherence,

producing improvements in disease outcomes. The aim of the present study was to assess patient's satisfaction with healthcare as well as treatment and patient-physician communication in Korea.

Methods: Self-administered, computer-aided internet-based questionnaires were distributed to members of Korean patients'organization for IBD from March to April 2014 by Korean Association for the Study of Intestinal Disease (KASID).

Results: Surveys were completed by 502 patients with IBD [Crohn's disease(CD): 276; ulcerative colitis(UC): 226]. Most (78%) of respondents received a final diagnosis within a year from noticing first symptoms. However, for 22%, it took longer than a year, for 4% longer than five years. Most common reason for the delayed hospital visit was lack of knowledge for IBD. Approximately half of patients (47%) had been hospitalized in the past 5 years due to IBD. One fourth (25%) patients had been operated for IBD, rising to 42% among the patients with CD. With regard to treatment, 51% of all respondents reported that they were very or somewhat satisfied with their current treatment, and 57% of the respondents reported that the doctors provide the best range of options for patients to get in touch. Considering accessibility to the hospital, 35% of patients have easily adequate access to a physician. As for communicating with physicians, 33% of the respondents felt that they were not able to tell their physician something potentially important about their illness. Furthermore, 75.3% of the respondents felt that their physician should have asked more probing questions to better understand their disease status. Only 37% of respondents say that their doctor service is best at giving them sufficient time at clinic. In addition, 44% of respondents feel that doctor best understand the impact that IBD has on their lives.

Conclusions: There is still room for improvement in healthcare services including access to the clinic and patient-physician communication for IBD patients in Korea. Social perspective and understanding of impact of IBD on patient's lives should be obtained to build better treatment and care system for Korean IBD patients.

P579
Hematologic Malignancies Among 1740 Inflammatory Bowel Disease Patients: Long term follow up Data from a Tertiary Center

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Background: There is a concern that inflammatory bowel disease (IBD) and medications especially thiopurines and anti-TNF agents used in the treatment may be associated with increased risk of various hematologic malignancies (HM). We aimed to describe IBD patients (pts) who developed HM.

Methods: Retrospective review of medical records from all 1740 pts treated for IBD at a single gastroenterology clinic from 1999 to 2014 was performed. Pts with HM were further evaluated for the following parameters; parameters in the table and MCV before AZA use, MCV at the time of HM diagnosis, duration of AZA use.

Results: A total of 6 pts (3/3, M/F) were identified with HM (5 MDS and 1 AML). Characteristics of the pts are summarized in Table. Median age at diagnosis of IBD and HM were 38.5 (18-55) and 48.5 (29-59) respectively. All of these 6 pts except one had been exposed to AZA and 4 were treated also with anti TNF. All 5 patients experienced leukopenia during AZA therapy. Median time of AZA treatment duration was 10 (6-18) months. Median time between IBD and HM was 6.5 years. At the time of IBD diagnosis MCV changed between 84-101. Only 1 patient had MCV > 100 before AZA treatment. In 4 patients MCV was ≤ 92 fl before AZA treatment.At the time of HM diagnosis 4 pts had a mean corpuscular volume (MCV) >98 fl Most of the patients (4/6) did not have active IBD at the time of HM diagnosis. Iron deficiency anemia with/without chronic diease anemia was exist in 5/6 pts.Median Hgb level was 11.7 (range:6.9-12.5)

Conclusions: Overall risk of myeloid malignancies may be increased in pts with IBD either as a consequence of AZA treatment(5/6)or in relation to unknown factors (1/6). Pts with leukopenia during AZA and MCV >98 fl (after exclusion of other causes) may be prone to develop HM and deserve increased awareness. Background iron deficiency may have some influence on the all values of MCV and MCV increment.

P580
Allogeneic hematopoetic stem cell transplantation to treat refractory Inflammatory Bowel Disease in an X-CGD carrier with non-random X-inactivation

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Background: Five genetic traits are known to cause chronic granulomatous disease (CGD), but the most common one is X-linked CGD (X-CGD) due to hemizygous mutations in CYBB. CGD is characterized by invasive bacterial and fungal infections accompanied by granulomatous inflammation. Inflammatory bowel disease (IBD) can be an additional or isolated manifestation. Allogenic hematopoietic stem cell transplantation (alloHSCT) is the standard curative treatment. X-CGD carriers normally show random X-chromosome inactivation and retain 50% of NADPH-oxidase activity. Nevertheless, they can develop aphthous stomatitis and discoid lupus erythematosus. In rare cases, X-CGD carriers present

Patients characteristics. AML, acute myeloid leukemia; Aza, azathioprine; GIBD gastointestinal Behcet disease, MDS, myelodysplastic syndrome; MTX, methotrexate; SSZ, salazopyrin; TNF, tumor necrosis factor.

sex	IBD	Age at diagnosis of IBD	AZA use	Other Tx	HM	Age at diagnosis	Time between IBD and HM (years)	Follow-up time (years)	Life statatus
M	CD	32	yes	Anti-TNF MTX	MDS	47	15	15	alive
F	CD	18	yes	Anti-TNF SSZ	MDS	29	11	11	alive
M	CD	45	yes	Anti-TNF	MDS	50	5	5	alive
F	GIBD	25	yes	steroids Anti-TNF	MDS	30	5	8	alive
F	UC	55	yes	SSZ	AML	59	4	5	alive
M	CD	52	no	SSZ	MDS	52	0.15	0.5	alive

with non-random X-chromosome inactivation and, depending on the remaining NADPH-oxidase activity, can develop invasive bacterial and fungal infections (activity <10%) or autoinflammatory manifestations (activity 10-15%).

Methods: We report on an X-CGD carrier with non-random X-chromosome inactivation and NADPH-oxidase activity of 30%. At the age of 12 years, she developed severe Crohn-like IBD that was refractory to treatment with exclusive enteral nutrition, immunosuppression (steroids, methotrexate, azathioprine and 3 different anti-TNF drugs. As her clinical course aggravated over time she received 03/2014 alloHSCT from a matched unrelated donor (10/10) after conditioning with submyeloablative targeted busulfan, fludarabine and alemtuzumab at the age of 20 years.

Results: The patient engrafted at day +15 without any major complications and no signs of graft versus host disease (GVHD). Four months post-tx being off any IBD-medication her colon had macroscopically healed with normalization of fecal calprotectin, but the known stenosis in the left colon remained. A recent clinical and endoscopic flare was successfully treated with short term antibiotics.

Conclusions: Screening for CGD is recommanded in young patients with refractory IBD. To our knowledge, this is the first case of an X-CGD carrier with non-random X-chromosome inactivation and IBD who has been successfully treated with alloHSCT.

P581
A Pharmacokinetic Study of Ferric Maltol (ST10; Fe-M) at 3 Dosages in Inflammatory Bowel Disease (IBD) Patients with Iron Deficiency

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Background: Fe-M (ST10) is a novel Fe3+ form of iron that has been shown to be well tolerated in IBD patients unable to use ferrous sulphate, and successfully correct Iron Deficiency Anaemia (IDA) at a 30mg twice a day (bid) dose (AEGIS 1 & 2). This study examined whether higher doses would result in greater iron absorption.

The aim was to investigate the single and repeat dose kinetics of iron and maltol components of Fe-M in IBD patients with iron deficiency.

Methods: Eligible patients were adults with IBD and iron deficiency, defined by ferritin <30 µg/L, or ferritin <50 µg/L and transferrin saturation (TSAT) <20%; and haemoglobin (Hb) ≥ 8.5 g/dL. Patients were randomised to Fe-M oral capsules 30, 60 or 90 mg bid for Days 1 to 8; taken on an empty stomach. PK blood and urine samples were collected after the first morning dose Day 1 and after a final dose morning Day 8.

Results: 24 IBD patients (UC: 11; CD 13; mean age: 39 y; 66% female; mean baseline ferritin 13.9ug/L; TSAT 17.9%; serum iron 12.5umol/L; Hb 13g/dL) were randomised.

For all doses plasma concentrations of maltol and maltol glucuronide (maltol-G) increased rapidly, reaching Cmax 1-1.5 hours post dose, declining to baseline after 3 and 6 hours. Exposure to maltol G was higher compared to maltol. Urine PK showed maltol is rapidly excreted as maltol G. Serum iron and TSAT increased after dosing, with maximum values between 1.5-3 hours post dose for all groups; the PK profiles were similar on Days 1 and 8.

Day 1 TSAT increase from baseline was higher in the 60 and 90mg groups compared to the 30mg (57.4 and 54.7 vs 24.8%). Ferritin increased in all groups by Day 8, but was greater in the 60 and 90mg groups (15.7 and, 17.1 vs 7.22µg/L). Reticulocyte Hb increased in all groups by Day 8; the rise was greater in the 60 and 90mg groups compared to the 30mg (3.37 and 3.07 vs 0.92pg).

The most common adverse events (AEs) were GI (7 subjects, 29.2%); non IBD-related GI AEs were more frequent in the 90mg group (57.1% of subjects vs 11.1% and 25.0% for 30 and 60mg). AEs were of mild or moderate intensity. Diarrhoea and abdominal pain were the most commonly reported AEs (12.5% and 8.3% of subjects).

Conclusions: The PK data from this study are consistent with previous data indicating that maltol is rapidly glucuronidated after Fe-M dosing, while iron is independently absorbed. 30mg Fe-M (ST10) has been shown to be well tolerated and effective in correcting IDA; however results of this study show 60mg bid resulted in greater iron absorption as evidenced by TSAT, ferritin and reticulocyte Hb rise. Additional clinical studies are needed to see if this would result in a more rapid Hb increase in IDA subjects.

P582
Serological monitoring for HBV infection and response to vaccination in Greek patients with IBD: a multi-centre study

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Background: Low vaccination rates and sub-optimal responses to vaccination against hepatitis B virus (HBV) have been reported in patients with IBD, raising questions regarding the appropriate management in this setting. We have initiated a multi-centre study to evaluate a) the percentage of Greek IBD patients with protective anti-HBs levels; b) the response to vaccination; and, c) the effect of various patient and disease-related parameters on the efficacy of vaccination.

Methods: We reviewed the clinical records of all IBD patients with a regular follow-up at 4 tertiary hospitals at the Athens Metropolitan area. All patients were tested for HBsAg, anti-HBs and anti-HBc antibodies. Patients less than 65-y-old with negative tests for both HBsAg and anti-HBc were managed as follows: a) negative anti-HBs without/unknown history of vaccination: 3-dose vaccination (0, 1, 6 mo) with 20 µg, b) history of vaccination: anti-HBs levels >100iu/l: annual follow-up of anti-HBs levels; anti-HBs 10-100iu/l, 1-3 20 µg doses with anti-HBs measurement after each dose; no anti-HBs, 1-3 40 µg doses with anti-HBs measurement after each dose. Vaccination

was considered complete when anti-HBs>100iu/l were detected. In patients with negative anti-HBs levels after 3x20 μg doses, vaccination was repeated with a double dose (40 μg).

Results: We have included 287 IBD patients so far in our study (CD=180, UC=104, IC=3, male=147, age: 42.9±16.0, 16-89). Among 213 patients with recent HBV serology, there were 3 with chronic HBV infection (HBsAg+) and 22 patients with previous exposure to HBV (HBsAg-, anti-HBc+). Protective immunity due to previous vaccination (HBsAg-, anti-HBc-, anti-HBs+>100iu/L) was detected in 23.5% (n=50). Sub-optimal anti-HBs levels were seen in 8.9% (n=19). The majority of tested patients were negative for all three markers (HBsAg, anti-HBc, and anti-HBs), indicating lack of effective vaccination (n=119, 55.8%). If only patients less than 65-y-old were analyzed (n=180), effective immunity was still absent in 54.4%. There was significant association ($p<0.001$) between age and presence of protective immunity that is probably due to the widespread application of HB vaccination at early ages in the last 2 decades in Greece. Vaccination was commenced in 64 patients so far, with 24 having finished their regimen. Response has been assessed in 10 patients with 6 (60%) achieving sufficient response and 4 requiring further vaccination.

Conclusions: A significant percentage of Greek IBD patients lack protective immunity against HBV. The "classical" vaccination regimen often fails to induce adequate levels of anti-HBs antibodies. Increased awareness, intensified vaccination protocols and frequent testing of response may be required in this population.

P583
Sequential Change of Endoscopic Findings and Therapeutic Efficacy of Anti-TNF alpha therapy for Patients with Intestinal Behçet's Disease

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Background: Behçet's disease (BD) is a systemic inflammatory disease characterized by repeated oral and genital ulcerations, ocular lesions, skin manifestations, arthritis, vasculitis, and gastrointestinal involvements. Intestinal BD is characterized by intestinal inflammation with round and oval ulcers typically in the ileocecum and is associated with gastrointestinal symptoms, which are often uncontrollable, relapsing, and can cause acute intestinal bleeding or perforation. Despite a wide range of treatment options, a significant proportion of patients with intestinal BD remain refractory to medical therapy. We conducted this study in an attempt to clarify the sequential change of endoscopic findings, and therapeutic efficacy of treatment options for patients with intestinal BD.

Methods: We retrospectively reviewed the medical records of 43 consecutive patients who regularly underwent colonoscopy and double-balloon enteroscopy for intestinal BD from January 2004 to September 2014. Diagnosis of intestinal BD was based on the Mason-Barnes criteria. For the endoscopic efficacy assessment, the volume of the largest ileocecal or colonic ulcer which was product of the largest and shortest ulcer diameter and ulcer depth was compared. The sequential change rate of ulcer volume was also assessed.

Results: 43 patients (M/F: 27/16) who underwent colonoscopy for intestinal BD were enrolled. Median age at diagnosis was 42 years (13-77 years). Median age was 51 years (23-82 years). Disease duration was 8.4±7.6 years. 32 patients (49%) have oral aphtus ulcer, 16 patients (37.2%) have skin lesions, 9 patients (20.6%) have uveitis, and 5 patients (11.6%) have genital ulcer (including overlapping cases). The disease locations (65 lesions) were 34 cases of ileocecal valve and cecum (52.3%), 8 cases of rectum (12.3%), 8 cases of ascending-descending colon (12.3%), 6 cases of small intestine (9.2%), 4 cases of sigmoid colon (6.2%), 4 cases of esophagus (6.2%), and 1 case of stomach (1.5%) (including overlapping cases). Among 34 ileocecal valve and cecum cases, 23 cases (67.6%) showed typical oval deep ulcer. Among several treatment options, anti-TNF alpha therapies (Infliximab and Adalimumab) showed the highest median improvement rate of ulcer volume (74.4%), and the lowest relapse rate (10%). Between patients treated with anti-TNF alpha therapy (group A, n=10) and patients treated with conventional therapy (corticosteroid, immunomodulators and 5-ASA) (group B, n=33), there was a statistically significant difference ($p<0.05$).

Conclusions: Anti-TNF alpha therapies have potentially positive effect in inducing and maintaining remission for patients with intestinal BD.

P584
Infliximab therapy for Japanese patients with ulcerative colitis: Efficacy, safety, and association between serum infliximab levels and early response in a randomized, double-blind, placebo-controlled study

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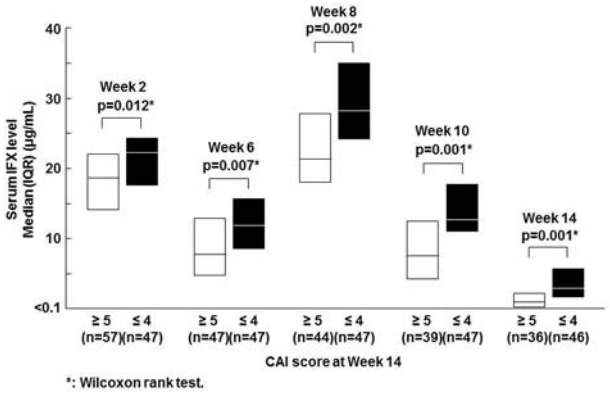
Background: Although infliximab (IFX) is reported to be effective for ulcerative colitis (UC), some patients show an inadequate response. Treatment in these cases should be immediately switched to another therapy. Here, we conducted a clinical trial to clarify the efficacy and safety of IFX in Japanese patients with UC (Japic CTI-060298). In addition, we conducted a post-hoc analysis to determine whether an early response to IFX is associated with serum levels of the drug.

Methods: The study was conducted under a randomized, double-blind, placebo-controlled design in 208 patients with moderate-to-severe active UC. Patients received placebo or 5 mg/kg IFX at Weeks 0, 2, and 6, and efficacy was assessed at Week 8. Patients with a lower Mayo score at Week 8 than at baseline were further treated with placebo or IFX at Weeks 14 and 22, and assessed for efficacy until Week 30, and for safety and pharmacokinetics until Week 38. Clinical response, clinical remission, and mucosal healing were defined by the Mayo score.

Results: At Week 8, clinical response rate, the primary endpoint, was significantly higher in patients who received IFX than in those who received placebo (54.8% [57/104] vs. 35.6% [37/104], p=0.005). Clinical remission rate showed a marginally significant difference (20.2% [21/104] vs. 10.6% [11/104], respectively; p=0.054) while mucosal healing rate showed a statistically significant difference (46.2% [48/104] vs. 27.9% [29/104], respectively; p=0.006). At Week 30, clinical response rate was significantly higher in the IFX group (46.2% [48/104]) than in the placebo group (31.7% [33/104]) (p=0.033). The incidence of adverse events and serious adverse events between groups was similar (IFX, 96.2% [100/104] and 17.3% [18/104]; placebo, 90.4% [94/104] and 18.3% [19/104],



"Figure: Serum IFX levels at Weeks 2, 6, 8, 10, 14 according to clinical efficacy at Week 14."

respectively). Serum IFX levels at Week 8 were highest in those with clinical remission, followed in order by those with a clinical response without remission and no response (p=0.009). Serum IFX levels at Week 14 markedly differed between patients with a Clinical Activity Index (CAI) of ≤ 4 and those with ≥ 5 (Figure). This significant difference in serum IFX level by CAI score at Week 14 was found from Week 2.

Conclusions: IFX was superior to placebo in achieving a clinical response and mucosal healing in Japanese patients with UC. An early response to IFX was associated with serum levels, and the relationship was seen even at the initial stage of administration.

P585
Preventing Crohn's Disease recurrence after resection with adalimumab: Role of drug and anti-drug antibody levels

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Background: Crohn's disease usually recurs after intestinal resection. Adalimumab post-operatively prevents recurrence in a majority of patients, but not in all. The cause of recurrence while on anti-TNF therapy is unknown. Low drug concentration and the development of anti-adalimumab antibodies (AAA) have been implicated in loss of response in established luminal disease, but their relationship to the efficacy of adalimumab in preventing postoperative recurrence is unknown.

Methods: Patients undergoing resection of all macroscopic Crohn's disease and receiving prophylactic adalimumab post-operatively were studied. Serum adalimumab levels and AAA were measured by homogenous mobility shift assay in adalimumab treated patients at 6, 12 and 18 months post-operatively. Endoscopic assessment was performed at 6 and/or 18 months post-operatively. IBDQ, CDAI, CRP and faecal calprotectin (FC) were measured at all time points.

Results: Adalimumab levels and AAA were measured over time from the time of surgery in 126 samples from 52 patients. 87 (69%) of samples were from patients on adalimumab monotherapy and 39 (31%) were from those on thiopurine combination therapy. 76 samples were matched to endoscopy: 29 (38%) and 47 (62%) of patients had recurrence (Rutgeerts score ≥ i2) at 6 and 18 months respectively. Combining 6 and 18 month endoscopic outcomes adalimumab concentration did not differ significantly between those in endoscopic remission compared to recurrence (10.0μg/mL vs 8.4μg/mL, p = 0.387). An adalimumab level of 9.3 was determined as the optimal cut-off for the prevention of endoscopic recurrence (Sensitivity 0.71, Specificity 0.51, PPV 0.33, NPV 0.84, AUROC 0.56). Of 4 patients with undetectable drug levels 2 were in remission and 2 had recurrent disease. Adalimumab drug level inversely correlated with FC (r = -0.2, p=0.038) but not with CRP (r = -0.11, p=0.364) or Rutgeerts score (r=0.04, p=0.734). AAA were present in 28% of all samples and 80% of samples with undetectable adalimumab level. AAA were more prevalent in those on monotherapy versus combination therapy (34% vs 13%, p=0.012). Median adalimumab levels were lower in patients with detectable AAA compared to those without (3.6μg/mL vs 12.0μg/mL, p<0.001).

Conclusions: Adalimumab drug levels post-operatively did not correlate with endoscopic recurrence after Crohn's disease resection. Drug levels did, however, correlate with FC, raising the possibility that higher drug levels prevent microscopic inflammation. Anti-adalimumab antibodies had a high prevalence and were associated with lower drug levels, suggesting that this may result in subsequent loss of protective effect and disease recurrence with prolonged treatment.

P586
Paradoxical psoriasis in a large cohort of IBD patients treated with anti-TNF alpha: 5 years-follow-up study

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Background: New onset of psoriasiform lesions is an emerging paradoxical side effect in a subgroup of patients with inflammatory bowel disease (IBD),treated with anti-TNF α. For patients with severe lesions unresponsive to topical therapy, it is necessary to withdraw from treatment with relevant impact on the management of IBD. The pathogenesis is not fully understood. Smoking seems to be a risk factor for developing these lesions. Aim of this study was to estimate the incidence of psoriasiform skin lesions in a large cohort of IBD patients treated with anti-TNF α and to analyze its clinical correlates.

Methods: A retrospective cohort study on all IBD patients who started anti-TNF α at our IBD center from January 2008 to December 2013 was performed. We recorded clinical characteristics at baseline:sex,type and duration of disease, extra-intestinal manifestations,smoking habit, type of anti-TNF α and concomitant immunosuppressive therapy. Information on time-dependent variables was updated at each clinical visit. Baseline characteristics of patients who did and did not develop psoriasis were compared with t-test, Mann-Whitney and Fisher exact test as appropriate. Proportional hazards regression models were used to estimate the association between each predictor and time to development of psoriasis. Time-dependent predictors were updated at each available time point.

Results: A total of 402 patients started anti-TNF α (both infliximab and adalimumab) between January 2008 and December 2013. There was preponderance of Crohn's disease (60%) and infliximab treated patients (60%),with a mean age at diagnosis of 40 ± 14 years. The median duration of disease was 6 years (range 0-29 years). Thirty-one percent of patients had also concomitant extra-intestinal manifestations and 21% were started on concomitant immunosuppressive therapy. Participants contributed a total of 839 person-years

of follow-up, during which 42 incident cases of psoriasis were recorded, all of them confirmed by punch biopsies, with an incidence rate of 5 per 100 person-years. Comparing IBD patients with and without skin lesions, we found higher rate of smokers in the subgroup of patients who developed psoriasis (18% vs 36%, p = 0.01). Cox-regression survival analysis confirmed smoking as independent predictor of psoriasis (HR 2.37, 95%CI 1.36, 4.48, p = 0.008). Concomitant immunosuppressive therapy was inversely related to psoriasis (HR 0.33, 95% CI 0.12, 0.92, p = 0.03).

Conclusions: New onset of psoriasis is a relevant side effect of anti-TNF α therapy with an incidence rate of 5 per 100 person-years. Smoking is confirmed as the main risk factor for developing lesions. The combination therapy with anti-TNF α plus immunosuppressants was associated with a reduced risk for psoriasis.

P587
Tacrolimus suppositories in therapy-resistant ulcerative proctitis - a single center experience

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Background: Ulcerative proctitis may be often managed with topical salicylates or budesonide alone, but in some patients, symptoms can be persistent, severe and have a profound impact on quality of life. Here we present an analysis from our outpatient clinic with add-on therapy of tacrolimus suppositories in patients who remained symptomatic despite conventional systemic and topical therapy.

Methods: We followed up 25 patients with ulcerative proctitis (E1, Montreal classification). Patients already received oral therapy consisting of an immunomodulator, prednisolone, salicylates and topical treatment with steroids or saliclyates. CAI according to Rachmilewitz was assessed at start of tacrolimus treatment and at every follow-up visit. The content of one 2 mg capsule of tacrolimus was moulded into suppositories by our pharamceutical department. Patients took 1 suppository BID. Tacrolimus serum levels, CRP, complete blood count and ESR along with creatinine were assessed via routine laboratory. Data was analyzed with Graph Pad Prisms.

Results: Median time from baseline to a consultation with assessment of CAI and tacrolimus serum level was 75 days. Three patients discontinued treatment after they experienced worsening of symptoms. Including these treatment failures, patients showed a significant decrease in CAI from 7,8 to 5,7 points (p=0,0279).

Mean tacrolimus trough level (n = 17) was 5,25 ng/mL (SD +/-2,601). The mean time from application of the last suppository was 17,6 hours (SD +/-6,862). The highest individual level was 10,2 ng/mL. We furthermore found a significant, moderate correlation between the change in CAI from baseline to follow-up and the height of tacrolimus trough level (Spearman r -0,555 (95% CI -0,8291 to -0,0657; p = 0,025). In terms of side effects, we registerd 1 case of hypertension, 2 cases of tingling sensation in hands and feet and tremor, 1 case of headache, muscle cramps at night and unspecific fatigue.

Conclusions: After addition of a topical formulation of tacrolimus (suppositories) in ulcerative proctitis refractory to standard treatment, we observed a significant decrease in CAI scores over a median treatment duration of 75 days. Mean tacrolimus serum levels were 5,253 ng/mL, and clinical benefit positively correlated with the height of serum levels. As envisioned by the use of topical treatment, side effects were rare and mild. On the other hand, tacrolimus serum levels were high enough to suggest that clinical benefit might be due to systemic tacrolimus effects. In this retrospective, observational study form our outpatient clinic, tacrolimus suppositories were used with success. Nevertheless, a further prospective study is needed to confirm these findings.

P588
A prospective evaluation of adalimumab drug levels and anti-drug antibodies using two commercial ELISA and the influence of 6-thioguanine nucleotides amongst patients with Crohn's disease

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Background: Some [1],[2] but not all [3] studies have demonstrated a relationship between therapeutic drug monitoring (TDM) of adalimumab (ADA) and outcomes in Crohn's disease (CD). We evaluated the utility of TDM of ADA in patients with CD using two commercially available ELISA

Methods: ADA drug levels (DL) and anti-drug antibodies (ADAb) were measured in CD patients (n=80) from 2 tertiary referral centres, between November 13 and February 14 using the Lisa-Tracker Duo ((LT) Theradiag, France) and Immundiagnostik ELISA ((IM) Germany). Faecal calprotectin (FC), C-reactive protein(CRP;<5ng/mL remission) and clinical activity (Harvey Bradshaw Index,(HBI)<5 remission)were also recorded. LT kits were provided by Theradiag at no cost.

Results: Neither assay showed a significant difference in ADA DL between remission and active disease (Table 1).

No significant differences in DL were observed in TDM performed at trough (day 13 or 14,n=13) or at any other time in the treatment cycle, nor amongst those receiving ADA every other week compared to weekly. Thiopurine metabolites (TGN) were performed in 51/52 patients taking thiopurines, (median 302, IQR 242-411pmol/8×10^8). There was no significant difference between DL and TGN according to TGN quartiles. ADAb were detected in 1(1.3%) patient using LT and 4(5%) using IM. Concomitant immunomodulation or therapeutic TGN(>235) did not significantly influence median DL or the detection of ADAb with either assay. IM ADA showed proportional positive bias (79.6%) against LT (Passing Bablok regression IM= 1.74 LT - 0.06)

Conclusions: No optimal cut-off could be identified that predicted clinical or biochemical remission or FC. Concomitant immunomodulation and TGN concentration was not associated with higher ADA DL . ADAb development was very rare whether measuring free (LT) or total (IM) ADAb. Further studies are needed to establish the cause of DL variation and understand differences in ADA pharmacokinetics in patients with CD.

"Table 1"

Outcome	Theradiag (LT)					Immundiagnostik (IM)				
	Remission		Active Disease			Remission		Active Disease		
	n (%)	DL*	n (%)	DL*	p value	n (%)	DL *	n (%)	DL *	p value
FCP<250 µg/g	57 (71)	6.2	23 (29)	5.7	0.3	57 (71)	11.1	23 (29)	10.1	0.2
FCP<59 µg/g	32 (40)	6.1	48(60)	5.9	0.4	32 (40)	11.3	48 (60)	10.4	0.6
CRP(<5) g/L	66 (85)	6.1	12(15)	5.4	0.6	66 (85)	11	12 (15)	9.8	0.6
HBI	66 (83)	6.1	14 (17)	5.5	0.7	66 (83)	11	14 (17)	10.4	0.6

*median DL (µg/mL),

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P589
Change in clinical features of Korean Crohn's Disease patients following the introduction of an anti-TNF-alpha agent: Results from the CONNECT study

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Background: Background: Anti-tumor necrosis factor-alpha (anti-TNF-alpha) agents have been known to alter the natural course of Crohn's disease (CD). Therefore, we aimed to compare the changes in clinical features and disease course according to the time of introduction of an anti-TNF-alpha agent in Korea.

Methods: Methods: We performed a retrospective analysis of 1,382 Korean CD patients diagnosed between 1982 and 2008 who were enrolled in the retrospective cohort of the CrOhn's disease cliNical NEtwork and CohorT (CONNECT) study. The anti-TNF-alpha agent was applied to national medical insurance in 2005, and has been more widely used in Korea since 2007. Accordingly, the patients were divided into three groups [Group A (1981-2004): 656 patients; Group B (2005-2006): 282 patients; and Group C (2007-2008): 362 patients].

Results: The average age (p = 0.251), disease location (p = 0.941), and disease behavior (p = 0.813) at the time of diagnosis with CD were not different among the three groups. The anti-TNF-alpha agent was administered to a total of 31.0% of patients (n = 403), which was not different among groups (p = 0.124). However, the 3- and 5-year cumulative probabilities for administering an anti-TNF-alpha agent were significantly higher in group C (p < 0.001). The 3- and 5-year cumulative probabilities of the occurrence of perianal fistula and CD-related surgery were higher in group A than in group C (perianal fistula, p = 0.032; surgery, p = 0.003).

Conclusions: Conclusions: After the introduction of the anti-TNF-alpha agent to the treatment of Korean CD patients, the natural history of CD changed. We found that early administration of an anti-TNF-alpha agent may help delay the occurrence of perianal fistula and the need for surgery in Korean CD patients.

P590
Inflammatory Bowel Disease Patient's Participation in Therapeutic Decision Making

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Background: Non-adherence to medical treatment in patients with inflammatory bowel disease (IBD) is a matter of a grave concern. Active participation in therapeutic decision making, as one of the aspects of patient empowerment, has potential to increase adherence to therapy. However, data from large studies on patients' participation in therapeutic decision making in IBD is scarce. Therefore, we aimed to evaluate the patients' role in therapeutic decision making.

Methods: A paper-based 15-item questionnaire was developed by IBD experts and sent to 2,100 members of the Swiss Association of IBD patients in September, 2014. In addition to patient baseline characteristics, the patients were asked about their experience in regards to developing a therapeutic concept together with their treating gastroenterologist.

Results: A total of 824/2,100 (39.2%) adult IBD patients sent back the completed questionnaires. Of these patients, 66% were female, 57% had CD, 41% had UC, and 2% had unclassified IBD. The age distribution was as follows: 31% were aged up to 40 years, 47% were between 41-60 years, and 22% were > 60 years old. When being asked "How actively were you involved in therapy decisions?" patients chose the following options: 50% told that their gastroenterologist proposed one particular therapy regimen which they followed, 23% told that their gastroenterologists provided them with several therapeutic options of which they chose one, 8% of patients told that they read about various therapeutic options on the internet before discussing their therapy of choice with the gastroenterologist, 7% told that due to their activity in the IBD patients organization they already made their mind about a particular therapy option which they proceeded to discuss with their gastroenterologist, 7% of patients told that they decided for another therapy than the one recommended by their gastroenterologist, and 5% of patients noted that their gastroenterologist provided them with several therapy options, but they thought it is upon the gastroenterologist to select the appropriate treatment. Older patients (55 years of age and older) were more likely to choose the option that it is upon the gastroenterologist to select the appropriate treatment when compared to younger patients (< 55 years) (12.7% vs.

3.6%, p < 0.001). The shorter the disease duration, the more frequently patients followed the therapy recommendation provided by their gastroenterologist.

Conclusions: Younger IBD patients tend to be more actively involved in therapeutic decision making when compared to older IBD patients. The knowledge of patient-specific information seeking behaviors may help gastroenterologists to improve adherence to medical treatments in the long-term run.

P591
The effect of Infliximab therapy on the Neutrophil-Lymphocyte and Platelet-Lymphocyte Ratios in Inflammatory Bowel Disease patients

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Background: Neutrophil-Lymphocyte Ratio (NLR) and Platelet-Lymphocyte Ratio (PLR) have been described as prognostic markers in many chronic inflammatory and malignant diseases. The aim of this retrospective cohort study was to investigate the effect of infliximab treatment on the NLR and PLR in patients with inflammatory bowel disease (IBD) and whether this effect was affected by other Disease Modifying Anti-Rheumatic Drugs (DMARDs), the sex of the patients and the type of IBD (Crohn's disease, CD, or Ulcerative colitis, UC).

Methods: Medical records of adult IBD patients on infliximab treatment were retrospectively studied. The NLR and the PLR were estimated at baseline T(-1), at the beginning of the treatment and before the 1st dose of infliximab (T0) and at 2 (T2), 6 (T6), 14 (T14) and 22 (T22) weeks, before the 2nd, 3rd, 4th and 5th dose, respectively. Wilcoxon-Signed Ranks test was used to determine the significance of the change of the NLR and the PLR between the aforementioned time intervals. Mann-Witney U test was used for the comparison of the change of the NLR and the PLR between patients pre-treated or not with sulfasalazine+/-azathioprine, between males and females and between patients with CD and UC. p<0,01 was considered to be significant. SPSS v22 was used for the analyses.

Results: 35 adult IBD patients (22 with CD) were included in the study (17 men). 17 patients were on mesalazine+/- azathioprine therapy at T0. At T(-1) (available data from 20 patients) the median NLR was 2.72 (1.66-3.98) and the median PLR was 120,68 (91,5-240,9). At T0 (available data from 35 patients) the median NLR was 2,84 (2,04-7,21) and the median PLR was 201,35 (128,59-263). From T(-1) to T0 both the NLR and the PLR were not significantly increased, p=0.1 and p=0.07, respectively. Two weeks after the introduction of infliximab, at T2, the median NLR was 2,13 (1,26-2,56), p<0,001 and the median PLR was 142,02 (90,43-186,66), p<0,001. The reduction of the NLR remained statistically significant up to T6 while the reduction of the PLR remained statistically significant up to T22. The decrease of the NLR and the PLR at T2 was the same between patients pre-treated or not with mesalazine+/-azathioprine, between males and females and between patients with CD and UC.

Conclusions: Infliximab therapy in IBD patients may result in a significant reduction of both the NLR and the PLR. This reduction seems to be independent of the pre-treatment with other DMARDs, particularly mesalazine+/-azathioprine, the sex of the patients and the type of IBD. Further larger studies are required to confirm the above results and determine whether these indices could serve as prognostic markers of response to infliximab therapy in IBD patients.

P592
Comparative assessment of the safety of stem cells and standard anti-inflammatory therapy of Crohn's Disease

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Background: Mesenchymal stromal cells (MSCs) are now widely used in clinical studies with various diseases, providing a positive effect due to the immunomodulatory and paracrine mechanisms.

Objective: to compare the safety of treatment of the patients with Crohn's disease (CD), receiving comprehensive anti-inflammatory therapy with the application of MSCs standard therapy with 5-aminosalicylic acid (5-ASA), glucocorticosteroids (GSCs) and immunosuppressive agents (IS).

Methods: Within the period from 2008 to 2013 the system transplantation of allogenic MSCs was carried out in 64 patients with CD. 47 patients were included in the first group. 124 patients with CD, who received standard anti-inflammatory therapy were included in the second group. The patients, who received anti-cytokine therapy, were not included in this group.

Results: In the first group of patients with CD the development of non-severe infectious complications or exacerbation of chronic inflammatory diseases were registered in 7 patients out of 56, that totaled 12.5%, in the second - in 14 (16,7%) patients out of 84. When comparing the two groups, no differences were found in the risk of the development of infectious complications and exacerbation of chronic inflammatory diseases on the background of the standard anti-inflammatory CD therapy or with the introduction of the MSCs (RR-0.75, 95% Cl 1.5-23.58; x2-0,16; p=0.66). Severe infectious complications (pneumonia, pleurisy, activation of latent TB) in the first group were detected in 1 patient (1,8%) out of 56, and in the second group in 5 (5,9%) out of 84. When comparing the two groups no differences in the risk of this type of complications were also found (RR-0,3; 95% Cl 0.04-2.5; x2-0.59; p=0.44). Colorectal cancer was registered only in one she-patient from the first group (1,8%). The time between the introduction of the MSCs and diagnosed colon cancer was 10 days. In the second group of patients over the 5 years of follow-up, malignant transformation was observed in 4 (4,8%) patients out of 84 (RR-0.5, 95% Cl 0.05-4.96; x2-0.01; p=0.97). Within 5 years of follow-up in the first and second groups of patients, fatal outcomes were registered on one occasion in each group, 1.8% and 1.2% respectively (RR-1.5, 95% Cl 0.1-23.49; x2-0.19, p=0.66).

Conclusions: The analysis did not reveal any differences in the development of severe infectious complications, exacerbation of chronic inflammatory diseases, serious infectious complications of malignant transformations and deaths in patients with CD, who received the MSCs and the standard anti-inflammatory therapy.

P593
Efficacy and safety of retreatment with vedolizumab in patients with Crohn's disease

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Background: Retreatment of patients (pts) with Crohn's disease (CD) after a drug holiday is a commonly encountered clinical situation. Vedolizumab (VDZ) is a monoclonal antibody to α4β7 integrin. The efficacy and safety of VDZ in pts with CD were investigated in the phase 3 GEMINI 2 study (NCT00783692).[1] This interim analysis (22 May 2009 - 27 June 2013) of data from the ongoing, open-label GEMINI long-term safety (LTS) study (NCT00790933) examined the effects of VDZ retreatment in pts who rolled over from the double-blind placebo (PBO)-controlled GEMINI 2 study after a drug holiday of up to 1 year.

Methods: In GEMINI 2, after 6 weeks of induction therapy, VDZ responders were re-randomised to PBO or VDZ every 8 or 4 weeks (Q8W or Q4W) during the 46-week maintenance period (maintenance intent-to-treat [ITT] population). Pts who completed the study (n=205) or withdrew early (due to sustained non-response, disease worsening, or the need for rescue medication; n=156) were eligible to enrol into GEMINI LTS to receive open-label VDZ Q4W. Here we evaluate rates of clinical response and remission with VDZ retreatment in these rollover pts in GEMINI LTS (prespecified analyses). Rates were calculated based on the number of pts at week 0 of GEMINI LTS. Adverse event (AE) and serious adverse event (SAE) rates were also evaluated.

Results: Pts from GEMINI 2 who were re-randomised to PBO in the maintenance phase (weeks 6-52; PBO completers) or those who discontinued due to loss of response or sustained non-response (VDZ

Table. Rates of clinical response and remission by GEMINI 2 treatment group (maintenance ITT population of GEMINI 2 completers and early terminators)

	GEMINI 2 Completers			GEMINI 2 Early Terminators[a]		
Visit	**PBO[b] (n=60)**	**VDZ Q8W (n=69)**	**VDZ Q4W (n=76)**	**PBO[b] (n=59)**	**VDZ Q8W (n=57)**	**VDZ Q4W (n=40)**
Number (%) of patients with clinical response[c]						
GEMINI 2						
Week 6	52 (86.7)	63 (91.3)	60 (78.9)	48 (81.4)	39 (68.4)	33 (82.5)
Week 26	51 (85.0)	64 (92.8)	62 (81.6)	21 (35.6)	10 (17.5)	6 (15.0)
Week 52	45 (75.0)	63 (91.3)	62 (81.6)	NA	NA	NA
GEMINI LTS						
Week 0	46 (76.7)	63 (91.3)	65 (85.5)	25 (42.4)	22 (38.6)	18 (45.0)
Week 28	48 (80.0)	56 (81.2)	62 (81.6)	33 (55.9)	31 (54.4)	15 (37.5)
Week 52	41 (68.3)	53 (76.8)	60 (78.9)	33 (55.9)	27 (47.4)	8 (20.0)
Week 84	34 (56.7)	40 (58.0)	47 (61.8)	31 (52.5)	22 (38.6)	9 (22.5)
Week 108[d]	25 (41.7)	22 (31.9)	30 (39.5)	25 (42.4)	19 (33.3)	10 (25.0)
Number (%) of patients with clinical remission[e]						
GEMINI 2						
Week 6	29 (48.3)	32 (46.4)	39 (51.3)	26 (44.1)	14 (24.6)	11 (27.5)
Week 26	30 (50.0)	49 (71.0)	47 (61.8)	13 (22.0)	3 (5.3)	3 (7.5)
Week 52	31 (51.7)	51 (73.9)	52 (68.4)	NA	NA	NA
GEMINI LTS						
Week 0	32 (53.3)	53 (76.8)	54 (71.1)	5 (8.5)	2 (3.5)	4 (10.0)
Week 28	42 (70.0)	50 (72.5)	57 (75.0)	28 (47.5)	13 (22.8)	11 (27.5)
Week 52	38 (63.3)	48 (69.6)	52 (68.4)	26 (44.1)	18 (31.6)	10 (25.0)
Week 84	31 (51.7)	35 (50.7)	42 (55.3)	25 (42.4)	15 (26.3)	9 (22.5)
Week 108[d]	22 (36.7)	22 (31.9)	26 (34.2)	20 (33.9)	14 (24.6)	9 (22.5)

Abbreviations: ITT, intent-to-treat; LTS, long-term safety; NA, not applicable; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; VDZ, vedolizumab.

[a] Early terminators include those who withdrew because of sustained non-response, disease worsening, or the need for rescue medication.

[b] The PBO groups received 2 doses of VDZ during the induction phase of the study. PBO completers received PBO during weeks 6 to 52. Time off drug before retreatment in GEMINI LTS varied in ITT PBO early terminators.

[c] Clinical response was defined as a ≥3-point decrease in Harvey-Bradshaw Index (HBI) score from baseline.

[d] At Week 108, the number of patients in the study was 26, 23, and 32 for PBO, VDZ Q8W, and VDZ Q4W completers and 27, 24, and 12 for PBO, VDZ Q8W, and VDZ Q4W early terminators, respectively.

[e] Clinical remission was defined as a HBI score ≤4.

Q8W or Q4W early terminators [ETs]) regained response when retreated with VDZ Q4W in GEMINI LTS (Table). Similar trends were noted with VDZ retreatment in the subpopulations of completers or ETs with prior tumour necrosis factor antagonist failure. No increase in AE or SAE rates was observed with VDZ retreatment. Rates of SAEs of anal fistula or abscess were ≤2% for PBO-treated pts (completers and ETs combined) retreated with VDZ (vs ≤1% in VDZ-treated completers and ETs combined).

Conclusions: Pts with CD from GEMINI 2 who responded to VDZ induction therapy and had a drug holiday for up to 1 year were safely retreated with VDZ Q4W in GEMINI LTS and experienced clinical benefits.

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P594
Systematic information to healthcare professionals about ECCO's vaccination guidelines improves adherence in patients with inflammatory bowel disease receiving anti-TNF α therapy

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Background: The European Crohn's and Colitis Organisation (ECCO) have developed guidelines for prevention of infectious diseases in patients with inflammatory bowel disease (IBD). However, implementation of vaccination routines in an everyday clinical setting is difficult. The aim was to investigate if systematic information to healthcare professionals about screening and vaccination guidelines improves patients' adherence hereto. Furthermore, to identify barriers for adherence to the guideline.

Methods: This study was carried out at a tertiary IBD center and consisted of three parts: 1) A cross-sectional study where baseline vaccination status was assessed in all IBD patients in ongoing anti-TNF α therapy as of March, 2013 (reference group n=130); 2) an intervention study where healthcare professionals received oral and written information about screening and vaccination guidelines every 2 months during a period of 6 months, and followed by assessment of vaccination status in all IBD patients in ongoing anti-TNF α therapy (intervention group n=99); and 3) a survey of Danish gastroenterologists' adherence to, knowledge of, and barriers for adherence to vaccination guidelines (n= 53 physicians from 7 centers). Validated questionnaires were used to assess the outcomes. European Crohn's and Colitis Organisation's (ECCO) guidelines served as gold standard. [1]

Results: Patients' adherence to recommended vaccinations during anti-TNF α therapy increased significantly after the period of systematic information to healthcare professionals about the guidelines. Hence, the percentage of patients completely adherent to all recommended vaccinations increased from only 5% to 26%, partial adherence increased from 38% to 56% and complete non-adherence decreased from 57% to 18% ($p<0.0001$). Adherence to all individual recommended vaccinations except human papilloma virus increased significantly ($p<0.05$). Prior to information about guidelines, only 8% of included physicians could identify all the recommended screening and vaccination measurements, and 89% were able to identify at least one recommendation. The most frequently reported patient barriers for adherence were high cost of vaccinations (35%) and forgetfulness (25%). The most frequent barriers reported by physicians were forgetfulness (29%) and insufficient consultation time (22%).

Conclusions: Gastroenterologist's limited knowledge of vaccination guidelines during anti-TNF α therapy can be overcome by systematic education, and this inexpensive and easily accessible intervention immediately results in markedly improved patient adherence. Remaining obstacles for adherence comprise high expenses for vaccinations and patient's forgetfulness.

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P595
Azathioprine is effective and safe in inducing and maintaining deep remission in Crohn's disease

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Background: Deep remission, defined as clinical remission, biomarker remission and mucosal healing (MH), is a new treatment target and might be the only way to alter disease course in Crohn's disease (CD). This retrospective study examined whether azathioprine(AZA) could be an effective and safe agent in inducing and maintaining deep remission.

Methods: The clinical data of all CD patients were reviewed from 2012 to July 2013. The patients who initiated AZA treatment and were followed for 1 year with complete medical data were included. All the patients were induced remission by glucocorticoid or operation. AZA was prescribed at the same time with glucocorticoid or within 2 weeks after operation. Deep remission rate at year 1was analyzed.

Results: Among 49 patients, 40 patients were induced by glucocorticoid and 9 patients received operation. The baseline characters were described as follow: high sensitive C-active protein (hs-CRP) 12.05 ± 4.04mg/l, PLT $360.65 \pm 117.17 \times 109$/L, CDAI 220.05 ± 82.84, Simple Endoscopic Score for Crohn`s Disease (SES-CD) was 12.09 ± 6.29. 12 patients derived AZA associated side effects during follow-up, 10 of them stopped therapy. The major side effects occurred was bone marrow suppression (9/12). 39 of 49 patients completed 1 year therapy on AZA. The steroid free remission rate was 74.36% (29/39), clinical remission rate was 87.18% (34/39), muscle healing rate was 33.33%(13/39) and deep remission rate was 23.07% (9/39). At year 1, the serum biomarkers were declined to normal range: hs-CRP 5.79 ± 0.87mg/l mg/l, PLT $265.94 \pm 15.39 \times 109$/L , CDAI was 102.97 ± 10.46, SES-CD was 4.97 ± 0.89. All the parameters were significantly improved compared with baseline($P<0.05$).

Conclusions: Azathiopurine is not only effective in maintaining clinical remission, but also could induce deep remission in CD. Side effects should be carefully monitored during follow-up.

P596
Efficacy and Nephrotoxicity of Long-term Maintenance Therapy with Tacrolimus in Patients with Ulcerative Colitis

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Background: Biological therapy has at least in the short term reduced the number of patients requiring colectomy for fulminant ulcerative colitis (UC). However, alternative medications are to be available for patients who are intolerant or lose response to biologics. Tacrolimus (Tac) has shown efficacy as remission induction therapy in UC patients, but the long term outcomes and safety of UC patients treated with Tac as maintenance therapy remain to be described. This study was to evaluate efficacy and nephrotoxicity of long-term maintenance therapy with Tac in patients with UC.

Methods: In a single tertiary centre setting, 139 patients with UC treated with oral Tac between 2009 and 2014 were included for evaluation. Blood Tac levels were maintained at 10-15 ng/mL for the initial 2 weeks, and at 5-10 ng/mL beyond 2 weeks. Among the 139 patients, 89 had received Tac for 3 to 4 months. At this time point, responders to Tac could discontinue with Tac, and patients who could not discontinue corticosteroids, patients who did not achieve remission, or mucosal healing, could continue receiving Tac as maintenance therapy. Nephrotoxicity was monitored by measuring serum creatinine and glomerular filtration rate (GFR), defined as >150% rise in serum creatinine or a reduction of >15% in GFR.

Results: Sixty-three patients received oral Tac maintenance therapy, 53 (90%) of these were taking aminosalicylates and 41 (69%) were taking thiopurines as concomitant medications. During a median follow up time of 29 months, range 4.1 - 69 months, 38 patients (60%) relapsed; 20 (48%) received biologics, and 15 (25%) underwent colectomy. The Kaplan-Meier survival analysis showed an overall relapse-free rate of 48% at 1 year, and 31% at 3 or 5 years. Non-switching to biologics was 74% at 1 year, 52% at 3 years, and 26% at 5 years. The colectomy-free rate was 91% at 1 year, 77% at 3 years, and 73% at 5 years. For patients who received oral Tac over 1 year, relapse-free rate was 64% at 1 year, 46% at 3 or 5 years. The rate of non-switching to biologics was an 80% at 1 year, 67% at 3 years, and 21% at 5 years. The colectomy-free rate was 100% at 1 year, and 81% at 3 years. Nephrotoxicity was found in 58% patients. Mostly reversible and no patient needed haemodialysis, but renal function did not fully recover in 13% of the patients 1 year after discontinuation of Tac.

Conclusions: Long-term maintenance therapy with Tac was significant in patients with refractory UC. However, nephrotoxicity by Tac is a serious issue in clinical settings and needs to be closely monitored during Tac therapy including a regular observations on Tac trough levels.

P597
The effects of infliximab treatment failure on health-related quality of life and work productivity in patients with Crohn's disease

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Background: A notable proportion of patients with Crohn's disease experience relapse of disease activity despite ongoing infliximab (IFX) therapy. While handling IFX treatment failure is clinically and financially demanding, little is known about the impact on health-related quality of life (HRQOL) and work productivity in this situation.

Methods: Pre-defined analysis of a 20-week randomized controlled clinical trial where 69 Crohn's disease patients (55 luminal, 7 fistulizing, 7 both) with IFX treatment failure (CDAI ≥220 or ≥1 draining perianal fistula) had been randomized to intensified IFX regimen or personalized therapy defined by IFX and anti-IFX antibody levels.(1) HRQOL was assessed using the Short Inflammatory Bowel Disease Questionnaire (IBDQ). Productivity was assessed by the Work Productivity and Activity Impairment Questionnaire for Crohn's disease (WPAI:CD). NCT00851565.

Results: The IBDQ score at manifestation of IFX treatment failure was median 40, and this concurred with impaired HRQOL. Patients with clinical response (CDAI decrease of ≥70 or ≥50% reduction of active fistulas) had significant improvement in IBDQ scores at all study visits: IBDQ score increased median 11 at week 4 and 8, and 13 at week 12 and 20 ($p<0.001$). In contrast, non-responders had a very modest increase in IBDQ scores and only at week 12 and 20 (median 4, $p< 0.05$). Among employed patients (55%), missed time on work due to Crohn's disease was very low both at time of manifestation of IFX treatment failure (median 0%) and throughout all subsequent study visits (all medians 0%, $p >0.05$). Furthermore, absenteeism was not significantly influence by clinical outcomes ($p>0.05$). On the other hand, impairment while working was relatively high at time of IFX failure (median 40%), and this figure decreased only among responders at subsequent study visits (week 4 median 10%, $p< 0.05$; week 8 30%, $p >0.05$; week 12 30%, $p<0.01$; week 20 10%, $p<0.01$). The overall daily activity impairment, irrespectively of employment status, was high at IFX treatment failure (median 70%), and decreased over time in responders (median at week 4, 8, 12, 20 was 20%, 30%, 30%, and 20%; $p<0.001$), and to a lesser extent also in non-responders (50%, $p< 0.01$; 55%, $p >0.05$; 30%, $p<0.05$; and 40%, $p<0.05$).

Conclusions: Therapeutic failure of IFX immediately causes major impairment of HRQOL and daily activity status, but patients who regain clinical response recover rapidly. Even though employed patients comprise a robust subgroup with a high threshold for absenteeism, IFX failure results in substantially lowered work productivity. Indirect disease related costs should be taken into account when evaluating consequences of IFX failure.

(1) Steenholdt et al. Gut 2014; 63:919-27

P598
Tuberculosis infection in IBD patients on antitnf therapy: an Algerian retrospective study

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Background: Algeria is a country considered as a high prevalence area of tuberculosis .

Our aim was to study the prevalence of latent tuberculosis infection and active tuberculosis in inflammatory bowel disease (IBD) patients before and during antiTNF therapy

Methods: . We conducted a retrospective study in 7 centers, collecting clinical data of IBD patients on anti TNF therapy (Infliximab or Adalimumab) from November 2010 to July 2014, identifying the cases with latent tuberculosis (LTB) and active tuberculosis infection.

Results: 214 patients received antitnf therapy ; 117 (54.7%) male ;177 (82.7%) crohn disease and 37 (17.3%)ulcerative colitis ;the mean age at introduction of antitnf therapy was 35.24(±11.54 range16 --73), 131(61.2%) patients were on concomitant immunosuppressive treatment ;the mean duration of antitnf therapy was 48.53±38.36 weeks (range 2 -182) . In the screening procedure, X-ray was performed in 87.85%, tuberculin skin tests (TST) in 79% and an interferon-gamma release assays (IGRA) test in 82% of patients. Based on the screening, LTB was found in 28 (13.1%) patients .All patients with positive screening for LTB received prophylactic treatment for 6 months.

Active tuberculosis infection occurred in 4 (1.86%) male patients , all with crohn disease, mean age 30.2 years.2patients have been treated for 6 months for latent tuberculosis,the two others were negative on initial screening .Tuberculosis infection appeared 6,19,52 and 67 weeks after starting antitnf therapy.

The localization of tuberculosis was peritoneal in one, pulmonary in one, and disseminated in two patients. They all received therapy and resolved,antitnf was definitively stopped in these patients.

Conclusions: Active tuberculosis in IBD patients on antiTNF therapy in a high prevalence area was 1.86%, this infection occurred despite screening and previous oral prophylactic treatment.

These cases highlight the need for periodical assessment and follow up of our patients.

P599
Adverse efffects in patients with Inflammatory Bowel Disease on biological treatment

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Background: Inflammatory bowel disease affects an increasing number of people. There are different treatments, including immunosuppressive drugs and biological therapy, which can be used both in monotherapy and in combined therapy.

However, using these drugs can lead to potential risks, as they have adverse effects that can be from mild to potentially severe. Nevertheless, they have a good safety profile if they are used properly.

The aim of our study is to analyse the frequency and characteristics of adverse effects of biological therapy (both in monotherapy and in combination) in our patients.

Methods: We have carried out a retrospective descriptive study of 170 patients who received biological treatment (adalimumab, certolizumab, infliximab or golimumab). 116 patients (68.2%) received concomitantly immunosuppressive treatment (azathioprine, 6-mercaptopurine or methotrexate).42.4% were women. 65.2% were diagnosed of Crohn's disease (40.5% inflammatory pattern, 34.2% stenosing pattern, 25.2% fistulizing pattern, 17.1% had perianal disease too). 34.8% had ulcerative colitis (6.7% rectitis, 33.9 left sided colitis and 59.4% pancolitis).

Results: 13 patients developed infectious complications, of which 38.4% received biological drugs in monotherapy and 61.6% in combined therapy. The infections consisted on the following: tuberculosis (7 patients), pneumonia (2 patients), sepsis (2 patients) and fever (2 patients).

11 patients presented infusional reactions: 10 (91%) received combined therapy and only 1 (9%) monotherapy with a biological drug. Infusional reactions were: local reaction (1 patient), fluctuations in blood pressure (2 patients), facial flush (3 patients), dyspnoea (1 patient), asthenia (2 patients) and arthralgia (3 patients).

3 patients developed tumours; 100% of them were under combined treatment. One of them developed colonic neoplasia (he did not follow endoscopic controls), another one developed laryngeal neoplasia (he had smoking habit and chronic alcoholism) and the third one developed a thyroid tumour.

Conclusions: Although in general the biologic treatment is safe, it has adverse effects that need to be known, so that they can be prevented and treated as long as it is possible. In our case, the percentage of adverse effects was 17%, and the rate of infusional reactions (6.47%) was similar to that described in other series (3-15%).

Tumours developed in our series are not typically associated to the treatment related neoplasia described in literature, and they could be related to other etiological factors.

Whether to continue, decrease or stop the therapy, it should be decided individually.

Furthermore, it has been described that doing an appropriate selection of the patients, the security profile of these drugs is accurate.

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Direct and indirect effects of tofacitinib on treatment satisfaction in patients with ulcerative colitis

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Background: Tofacitinib is an oral, small molecule Janus kinase inhibitor being investigated as a targeted immunomodulator for inflammatory bowel disease (IBD). We assessed direct and indirect effects of tofacitinib on patient treatment satisfaction via clinical and patient reported outcomes (PROs).

Methods: Clinical and PRO data were collected from a randomised Phase 2 trial (NCT00787202, A3921063) in adult patients with moderately to severely active ulcerative colitis treated with tofacitinib 0.5,

3, 10 or 15 mg (n=146) or placebo (n=48), twice daily for 8 weeks. Two statistical mediation models were considered: a PRO-based and a clinical based model. In both models, treatment was the binary predictor variable (pooled active treatment vs placebo); the eventual dependent variable was patient treatment satisfaction at Week 8 (5-point Likert scale: extremely satisfied-extremely dissatisfied). For the PRO-based model, mediators of treatment effect on patient satisfaction were IBD Questionnaire (IBDQ) domains at Week 8 (Bowel Systems, Emotional Health, Social Function, Systemic Symptoms). For the clinical-based model, corresponding mediators were Mayo scale domains at Week 8 (Endoscopic disease activity, Physicians Global Assessment [PGA], Stool Frequency, Rectal Bleeding).

Results: With the PRO-based mediation model, 52.2% of treatment effect on patient satisfaction was direct ($p<0.05$). With the clinical-based mediation model, only 16.0% of treatment effect was direct (not statistically significant; $p=0.56$). For indirect effects, both models revealed bowel function as the most important domain for patient satisfaction (PRO based model, 35.1% of treatment effect on satisfaction mediated via Bowel Systems domain; clinical-based model, 30.0% via Stool Frequency; both $p< 0.05$); other indirect effects of treatment were not statistically significant (PRO-based model: via Emotional Health -1.3%, Systemic Symptoms 5.7%, Social Function 8.4%; clinical-based model: via Endoscopic disease activity 12.8%, PGA 24.5%, Rectal Bleeding 16.8%; all $p >0.05$). Overall indirect effect in the PRO-based model was 47.8% ($p<0.05$), indicating ~50% of treatment effect on satisfaction is mediated via IBDQ domains. Overall indirect effect in the clinical-based model was 84.0% ($p<0.01$), indicating most of the treatment effect on satisfaction is mediated via Mayo scale domains.

Conclusions: Mediation models, which can help to identify mediators of therapeutic response, identified bowel function as an important factor for patient treatment satisfaction with tofacitinib. Treatment effect on patient satisfaction was substantially mediated via improvement in Mayo scale domains, and partially mediated by improvement in IBDQ scale domains.

P601
Postoperative Crohn's Disease, Recurrence Rate and Risk Factors

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Background: Surgery for Crohn's disease (CD) is not a cure and postoperative recurrence is common. There are numerous studies that report numbers of postoperative recurrence after ileocecal resection, but with varying results. Endoscopy is the gold standard and endoscopic recurrence predicts clinical relapse. We retrospectively determined the postoperative endoscopic recurrence rate as well as risk factors for endoscopic recurrence.

Methods: Patients with CD who underwent an ileocecal resection between 2008 and 2013 in two referral centers in the Netherlands were included. Patients who did not undergo an ileocolonoscopy within two years postoperatively were excluded. The modified Rutgeerts score was the primary outcome to determine endoscopic recurrence (modified Rutgeerts score>i2a, i2a: lesions confined to the ileocolonic anastomosis). Secondary outcome was to identify risk factors like Montreal classification, smoking behaviour, previous resection(s), gender, family history of inflammatory bowel disease (IBD), surgery indication, type of anastomosis, ileum length resected and postoperative use of medication.

Results: The overall endoscopic recurrence rate was 38.1% in the 105 included patients. The recurrence rate in patients who used postoperative biologics was 26.3%, 23.8% in patients who used immunomodulators and 51.9% in patients without postoperative medication. Only smoking the year before surgery (OR; 3.590, 95% CI 1.269-10.233, $p=0.017$) seemed to be a significant risk factor in the multivariate analysis for risk factors for endoscopic recurrence. Postoperative use of medication was a protective factor (not significant, but a trend OR; 0.381, 95% CI 0.142-1.018, $p=0.054$), which reduced the risk with 61.9%.

Conclusions: This retrospective multicenter cohort study is the first study that used the modified Rutgeerts score to evaluate endoscopic recurrence. The endoscopic recurrence rate found was lower than in previous studies. Based on this study, special attention should be paid in the preoperative phase to patients with smoking habits. Postoperatively, an early start with immunomodulators or anti-tumor necrosis factor (TNF) therapy should be taken into consideration.

P602
Secondary healthcare use following major abdominal surgery employing an acellular reconstructive tissue matrix

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Background: An analysis of pre- and post-intervention secondary healthcare use for major reconstructive surgeries involving the use of Strattice™ Reconstructive Tissue Matrix (TM), an acellular porcine dermal matrix.

Methods: A before-after analysis of secondary healthcare use was conducted for 154 major abdominal surgeries undertaken at University College London Hospitals Trust (UK) between February 2010 and October 2013. All interventions employed Strattice™ TM. Pre- and post-intervention pathways (inpatient (IP), outpatient (OP), and Accident & Emergency (A&E)) were quantified using Hospital Episode Statistics covering NHS hospitals in England (data April 2008 - December 2013). Non-parametric t-tests were used to assess for significance.

Results: Mean age at intervention was 57.5 years (SD 12.9). 54% of surgery recipients were female. Three-quarters of interventions occurred as part of an elective admission. The most common primary diagnosis at intervention was ventral hernia (31%), followed by intestinal fistula (15%). Interventions were primarily for incisional hernia repair (36%). A total of 11,798 pre- and post-intervention observations were recorded in the sample period. An average of 3.4 years' worth of data was available pre-intervention; average follow-up was 2.4 years.

IP admissions decreased between pre- and post-intervention periods (mean 2.0; SD 12.7; $p<0.001$), representing a reduction in bed-days (BD) and excess BD of 31.0 (SD 104.6; $p<0.001$) and 15.0 (73.4; 0.002) respectively. OP appointments post-intervention decreased by an average of 10.6 (42.2; 0.001). No significant impact on A&E attendances was observed (mean 0.6; SD 9.3; $p=0.26$).

In order to balance the pre- and post-intervention observation windows, an analysis of 12-month resource use was conducted on pathways for individuals with 12 months of data pre- and post-intervention (window of analysis: 720 days; observations n=4,367; interventions n=129). Excess BD decreased by mean 12.3 (SD 48.0; p=0.01). IP admissions and BD decreased, although neither result was significant ((mean reduction; SD; p-value) (0.5; 5.2; 0.19) and (20.4; 57.4; 0.25), respectively). A&E attendances increased, again insignificantly (mean 0.4; SD 2.4; p=0.5). OP appointments decreased significantly, albeit marginally (mean -0.01; SD 15.5; p=0.02).
Conclusions: This is the first work in a larger study intended to assess the effectiveness of Strattice™ TM in 'real-world' major surgery. The sample exhibits substantial clinical heterogeneity, which may limit the interpretability and generalisability of the results. However, the results of this work support the proposition that abdominal surgeries employing biological mesh result in decreased secondary healthcare use.

P603
Efficacy of the new infliximab biomarker CT-P13 induction therapy on mucosal healing in ulcerative colitis patients

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Background: CT-P13 is the first biosimilar to infliximab that has been approved for the same indications than infliximab in June 2014 in Hungary. Studies examining whether CT-P13 is identical to that of reference infliximab will have a high importance. The aim of this study was to examine the efficacy of CT-P13 induction therapy on mucosal healing in patients with ulcerative colitis (UC).
Methods: Patients diagnosed with UC, who were administered CT-P13 from June 2014 at the First Department of Medicine, University of Szeged, were prospectively enrolled. Medical records analyzed included patients' characteristics, previous history of infliximab administration, response to CT-P13, concomitant medications, and adverse drug reaction. Serum activity markers, trough levels and antibody titers have been measured. Sigmoideoscopy was performed at the end of the induction therapy in patients who agreed.
Results: Twelve UC patients were treated with CT-P13 between June and November 2014 at our centre. The indication of the therapy was acute, severe flare up and chronic, refractory activity in 6-6 patients. Male-female ratio was 5:7. Mean age was 34 years (range 20-68). Induction treatments have been done in 9 patients until now. Two patients discontinued the therapy after the second infusion: one, who was previously treated with infliximab and developed high antibody level, because of hypersensitivity reaction and one because of septic complications. Clinical response and remission at week 6 were achieved in 2 and 5 patients. Two patients did not respond to CT-P13 at week 6 (one previously treated with infliximab). Sigmoideoscopy was performed in 9 of the 12 patients. Severe activity was detected in 2 patients; one of them discontinued the therapy after the 2nd infusion and the other did not show response at week 6. Seven patients (four with eMayo score of 1 and three with eMayo score of 0) showed mucosal healing at the end of the induction therapy.
Conclusions: This was the first study examining the efficacy of CT-P13 induction therapy on mucosal healing in UC. CT-P13 induction therapy showed clinical response and remission in 58% of the UC patients. Mucosal healing was revealed in 78% of the patients during or after the induction therapy. Although the number of the enrolled patients is not so high yet, our results indicate that the induction with CT-P13 can result mucosal healing in similar proportion as the originator infliximab.

P604
Stigma in Inflammatory Bowel Disease

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Background: A stigma is 'an attribute that is deeply discrediting ', often contravening social norms, and perceived by others as being undesirable. Inflammatory Bowel Disease (IBD) is a chronic illness characterised by symptoms of diarrhoea, urgency, and vomiting occurring in a relapsing and remitting pattern. Regular or temporary loss of bowel control leading to faecal incontinence (FI) is a prominent feature of disease and may lead to stigmatisation through infringement of social hygiene rules. Although stigma in IBD has been measured in quantitative studies, there is a dearth of qualitative evidence. This Heideggerian (interpretive) phenomenological study explored the lived experience of IBD-related stigma.
Methods: Using purposive stratified sampling, 40 members of a national IBD charity were recruited. Participants did or did not experience FI, and did or did not feel stigmatised. This variation in the sample enabled exploration of the relationship between IBD, FI and stigma, and identification of features in the non-stigmatised which contributed to their transcendence of stigma. Unstructured individual interviews (digitally recorded and professionally transcribed) took place in consenting participants' homes between May and November 2012. Data was analysed using Diekelmann's hermeneutic method.
Results: Eight relational themes (present in some transcripts) and three constitutive patterns (present in all transcripts) emerged. IBD-related stigma is a complex experience, mostly of anticipated or perceived stigma, which changes according to social setting and is fuelled by the antisocial nature of the disease. The more affected report more negative aspects of the themes outlined above. Many types of stigma are reported, including kinship stigma - that uniquely directed at the person by someone with whom they have a close biological or intimate bond. Certain characteristics or childhood experiences seem to contribute to stigma reduction and stigma resistance is most likely in those with a positive sense of control, a support network which suits their needs, and mastery over life and illness. These people recognise, expect and experience stigmatising attitudes from others but are not negatively affected by these.
Conclusions: IBD-related stigma occurs regardless of continence status, negatively affecting the chronic illness experience. Time, experience, and suitable support enhance stigma resilience. IBD nurses and clinicians can direct patients towards stigma resilience by helping those who struggle the most to identify ways of achieving a sense of control, building support networks, and becoming increasingly competent and masterful in managing their condition.

P605
Serum hepcidin and its relation to anaemia in inflammatory bowel disease

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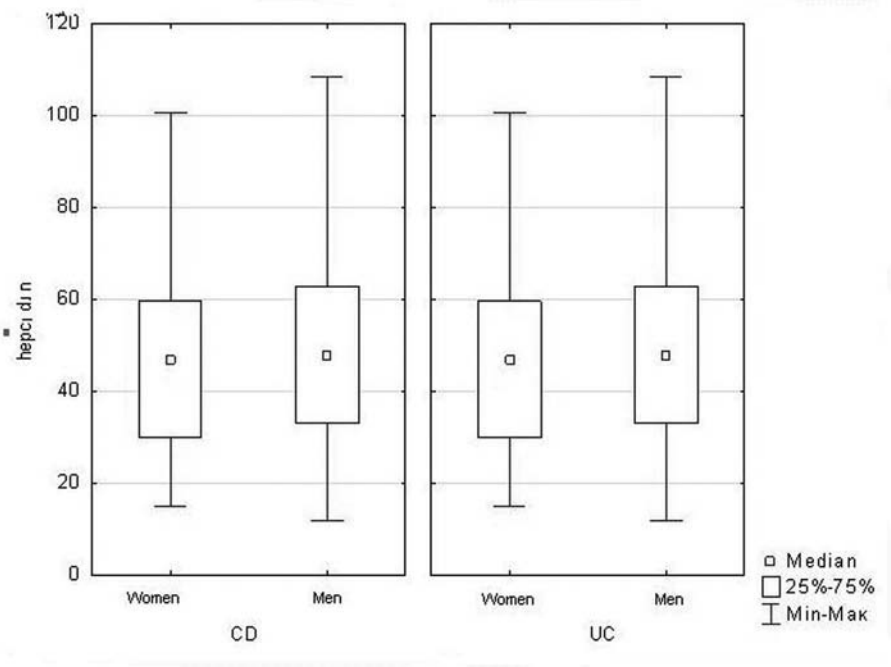

"Hepcidin values in groups with respect to gender."

Background: Hepcidin is the most important mediator of anaemia. Stimulation of hepcidin production has a casual role in the pathogenesis of the aneamia of inflammation. Anaemia is the most common complication of inflammatory bowel disease (IBD). Anaemia in IBD is pathogenically complex, with several factors contributing to its development. Because the right diagnosis of anaemia in IBD often presents a challenge, combination of several hematimetric and biochemical parameters should be used and hepcidin is one of them.

Methods: The study comprised 51 patients with CD (24 women, 27 men) and 46 patient with UC (23 women, 23 men) hospitalized in gastroenterology ward. Serum hepcidin levels were measured using a commercially available ELISA. All patient underwent blood investigation comprising hemoglobin (Hgb), ferritin, transferrin, serum iron and serum soluble transferrin receptor levels. Anaemia defined as a Hgb level of less than 12.0 g/dl in females and less than 13.0 g/dl in males has been established in 18 patients with CD (35%) and 22 patients with UC (48%). According to Weiss and Goodnough [1] ferritin, transferrin saturation and sTfR-Fer Index were used for further group stratification on iron deficient anaemia (IDA), anemia of chronic disease (ACD) and mixed form (MIX).

Results: The mean hepcidin level in patients with CD was 51,74 ng/ml compared with a mean of 43,38 ng/ml in patients with UC and this difference was statistically significant (p=0,039). Significantly more cases of hepcidin values above the upper limit of norm was observed in the CD group (23 vs. 12). There was no statistically significant difference in the distribution of hepcidin in relation to sex, both within groups and between them (Fig.1)

. The group of anaemic patients consisted of 19 patients with MIX, 13 patients with IDA and 8 with ACD. A statistically significant difference between patients with CD and UC was demonstrated in the case of ACD and MIX (p <0.02). The mean hepcidin level was the highest in patients with ACD (63,32 ± 24,35 ng/ml) and statistically significant compared to IBD patient without anaemia (p=0,038) and patient with MIX (p=0,033). The relation between mean hepcidin level in patient with ACD and IDA (43,4 ± 16,4) was not statistically significant (p=0,062).

Conclusions: Our data suggest that high hepcidin level is more specific for ACD and IDA/ACD. This relationship should influence on the choice of an appropriate method of treatment anemia, depending on the disease activity in patients with IBD.

References:

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P606
Is it necessary to include disease extent in endoscopic scoring in ulcerative colitis?

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Background: Colonoscopy plays a crucial role in the establishment of diagnosis, management and follow-up of ulcerative colitis (UC). None of the current endoscopic scores consider the disease extent, and therefore does not correlate with the disease extension and does not reflect the real severity of UC. Our aim was to assess accuracy of a modification of widely used Endoscopic Mayo Score (eMayo) to reflect not only the severity, but the extension of acute flare in UC.

Methods: Pancolonic Modified Mayo Score (panMayo) was calculated. The eMayo scores of the involved area of the five colorectal segments (ascendens, transversum, descendens, sigma and rectum) were added, however to clearly distinguish the almost healing mucosa (eMayo 1 in each segment would effect a larger score than severe proctitis) from active inflammation, the sum was multiplied by 3.5 in the case of eMayo equal or greater than 2 (range 0 [normal] to 52.5 [most severe]). Fiftyfour UC patients were enrolled in this prospective study (the mean age: 42.9 years; male/female: 26/28). We

compared panMayo score, eMayo and Ulcerative Colitis Endoscopic Index of Severity (UCEIS) with serum and faecal inflammatory parameters and Riley score.

Results: All of tree assessed scores significantly correlate with Riley score (p<0.001). The panMayo score correlates with CRP (p<0.001), hematocrit (p=0.008), haemoglobin (p=0.002), trombocytes (p=0.035), serum iron (p<0.001) and MMP-9 (p<0.001). This score do not associate with number of leukocytes. Tendency correlation was shown with faecal calprotectin (p=0.08). Endoscopic Mayo score and UCEIS was also correlated with CRP (p=0.012 and p=0.016), MMP-9 (p=0.003 and p=0.004), leukocytes (p=0.047 and p=0.011), serum iron (p=0.003 and p=0.007), but not with hematocrit, haemoglobin, trombocytes and faecal calprotectin.

Conclusions: We suggest that panMayo score could be favourable due to it gives an additional information about disease location besides disease activity; in addition, it revealed a stronger correlation with laboratory parameters of inflammation than the other scores.

P607
Histologic activity after acute treatment with multimatrix mesalazine for ulcerative colitis may predict long-term remission status

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Background: For patients with active mild-to-moderate ulcerative colitis (UC), mesalazine (5-aminosalicylic acid) is recommended first-line treatment. While endoscopic assessments are commonly used to assess treatment efficacy in UC, relatively few studies have examined histology scores over the course of treatment. Results of a post hoc analysis are presented, examining the relationship between remission status and histology scores in patients with UC during acute and maintenance treatment with multimatrix mesalazine.

Methods: In this open-label, multicenter, prospective phase 4 study (ClinicalTrials.gov ID: NCT01124149), adult patients with active mild-to-moderate UC were administered multimatrix mesalazine 4.8 g/d once-daily (QD) for 8 weeks (acute phase); those in complete or partial remission following acute treatment were eligible for 12 months of maintenance treatment with multimatrix mesalazine 2.4 g/d QD. Complete or partial remission was defined using a modified UC-Disease Activity Index that evaluated symptom, endoscopy, and Physician's Global Assessment scores. At Baseline (Week 0) and endpoints for the acute (Week 8/Month 0) and maintenance (Month 12) phases, 2 or 4 biopsies were taken (when endoscopy was performed) and evaluated by 2 blinded pathologists. Histology scores were based on a modified Geboes grading scale (range 0-6) for assessment of inflammation. Inter-rater reliability of matched sample pairs was examined using Cohen's kappa with Fleiss-Cohen weights. Remission status (complete, partial, or none) at Month 12 was stratified by maximum histology score (cutoff score at 3.1) at Month 0.

Results: Measurement of inter-rater reliability between histology readers produced a Cohen's weighted kappa coefficient of 0.60 (moderate strength of agreement; 95% confidence interval, 0.33-0.87). A higher proportion of patients with low (<3.1) versus high (≥3.1) maximum histology scores at Month 0 were in complete remission at Month 12 (41.3% vs 27.4%). Also, fewer patients with low versus high histology scores at Month 0 were not in remission at Month 12 (8.1% vs 14.4%).

Conclusions: A low degree of inflammation (maximum histology score <3.1) prior to maintenance treatment with multimatrix mesalazine was associated with a higher likelihood of complete remission after 12 months of maintenance therapy. These findings suggest that histology may be considered as a viable UC treatment endpoint.

P608
Hypovitaminosis D correlates with a more severe disease course in Inflammatory Bowel Disease patients

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Background: Increasing evidences suggests an implication of hypovitaminosis D in immuno-mediated disease, including Inflammatory Bowel Disease (IBD). Moreover, some authors reported a correlation between hypovitaminosis D, disease history and clinical features in Crohn's Disease (CD) and Ulcerative Colitis (UC). The aim of this study is to evaluate vitamin D serum levels in a IBD patients population and to correlate the prevalence of hypovitaminosis D with disease history and clinical features

Methods: Patients from our center affected by UC or CD were enrolled from october 2013 to november 2014. Exclusion criteria were age below 18 and over 60, concomitant vitamin D replacement therapy and concomitant gastrointestinal or endocrinological diseases which may alter vitamin D metabolism. Enrolled patients underwent 25-OH-vitaminD and C-reactive protein (PCR) plasmatic assay. According to 2012 Osteoporosis Italian Society Guidelines, we defined as hypovitaminosis D plasmatic values below 30 ng/mL, vitamin D levels were considered as insufficient if between 20 and 30 ng/mL and deficient if < 20 ng/mL. We collected data regarding patients life habits and clinical history, disease course and disease clinical activity at enrollment

Results: We enrolled 88 patients (62 CD, 26 UC), median age at enrollment was 42 years for CD and 43 years for UC. Mean Body Mass Index (BMI) was 22.6 in CD and 23.7 in UC patients. Age at diagnosis was 29.8 years for CD and 33.5 years for UC, with mean disease duration of 12.8 years for CD and 9.1 years for UC. Hypovitaminosis D was observed in 84.1% of cases with insufficient and deficient vitamin D levels in 31.8% and 57.3% of patients respectively. Mean vitamin D level was 20.4 ng/mL and no difference has been found according to patients' sex or disease type. In our study hypovitaminosis D did not correlate with disease duration nor patients' age at diagnosis. A statistically significant correlation has been found between hypovitaminosis D and history of steroid-dependancy (p = 0.03), need of biological therapy (p = 0.01) and cigarette smoke habit in CD patients (p = 0.01). Furthemore, in CD patients we found a correlation, at the limit of statistical significance, between hypovitaminosis D, altered PCR values and Harvey-Bradshaw Index (HBI) at enrollment (p=0.05)

Conclusions: In our study we found a high prevalence of hypovitaminosis D in a young IBD population regardless of patients' sex, disease type and duration. Our data showed a strong correlation between hypovitaminosis D and a more aggressive disease course in terms of history of steroid-dependancy, need of biological therapy

and smoke habit in CD patients. Hypovitaminosis D may be crucial in determining a more severe clinical behavior of IBD

P609
Efficacy of cytapheresis for remission induction therapy and dermatological manifestations of active ulcerative colitis

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Background: Erythema nodosum (EN) and pyoderma gangrenosum (PG) are the two major cutaneous ills of extraintestinal manifestations of ulcerative colitis (UC). The biologics and corticosteroids have significantly changed the management of these conditions. However, many patients show loss of response to biologics or their UC becomes refractory to corticosteroids. Cytapheresis can deplete elevated and activated leucocytes in UC patients, and is expected to ameliorate intestinal inflammation. This study was to assess the efficacy of cytapheresis for remission induction and dermatological manifestations of active UC.

Methods: A total of 193 cases received cytapheresis for UC between 2008 and 2014. Among these, 172 were for inducing remission including 12 with cutaneous lesions and 21 with quiescent UC for maintenance therapy and corticosteroid tapering. Each patient received weekly or intensive (2-3 sessions/week) cytapheresis up to 10 sessions with either a granulocyte-monocyte apheresis (GMA) column or with a leucocyte removal filter (LCAP). Lichtiger's clinical activity index (CAI) 4 and under meant clinical remission, while 3 and over decrease in CAI meant clinical response. Corticosteroid dose was to be tapered in responders. Remission induction rate, corticosteroid sparing, and the response to skin lesions were factored into our assessment of cytapheresis efficacy.

Results: Relative to baseline, the overall CAI fell from 9.3±3.3 to 4.9±3.5 (P<0.001). The clinical response and remission rates for cytapheresis were 76.2% (GMA 78.2% vs LCAP 70.8%, P=0.31), and 57.6% (GMA 57.3% vs LCAP 58.3%, P=0.90), respectively. Eighty-four patients were receiving systemic steroid, the average daily prednisolone dose at baseline was 19.3±13.1mg, and was reduced to 12.9±10.0mg after cytapheresis (P<0.001). The response and remission rates between the patients with concomitant steroid, biologic or tacrolimus and without concomitant medication were 80.6% and 70.9% (P=0.28), 61.3% and 53.1% (P=0.13), respectively. Patients with skin lesions associated with UC were 12, EN (n=5) and PG (n=7). All 12 cases responded to cytapheresis, notably, 4 EN patients showing rapid remission after the first 2 cytapheresis sessions. Six of 12 cases (1 EN and 5 PG), received concomitant steroid or infliximab. Extracorporeal related non-severe adverse events were observed in 7 of 193 patients.

Conclusions: In this study, cytapheresis was effective as remission induction therapy with significant steroid sparing effect. Additionally, patients with dermatosis associated with UC responded well to cytapheresis. We believe that cytapheresis has a clear efficacy in patients with skin lesions reflecting extraintestinal manifestations of UC.

P610
OSTEOPATHY AND IMPROVING THE QUALITY OF LIFE IN CROHN'S DISEASE

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Background: Crohn's disease, chronic inflammatory disease characterized by periods of flares and remissions, is very debilitating for patients.

The objective of this study is to evaluate the improvement of the quality of life of patients with Crohn's disease with visceral osteopathic technique, the root of the mesentery.

Methods: Groups

This study examined 27 patients (18 to 75 years), followed in the hepato-gastroenterology service at North Hospital (Marseille) and randomized into two groups:

- G1: 14 patients in the group receiving visceral osteopathic technique
- G2: 13 in the control group without treatment osteopathic

Patients meet the following inclusion criteria:

- Crohn's Disease diagnosis established by a gastroenterologist
- Crohn's located at the small intestine and / or colon
- Topics stable, in remission, following appropriate treatment

Excluded from the study, subjects with other recognized medical condition, or according to any other treatment.

Material and Methods

This study, single-blind test, has two assessments of the quality of life conducted at three-week intervals (D0 and D21) from IBDQ (Inflammatory Bowel Disease Questionnaire), whose score ranges from 32-224.

At D0, the patient responds to the IBDQ and receives treatment:

- G1: visceral osteopathic technique on the root of the mesentery
- G2: control, "virtual manipulation" (palpation of the small intestine and colon framework without action on the vasculature and innervation)

On D21, the two groups match in the new IBDQ

Results: To evaluate the effect of visceral osteopathic technique on the quality of life of patients, we perform a paired t-Student test.

G2 control group shows no variation in the evolution of the IBDQ ($p = 0.22$). However, the score of the patients in group treated with osteopathy G1 increased significantly between D0 and D21 ($p < 0.001$), indicating a significant improvement in their quality of life.

Conclusions: Visceral osteopathic technique on the root of the mesentery significantly improves the quality of life of patients with Crohn's disease.

As an osteopath, we can not limit ourselves to a single technique in our treatment. A full osteopathic care would reduce other symptoms of Crohn's disease, such as bone and joint pain, and further improve the quality of life of patients.

P611
First intestinal resection in Crohn's Disease . A long term prospective study

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Background: Surgical resection rates in Crohn's disease (CD) are high ranging from 25 to 61% at 5 years .Need for surgery remains impredictable. Identifing of predictors for surgery may be of interest for medical therapeutic strategies.

Methods: To determine surgical rates, characteristics and predictive factors of the first intestinal resection in CD, we have studied the outcome of a cohort of 226 CD patients (103 males: M ;123 females :F) , hospitalized in 3 Gastroenterological units in Algiers from 1/1/2000 to 31/12/2004 and included in a prospective follow-up for at least 5 years or until surgical resection. Mean age at

inclusion was 30,6 ± 6,5 years. 41 patients(18,1%) were smokers. Disease was located in both colon and small intestine (CSI ; n=116 ;51,4%), small intestine alone (SI ;n= 67;29,6%) or colon alone (C ; n=43 ;19%). Lesions were of inflammatory (I) ,stricturing (S) or penetrating (P) type in 92 (40,7%), 76 (33,6%), 58(25,7%) cases respectively . Medical treatment of flares was a conventional one and adapted to their severity ;relapses were prevented by 5ASA (n=125 ; 65,3%) or immunosuppressive drugs (n=32 ;14,1%) ;69 patients (30,5%) received no maintenance treatment. Statistical analysis:Student Fisher's test and Mann Whitney's U test.

Results: The 5-year intestinal resection rate was 29,6% (n=67/226). Annual rate of surgery increased according to duration of disease and varied from 4% between the first and second year to 7% between the forth and the fifth year of follow-up. Emergent surgery was needed in 24/226 patients (10,6%) and elective one in 19%(n=43/226) of all the cases. During the follow-up surgical resection was more frequent : 1/ when disease begun before 20 years old (n=13/29 ; 44,8%) comparatively to patients aged between 20 and 40 years (n=46/160 ; 28,7% ; p<0,001) or over 40 years (n=8/37 ; 21,6%) :p< 0,1103 ; thus 31,2% (n=59/189) were operated upon before 40 years. 2/ in patients with SI (n=35/116 ; 37,5%) or CSI (25/67 ;30,4%) location compared to patients with C location of the disease (n=7/43 ;16,3%) : p=0,06 ; 3/ in patients with S (n=38/76 ;50%) or P disease (n=23/53 ;43,4%) comparatively to I type of lesions at inclusion (n=6/92 ;6,5%) : p=0,0019. In return, rate of surgical resection was not influenced by : 1/ gender (F=37/123=30%, M=30/103 = 29,1% ; p >0,05) ; 2/ Smoking status of patients (smokers :10/33 ; 30,3% , previous smokers (n=5/15 ; 33,3%) and non smokers (52/170 ; 30,5%) ; p>0,05.

Conclusions: In this prospective study,the 5-year surgical rate of the first intestinal resection in Crohn's disease was 29,6%. The need for surgery was more frequent, but not statistically significant when disease begun before 20 years, in stenosing and penetrating disease and in SI or CSI location.

P612
Human safety, pharmacokinetics and pharmacodynamics of the GPR84 antagonist GLPG1205, a potential new approach to treat IBD.

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Background: Free fatty acids (FFAs) have been shown to act as signaling molecules through a family of G protein-coupled receptors, which are involved in the pathophysiology of a variety of diseases, including metabolic and inflammatory disorders. GPR84 is activated by medium chain FFAs. The receptor is primarily expressed on white blood cells (PMN, monocyte/macrophage) consistent with a reported role for GPR84 in inflammation.

GLPG1205 is a potent and selective antagonist of GPR84, inhibiting GPR84 activation in a functional GTPγS binding assay, as well as GPR84-induced neutrophil and macrophage migration. In the DSS mouse IBD model, GLPG1205 dose-dependently prevented disease progression, to a similar extent as sulfasalazine and cyclosporine. The histological score for colon lesions, neutrophil influx as well as colonic MPO content was substantially reduced.

Methods: The safety, tolerability, pharmacokinetics (PK) and target engagement (TE) of orally administered GLPG1205 (liquid formulation) were evaluated in healthy volunteers after single dosing (10-800 mg) and multiple ascending dosing for 14 days (50, 100, 200 mg QD) (NCT01887106). TE was assessed by a competitive radiometric displacement assay in whole blood (*ex vivo*). The bioavailability of a solid formulation (capsule) of GLPG1205 was determined in fasted and fed state after single oral dose administration (NCT02143856).

Results: In healthy volunteers, GLPG1205 was generally safe and well tolerated up to 100 mg QD for 14 days, with no adverse effects on ECG, vital signs or laboratory parameters. The most relevant adverse event was headache. The PK of the compound showed a rapid absorption, a long apparent terminal half-life (> one day) and a dose-proportional increase in exposure from 50 to 100 mg QD. Steady state was reached after 10 days. GLPG1205 showed dose-dependent target engagement, with a similar potency as in *in vitro* assays. The single-dose PK/TE data demonstrated a clear relationship between drug exposure and TE. At steady state, sustained target occupancy for 24 hours after once daily dosing was observed. Exposure and absorption rate of the capsule was similar to the liquid formulation and no food effect was observed.

Conclusions: GLPG1205, a potent and selective inhibitor of GPR84, is safe and generally well tolerated in healthy volunteers. It shows a favourable PK/PD profile, clearly demonstrating the ability of the compound to antagonize GPR84, a target which might be implicated in several neutrophil- and macrophage-driven inflammatory conditions. At steady state, a sustained 24-hour inhibition was observed. The efficacy and safety of GLPG1205 will be evaluated in Proof of Concept studies in IBD patients.

P613
Long side-to-side isoperistaltic strictureplasty over the ileocecal valve: a prospective analysis of feasibility and medium term outcome

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Background: A modified side-to side isoperistaltic strictureplasty over the ileocecal valve could be a valid alternative for ileocecal resection in patients with Crohn's disease (CD) and a long involved ileal segment. We explored the safety and efficacy in a prospective group of patients.

Methods: All CD patients with a long stenotic terminal ileum (>25cm) were included. Early ileocolonoscopy and magnetic resonance enterography (MRE) were performed to assess healing. Data were retrieved from a prospectively maintained institutional IBD database.

Results: Between June 2009 and September 2014, 29 patients, with a median age of 38 years (range: 16 - 68) and a median disease duration of 8 years (range: 0 - 34) underwent surgery. Nine male patients were included. Eleven patients were active smokers. Twenty six patients had primary surgery with a strictureplasty over the ileocecal valve. Three patients had a strictureplasty over the ileocolic anastomosis after previous ileocecal resection. Most patients had a laparoscopic approach (n = 24). The median length of the strictureplasty was 50cm (range: 27 - 110). 12 patients had 29 additional procedures: 22 strictureplasties, 6 segmental small bowel resections and 1 reversal of Hartmann's resection. Median length of stay was 9 days (range: 6 - 17) with prolonged postoperative ileus being the main cause of delayed discharge (median: 5 days, range: 2 - 12). Two patients developed a leak requiring additional suturing with successful salvage of the strictureplasty. Twenty-four patients underwent a postoperative colonoscopy at a median follow up of 6 months (range: 2 - 21) with significant improvement of the 'simple endoscopic score in Crohn's disease (SES-CD score). Postoperatieve MRE at a median interval of 6.7 months (range: 2 - 27) showed a significant regression of inflammation, bowel wall thickness and adequate luminal patency. At a median follow up of 10 months (range: 1 - 47), clinical recurrence was reported in 10 patients at a median interval of 14 months (range: 4 - 28). One patient had a surgical recurrence requiring additional strictureplasty after 48 months. Another patient needed adhesiolysis for small bowel obstruction.

Conclusions: A modified long side-to-side isoperistaltic strictureplasty over the ileocecal valve represents a valuable bowel sparing technique in Crohn's disease patients with a long stenotic segment. Surgery is safe and efficient at medium term follow-up.

P614
Anti-TNF-induced skin manifestations in IBD patients: role for increased drug exposure?

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Background: A subgroup of patients treated with anti-tumor necrosis factor (anti-TNF) develop paradoxical inflammation of the skin. While in most patients these lesions can be controlled with topical or systemic treatment, in a subset of patients anti-TNF treatment needs to be discontinued. Although the pathogenesis of these skin lesions is not fully understood, these side-effects mostly seem to occur while the intestinal inflammation is controlled. We therefore aimed to study if drug exposure in those patients developing a skin lesion is higher than in patients without skin lesions.

Methods: We performed a retrospective study on 604 IBD patients under anti-TNF maintenance therapy (≥ 4 infusions in ≥ 6 months), and studied the influence of infliximab trough concentrations (TC) and development of antibodies to infliximab (ATI) on the development of skin lesions. A skin lesion was defined as either xerosis cutis, eczema, psoriasis, psoriasiform eczema, palmoplantar pustulosis or other (folliculitis, acne, alopecia areata, tinea pedis...) with the need to consult a dermatologist. A total of 8350 TC measurements (ELISA) were available in 433 individuals with a median of 18 (IQR 5-32) per individual. 2770 ATI measurements were available in 325 individuals with a median of 5 (IQR 3-13) per individual.

Results: Of the 604 patients, 230 (38.0%) developed a skin lesion related to anti-TNF therapy. Of these, 176 (29%) developed under infliximab after a median time of 1.7 years (8.7/100 patient years, pyrs), and 54 (9%) after switch to adalimumab or certolizumab pegol with a median time of 1 year after switch (7.3/100 pyrs). The cumulative infliximab dose in patients developing a skin lesion under infliximab was 2833 [2198-3864] mg/year, compared to 2927 [2372-3670] mg/year in the other patients (p=NS). The median infliximab TC in skin lesion patients was 4.2 µg/ml, and 4.0 µg/ml in non-skin lesion patients (p=NS). There was no difference in the number of subtherapeutic TC (at least twice TC < 3 µg/ml), supratherapeutic TC (at least twice TC > 7 µg/ml), or ATI positive (at least once > 1 µg/ml equivalents) patients in the skin lesion group compared to the non-skin lesion group (Table 1). Quartile analysis of the median TC per individual did not show differences between skin lesion and non-skin lesion patients (Table 1, p=NS).

Table 1: Comparison of TL and ATI between patients developing a skin lesion during infliximab treatment or not

Variable	No skin lesion (n=374)	Skin lesion (n=176)
Median TC (µg/ml)	4.0 (1.6–5.9)	4.2 (2.6–5.8)
TC subtherapeutic	184 (69.7%)	113 (68.5%)
TC supratherapeutic	221 (81.8%)	135 (83.7%)
ATI positive	53 (39.0%)	34 (32.7%)
Q1 (<1.8 µg/ml)	70 (26.5%)	32 (19.4%)
Q2 (1.8–4.0 µg/ml)	65 (24.6%)	48 (29.1%)
Q3 (4.0–5.9 µg/ml)	64 (24.2%)	46 (27.9%)
Q4 (>5.9 µg/ml)	65 (24.6%)	39 (36.3%)

Conclusions: Our data show that differential drug exposure does not play a role in developing skin adverse events in patients treated with anti-TNF.

P615
Post-marketing experience of vedolizumab for IBD: The University of Chicago experience

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Background: Vedolizumab, a monoclonal antibody to alpha-4 beta-7 integrins was recently approved for both Crohn's disease (CD) and ulcerative colitis (UC). Its post-marketing experience in adults has not yet been described.

Methods: This was an IRB-approved post-marketing study of University of Chicago patients with CD and UC who received vedolizumab. Patients followed for at least 12 weeks were fully characterized and included. Clinical activity was assessed using Harvey-Bradshaw Index (HBI) or Simple Clinical Colitis Activity Index (SCCAI) at baseline and at pre-defined times of follow-up. Clinical response was defined as a reduction of 3 or more in HBI or SCCAI and clinical remission was defined as HBI less than or equal to 4 or SCCAI less than or equal to 2. Variables influencing clinical response were examined using Chi-square test, Fisher's exact test and Wilcoxon rank-sum test.

Results: From May 2014-November 2014 130 patients (62% CD) started vedolizumab at our Center. At the time of this abstract, 69 patients (61% CD) had post-induction follow-up (45% male, median age 35 years). Of 46 patients with active disease at baseline, 39% achieved clinical remission and 54% achieved clinical response by week 14. Of 23 patients who were in clinical remission at baseline, the indications for vedolizumab included steroid/tacrolimus dependence (n=8), active disease on endoscopy (n=5), intolerance to anti-TNF therapy (n=2), transition from natalizumab (n=6), perianal disease (n=1) and active PSC (n=1). Clinical remission rates in those with UC and CD increased from 26% to 52% and 38% to 62%, respectively (CD v UC n.s.). Of 37 patients on prednisone at induction, 10 (27%) were steroid-free by week 14. Numerical but non-significant differences were found for response in ileocolonic CD v isolated ileal or colonic disease (44% v 100% v 67%, p = 0.109), pan UC v less extensive disease (40% v 80%, p = 0.303), number of failed anti-TNF therapies (71% v 67% v 46% for TNF-naïve, 1 failed TNF or 2 or more failed TNF therapies, respectively, p=0.602) and combination v monotherapy (59% v 52%, p = 0.641). 5/15 (33%) with arthralgias and 5/10 (50%) patients with active perianal disease had improvement. 30% of pts described an adverse event including worsening GI symptoms (n=10, 5 colectomies), minor infections, aches and pains, and one pt with an allergic reaction to vedolizumab

Conclusions: In this post-marketing experience of vedolizumab for IBD in a tertiary center, vedolizumab therapy demonstrated similar efficacy and safety as seen in the pivotal trials, with clinical response in the majority of patients, including those with

complex disease phenotypes and those who have failed anti-TNF therapy. We did not see differences in response between CD and UC.

P616
Different profile of efficacy of thiopurines in Ulcerative Colitis and Crohn's Disease

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Background: Azathioprine (AZT) and 6-mercaptopurine (6-MP) are effective drugs in treating ulcerative colitis (UC) and Crohn's disease (CD) as they can induce/maintain clinical remission (CR) and mucosal healing (MH) in steroid-dependent patients. Nevertheless, studies directly investigating a possible different profile of efficacy in UC in comparison with CD are scarce. Aim: to explore the rate of CR and MH in UC patients treated by thiopurines compared to that of subjects with CD.

Methods: We performed an observational longitudinal study evaluating steroid-free CR and MH in all UC and CD patients who would complete 2 years of maintenance treatment with thiopurines. Patients characteristics were classified according to the ECCO guidelines. CR and MH were assessed before starting treatment and 2 years later by Mayo score for UC (CR= Mayo score <2; MH= Mayo sub-score <1); CR and MH were assessed at same time-points by Crohn's disease activity index (CR=CDAI< 150) and Simplified Endoscopic Score for Crohn's Disease (MH=SES-CD <2) for CD. Statistical analysis was performed using chi-square, Mann-Whitney U test and odd ratio(OR) where appropriate. To test the concordance between CR and MH in UC and CD, the Cohen's k measure was applied. Regarding the differences in outcomes for CR and MH we estimated that a total sample size of 120 patients would allow detection of a 20% difference between the 2 groups.

Results: The study included 70 patients with UC (AZT/6-MP=60/10; M/F=37/33; mean age=39 years; E1=0, E2=24, E3=46;mean baseline Mayo score=8.5) and 70 subjects with CD (AZT/6-MP=62/8; M/F= 39/31; mean age=33 years; L1=34, L2=26, L3=10;B1=54, B2=10, B3=6; mean baseline CDAI=290) treated with thiopurines for 2 years. At the end of the study, steroid-free CR was recorded in 43 patients with UC and 37 with CD (61% vs 53%; p=0.3). MH was obtained in 38 patients with UC and 17 with CD (54% vs 25%; p<0.01; O.R.=4.5). The concordance between CR and MH was higher in UC patients than in subjects with CD (k=0.71in UC; k=0.41 in CD).

Conclusions: Thiopurines are equally effective in maintaining steroid-free clinical remission in both UC and CD even if with a better profile of efficacy in UC in terms of mucosal healing. Our data confirm the higher concordance between clinical and endoscopic findings in UC compared to that observed in CD patients.

P617
Analysis of Patient Perception of Pain and Management Strategies in IBD

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Background: Pain is a common reason for poor quality of life (QOL) in inflammatory bowel disease (IBD) patients. Inflammation, mechanical obstruction, functional impairment, psychological and psychosocial factors influence patient perception of pain. The objective of this study was to establish the prevalence of and factors associated with pain in IBD patients and how they perceive and manage their pain.

Methods: A cross-sectional study of consecutive patients with IBD attending out-patient review at two academic centres. A 127 item anonymous questionnaire was distributed to 253 patients and complete responses were obtained in 200 (79%). Physician assessment of disease activity based on recording of biochemical, endoscopic, histologic and radiological parameters was performed, blinded to patient responses. Physicians recorded their opinion on whether pain related to stricture, inflammation, prior surgery/adhesions and/or functional disorder. The validated SAD-21 score, brief pain inventory and CCKnow questionnaires were used to assess stress, anxiety, depression, pain frequency and intensity, and knowledge of IBD. 39 questions related to pain management methods and patient beliefs regarding pain. Data was analysed using SPSS.

Results: Data were collected from 200 patients (mean age 41 years; 55% male; 43% UC, 53% CD, 4% IBDU). Medications: steroids 9%, 5-ASA 43%, biologic 23%, azathioprine 43%. 35% had previous surgery, 22% smoked, 54% in current employment, 46% had third level education. 58% felt well and 64% reported no abdominal pain. 30% had CRP elevation, 61% had endoscopic activity, 34% had radiological activity , 61% had histological activity. Overall 64/200 (32%) of respondents reported pain with average intensity of 3/10 or greater ('pain reporters'). Compared to those without pain, these patients showed no difference in age, disease duration or diagnosis, but more were female (58% versus 40%, p=0.02). Pain reporting was not associated with physician rating of active disease or raised inflammatory markers. Trends to pain reporting were noted in patients with radiological activity (p=0.07), stricture (p=0.08) and with functional bowel disease (p=0.06). The mean scores in the SAD-21 for anxiety (mean = 4.6 versus 1.9, p<0.001), depression (mean = 5.6 versus 2.6, p<0.001) and stress (mean = 7.0 versus 4.1, p<0.001) were significantly greater in pain reporters. 37% of patients reported pain relief interventions in the previous week. Alcohol was second only to paracetamol as the most commonly used pain relief intervention.

Conclusions: Pain is a common symptom in IBD patients and is associated with significantly increased stress, anxiety and depression and may be associated with problem alcohol use.

P618
Adalimumab dose escalation is effective for managing loss of response in Ulcerative Colitis

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Background: The outcomes of adalimumab dose escalation in ulcerative colitis (UC) are not well known. The aim of this study was to assess the short- and long-term outcomes of adalimumab dose escalation in a cohort of UC patients who had lost response to the drug.

Methods: This was a retrospective multicentre cohort study. All consecutive UC out-patients who required adalimumab dose escalation for loss of response were included. Post-escalation short-term clinical response and remission were evaluated. Clinical response was defined as a 3-point decrease in the Partial Mayo Score (PMS) or a decrease of at least 50% in the PMS and a final PMS of 2 or less. Clinical remission was defined as a PMS of 0 or 1. In the long-term, the cumulative probabilities of adalimumab failure-free survival and colectomy-free survival were calculated. Predictors of short-term response and event-free survival were estimated using logistic regression and Cox proportional hazard regression analysis.

Results: Of the 200 UC patients who received adalimumab therapy, 76 (38%) required escalation to weekly adalimumab dosing and composed the study population. Of these escalated patients, 41 (54%) were male, with a mean age of 46 (SD 14) years and a median disease duration of 11 (interquartile range [IQR] 2-20) years. Sixty-two patients (81%) had previous anti-TNF use. Thirty-six (47%) achieved short-term clinical response, of these 15 (20%) entered into clinical remission. The mean PMS was 6 (range 4-9; standard deviation [SD] 1.5) at baseline and 3.6 (range 0-8; SD 2.3) at week 8-12 ($p<0.001$). There were no factors associated with short-term response. After a median follow-up of 9 months (IQR 8-26), 43 patients (56%) had adalimumab failure. Patients with short-term response had a significantly lower adjusted rate of adalimumab failure (hazard ratio [HR] 0.60; 95% confidence interval [CI] 0.12-0.80; $p<0.01$). During a median follow-up of 17 months (IQR 13-34), 16 patients (21%) needed colectomy. Median time to colectomy was 5.9 months (IQR 4-14). Short-term response was identified as a predictor of colectomy avoidance (HR 0.53; 95% CI 0.03-0.69; $p<0.007$).

Conclusions: Adalimumab dose escalation was required in 38% of UC patients. Nearly 50% of patients regained response with weekly adalimumab dosing. In the long term, 44% of patients maintained sustained clinical benefit, and 8 of 10 avoided colectomy. Short-term response was associated with a 50% reduction in the relative risk of colectomy.

P619
Evaluation of a service to manage Inflammatory Bowel Disease (IBD) in Pregnancy.

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Background: Following the publication of the ECCO consensus [1] for management of IBD in pregnancy a service was set up in our institution to optimise management of this group. Its' aim is to enable multidisciplinary management of patients with a gastroenterologist, obstetrician, colorectal surgeon and IBD specialist nurse. It provides a baseline health check in the early stages of pregnancy, more intensive foetal growth monitoring (additional growth scans at 28 and 32 weeks), discussion of delivery methods and anticipation of potential peripartum problems. A review of the service was performed after 18 months.

Methods: A retrospective review of medical notes was performed. Information was gathered on: diagnosis, previous surgery, parity, previous pregnancies, medication and disease activity both preconception and during pregnancy.

Results: Data was collected on 39 patients. 18 Crohns disease (CD), 21 ulcerative colitis (UC). Surgery: UC group 3/21 had previous surgery:2 ileoanal pouch, 1 subtotal colectomy. CD group 10/18 had previous surgery: 9 ileocolonic resections and 1 subtotal colectomy. Parity: 11=para 1,14=para 2, 11=para 3, 3=para 4, 1=para 1.

Medication: 17/39: no medication (8 UC, 9 CD). 4:infliximab, last infusion approximately 20/40, 12: azathioprine, 12: 5ASA.

Disease activity: 36/39 were well preconception; 1 was unwell around time of conception and had miscarriage at 11/40. 15/39 had a flare of disease activity: 1 settled with topical treatment, 3 with 5ASA, 11 required oral steroids. 3 of 4 patients on infliximab had a flare and all 3 required oral steroids. 1/4 had a stillbirth shortly after commencing steroids for a flare although had responded well.

Outcomes: 8/39 have not yet delivered; 3 are planned for elective CS (Caeserian section)for obstetric reasons, 1 planned for induction (small baby). 15/31 had CS; 2 ileo-anal pouches, 2 ileo-rectal anastomosis, 3 perianal disease, 8 for obstetric reasons. 1 stillbirth, 2 miscarriages, 13 normal vaginal delivery (NVD). No preterm births or low birth weights reported to date

Conclusions: Those with ileo-anal pouches and perianal disease are being appropriately considered for a planned CS. 42% of our patients have a NVD which as expected is lower than the general population. 38% of patients had a flare in disease during pregnancy which is higher than literature (30%). 73% required oral prednisolone. 2/3 adverse outcomes appear to be related to a flare in disease. Those on infliximab appear to be at high risk of flaring after their last dose around 20 weeks.

A combined service with a dedicated Gastreoenterology and Obstetric team is an essential part of a tertiary referral centre in order to pre-empt and pro-actively manage complications in pregnancy in IBD.

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P620
Granulo-monocytes Apheresis Induce TGFbeta1 Modulation in Neutrophils of Patients Suffering from Ulcerative Colitis: A Possible Role of Soluble HLA-I Molecules.

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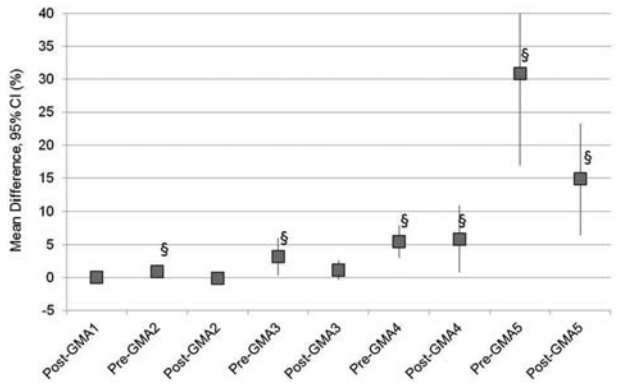

Fig 1 TGFβ_1 Cytofluorimeter differences in CD66b cells respect with previous sample timing

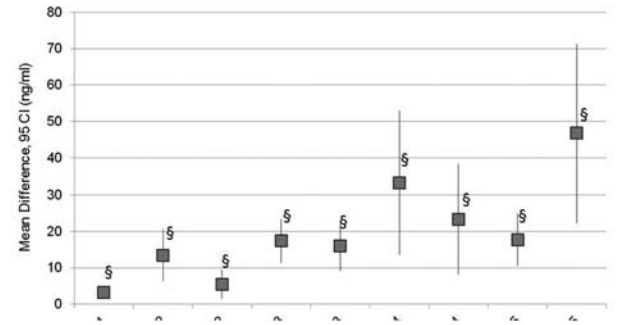

Fig 2 Plasma TGFβ_1 differences respect with previous sample timing

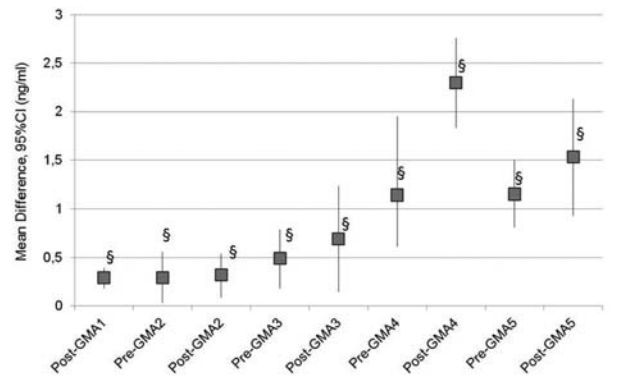

Fig 3 Plasma sFasL differences respect with previous sample timing

Background: Plasmapheresis is used in immune-mediate disease in order to remove humoral factors and, in addition, to modulate cellular immunity. It has been shown that during aphaeretic centrifugation , whole and/or re-folded soluble HLA class I molecules (sHLA-I) bind to the circuit surfaces. Similarly, neutrophils can bind sHLA-I molecules with immunoglobulin-like transcript (ILT) membrane receptors, becoming hereafter sensitive to the immunomodulation of sHLA-I such as transcriptional and post-transcriptional transforming growth factor (TGF)-beta1 modulation. On the other hand, TGFbeta signaling plays a major role in the pathogenesis of inflammatory bowel diseases and it is known to directly induce Foxp3 expression. Besides, Foxp3 expression has been reported increased in patients who responded to granulocytes apheresis with remission of clinical symptoms.

The aim of this prospective study was to evaluate a possible sHLA-I mediated immunomodulation in granulocytes and monocytes apheresis in ulcerative colitis patients who responded to therapy.

Methods: We prospectively enrolled a total of 10 patients (4M/6F; mean age 49, range 27-73) who achieved clinical remission with GMA. The GMA sessions (5 cycle/session) were performed using Adacolumn device. Instantly before each single apheresis and immediately after each procedure, neutrophils were analyzed for a possible in vivo aftermath of sHLA-I binding with corresponding ligands Ig-like-transcripts. The concentrations of sFasL molecules were determined by double-determinant immunoassay (DDIA) and the concentrations of TGFb1 were determined by double-determinant immunoassays utilizing a commercially available kits.

Results: Between every GMA cycle a significant upregulation of intracytoplasmic TGFbeta1 molecule or TGFbeta1-mRNA was observed in neutrophils and CD8+ T lymphocytes drawn along the apheretic therapeutic treatments. In particular, the greatest mean increase was found after the first and the forth GMA cycles (from +1% to +30%) (IMAGE.01). A significant up-regulation of sFasL and TGFbeta1 concentrations in plasma was observed along the procedures. Similarly, the mean difference increases in comparison with previous samples were constantly found raising during scheduled blood sampling for both molecules (IMAGE.02 and 03). In CD4+ T lymphocytes, unable to bind sHLA-I, the aphaeretic procedures never induced TGFbeta1 modulation

Conclusions: Our findings suggest that the immunosuppressive effects following therapeutic apheresis might at least in part depend on activated leukocyte sensitivity to sHLA-I molecule bioactivity.

P621
Comparison between total abdominal colectomy and segmental colectomy in Crohn's colitis patients: Recurrence and re-resection rates. A retrospective cohort study

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Background: Crohn's disease (CD) may potentially affect any part of the gastrointestinal tract. Crohn's colitis is a subgroup of CD involving the colon and rectum. Although medical management has evolved greatly, patients with CD still require surgery as disease progresses. Recent studies that compared segmental colectomy and total abdominal colectomy presented equivocal data regarding recurrence and re-resection rates. The aim of this study was to compare long-term outcomes in regard to recurrence rates and re-resection rates, of segmental versus total/subtotal colectomy in patients with Crohn's colitis (CC), and to identify risk factors associated with post-operative recurrence.

Methods: The medical records of all CC patients who underwent colectomy between 1995 and 2013 and were followed at the Tel Aviv Medical Center were identified. Data on age at diagnosis, gender, smoking, disease location at diagnosis, perianal and rectal disease status, indication for surgery, disease duration before operation, type of operation, primary anastomosis at first operation, length of resected specimen, recurrence of symptoms, medication after surgery, re-operation, and total follow-up time were retrieved.

Results: Thirty-five patients (segmental colectomy-18, total/subtotal colectomy-17, male-17, mean age at operation 36.6) were identified. All parameters were comparable between the groups. Mean disease duration prior to first operation was 122.83 months before segmental colectomy and 131.89 months before total/subtotal colectomy (p=0.456). Resuming of medical treatment following surgery was significantly higher in CC patients undergoing segmental colectomy (n=10, 55.55%) compared to those undergoing total/subtotal colectomy (n=15, 88.23%) (p=0.01). Patients undergoing segmental colectomy had significantly longer re-operation-free survival compared to those undergoing total/subtotal colectomy, (p=0.02). A trend towards longer symptom-free survival after segmental colectomy was observed as well, 59+/-13 and 24+/-8 months, respectively (p=0.105); surprisingly, no correlation between the length of resected bowel and survival outcomes was observed (p=0.997 and p=0.319, respectively).

Conclusions: Disease recurrence rate and re-resection rate are not higher after segmental colectomy and therefore segmental resection can be safely performed in limited Crohn's colitis. Further studies should be conducted to explore these potential culprits.

P622
Infusion-related reactions with vedolizumab treatment in patients with UC or CD during the GEMINI 1 and GEMINI 2 clinical trials

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Background: Vedolizumab (VDZ) is a monoclonal antibody that specifically targets the α4β7 integrin. The efficacy and safety of VDZ in patients with ulcerative colitis (UC) and Crohn's disease (CD) were demonstrated in the phase 3, placebo (PBO)-controlled GEMINI 1 (NCT00783718)[1] and GEMINI 2 (NCT00783692) [2] studies, respectively. In these studies, ≤5% of VDZ-treated patients experienced adverse events (AEs) defined by the investigator as infusion-related reactions (IRRs). Here, we describe the reported IRRs and use of premedication in GEMINI 1 and 2.

Methods: GEMINI 1 and 2 both consisted of a 6-week induction phase followed by a 46-week maintenance phase. Post hoc analyses were performed for patients who received either PBO or VDZ continuously throughout the induction and maintenance phases to identify the AEs reported as investigator-defined IRRs in each study. Time of onset for IRRs was also evaluated. Premedication use was summarised by study visit.

Table. Adverse events defined by the investigator as infusion-related reactions in ≥2 patients with ulcerative colitis or Crohn's disease

GEMINI 1 Ulcerative Colitis			GEMINI 2 Crohn's Disease		
	PBO[a]	VDZ[b]		PBO[a]	VDZ[b]
Adverse Event	n=149	n=620	Adverse Event	n=148	n=814
Preferred Term	Patients, No. (%)		Preferred Term	Patients, No. (%)	
Arthralgia	0	2 (<1)	Nausea	2 (1)	8 (<1)
Fatigue	0	2 (<1)	Headache	2 (1)	4 (<1)
Headache	0	2 (<1)	IRR	0	3 (<1)
Pruritus	0	2 (<1)	Dizziness	1 (<1)	3 (<1)
Tinnitus	0	2 (<1)	Pruritus	0	3 (<1)
Urticaria	0	2 (<1)	Fatigue	0	2 (<1)
Vomiting	0	2 (<1)	Pyrexia	0	2 (<1)
			Rash	0	2 (<1)

Abbreviations: IRR, infusion-related reactions; PBO, placebo; VDZ, vedolizumab.

[a] Patients received PBO in both induction and maintenance phases.

[b] Patients received VDZ in both induction and maintenance phases.

Results: IRRs were reported for 28 (5%) and 33 (4%) patients treated with VDZ in GEMINI 1 (UC) and GEMINI 2 (CD), respectively. In each study, >70% of all IRRs occurred during or within the first 2 hours after the end of an infusion. The most common IRRs were nausea (CD n=8; <1%) and headache (UC n=2, <1%; CD n=4, <1%; Table). One patient with CD had an IRR that was considered serious and resulted in study drug discontinuation. Her symptoms, including dyspnoea, bronchospasm, hives, flushing, rash, and increased blood pressure and heart rate, began 13 minutes after the start of an infusion and resolved about 3 hours later with treatment. No serious IRRs were reported in patients with UC. Premedication, predominantly antihistamines and corticosteroids, was used in 5% and 7% of VDZ-treated UC and CD patients, respectively, a rate similar to that in PBO-treated patients (5% UC and 6% CD).

Conclusions: IRRs occurred in ≤5% of patients receiving VDZ infusions; 70% of all IRRs occurred within 2 hours. Premedication was administered infrequently. These results indicate that VDZ infusions were generally well tolerated by patients.

The clinical study was funded by Millennium Pharmaceuticals, Inc. (d/b/a Takeda Pharmaceuticals International Co.). Medical writing assistance was provided by inVentiv Medical Communications and supported by Takeda Pharmaceuticals International, Inc.

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P623
Steroids no more! Exclusive Enteral Nutrition therapy in pediatric patients with Crohn's Disease Results in long-term avoidance of corticosteroid therapy

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Background: Exclusive Enteral nutrition (EEN) has been used as a primary therapy for the treatment of pediatric Crohn's Disease (CD). However, it has yet to be widely endorsed as a primary therapy by North American gastroenterologists despite evidence of its efficacy.

Aim: To compare the long-term outcomes of CD patients initially managed with EN versus corticosteroids in a large retrospective cohort.

Methods: A single centre, retrospective analysis (1985 to present) of 229 pediatric patients with CD receiving either EEN (n=153) or steroid induction therapy (n=76). EEN was used for a 12 week induction, followed by EN (50% total daily calories) + regular diet as maintenance. Clinical remission was defined as PCDAI ≤ 7.5 without height at baseline and at the 4-8 week follow-up, and ≤ 10 at the 6-, 12-, 24-, and 36-month follow-up visits. A propensity analysis with nearest-neighbour matching, using a 1:2 replacement, and small caliper (.15; allowable standard deviation of estimated propensity score) was carried out. Matched baseline characteristics included gender, age, weight, height, PCDAI and Paris disease locations.

Results: The propensity analysis reduced the sample size of each group, EEN (N=69) and corticosteroid (N = 70), yet reduced bias in initial assignment to therapy. EEN and Steroid patients (33% female in each group) were very similar in age (11.9 ± 3.0, 12.0 ± 2.5 years respectively), Height (146.6 ± 19.6, 147.4 ± 14.5 cm), Weight (36.5 ± 13.7, 37.9 ± 12.3 kg), and disease activity measured by PCDAI (31.1 ± 10.9, 31.8 ± 10.4) at baseline. Initial EEN therapy significantly decreased the risk of exposure to corticosteroids, as 76% and 66% of EEN matched patients remained steroid free over 1 and 3 years, respectively. EEN patients had a quicker induction of remission (4-8 weeks) with 80% of patients achieving clinical remission versus 63% of steroid patients ($p < .05$). There was a significant growth x group interaction over time, showing that EEN patients height z-score trajectory (-.14 at baseline to .11 at 36 months) was larger than Steroid group patients ($p = .02$) whose growth remained relatively unchanged from baseline to 36 months (z = -.14 to -.13).

Conclusions: EEN therapy showed more positive effects over time via quicker induction of remission, significant changes in linear growth, and avoidance of corticosteroids over a 3-year follow-up period.

P624
Impaired intestinal barrier function promotes procoagulatory state in Inflammatory Bowel Diseases

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Background: Inflammatory and immune mediated disorders are risk factors for arterial and venous thromboembolism. Inflammatory Bowel Diseases (IBD), namely Crohn's disease (CD) and ulcerative colitis (UC) confer an even greater risk of thromboembolic events than other inflammatory conditions. It has been shown that IBD patients display defective intestinal barrier functions. Thus, pathogen-associated molecular patterns (PAMPs) coming from the intestinal bacterial burden might reach systemic circulation and activate innate immunity receptors on endothelial cells and platelets, promoting a procoagulative state.

Aim of the study was to test this hypothesis, correlating the presence of circulating PAMPs with the activation of innate immune system and the activation of the coagulatory cascade in IBD patients

Methods: Lipopolysaccharide (LPS), Toll-like receptor (TLR) 2, TLR4 and markers of activated coagulation (i.e. D-Dimer and prothrombin fragment F1+2) in the serum and plasma of IBD patients (N=35 CD and 25 UC) and controls (CONT) (N=20) were measured using commercially available immunoassays.

Results: LPS levels were more elevated in CD (0.400 [0.333-0.540] EU/ml) and UC (0.410 [0.275-0.659] EU/ml) patients vs. CONT (0.325 [0.264-0.411] EU/ml; P=0.048 and P=0.253, respectively). TLR2 was more abundant in CD (517.21 [412.07-890.73] pg/ml) and UC (438.43 [286.63-699.98] pg/ml) sera vs. CONT (281.15 [122.23-412.05] pg/ml; P=0.002 and P=0.055, respectively). LPS and TLR4 levels significantly correlated in IBD patients (r=0.408, P=0.001) with a more robust correlation for UC (r=0.512, P=0.008), than for CD (r=0.332, P=0.054). Only a weak correlation between circulating LPS and CRP concentrations (r=0.274, P=0.046) was found, whereas, no correlations were observed between Harvey-Bradshaw and CAI scores and circulating LPS and TLR4. Interestingly, LPS levels significantly correlated with both D-Dimer (r=0.398, P=0.002) and F1+2 concentrations (r=0.395, P=0.002).

Conclusions: Taken together, our data support the role of an impairment of intestinal barrier in triggering the activation of the coagulatory cascade in IBD.

P625
Use of infliximab (Remicade®) for IBD within a patient support program: Positive perception of i.v. infusions from patient's perspective

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Background: In Canada, IBD patients treated with infliximab (IFX) are primarily managed through a nationwide patient support program (PSP) where a case coordinator manages treatment between the patient, physician and a network of infusion clinics. The aim of this study was to assess patients' experience of IFX therapy administered in this PSP.

Methods: In this nationwide, cross-sectional survey, patients currently receiving IFX within the PSP were given an information brochure to access a web-based survey (May 5-July 18, 2014) of demographic and disease characteristics, respondents' lifestyle and health ratings, and their perception of IV infusions before and after initiating therapy. The analysis was exploratory and descriptive; data collected was a self-reported ordinal scale (low to high, 1 - 10) with median (IQR) and mean (range) reported. The Wilcoxon signed-rank test was used for assessment of statistically significant differences in responses over time.

Results: Of 10,000 brochures distributed in 192 clinics, there were 1,762 respondents (18%); >75% were treated for IBD. 49% were males, and median age was 41 (30-53) and 98% treated with IFX. 62% of respondents were employed, 8% unemployed, 11% retired, 9% on disability, 9% were students. 57% of respondents reported receiving therapy for >2 yrs, 18% for 1-2 yrs and 25% <12 mo. 73% of respondents were receiving their 1st biologic therapy. Regarding lifestyle, 57% of respondents stated that they travel for personal/work reasons and 76% of all responders self-categorized as living a busy/active lifestyle. Median health rating was high 8(6-9), with higher values observed for patients enrolled in the program for longer periods of time (p<0.0001). Changes in the initial vs. current patient impressions on specific attributes of the program were notably positive. Experience of having multiple infusions revealed how worthwhile the time commitment was and hence improved patients' perception on of the value of the time required to complete an infusion. The overall perception of IV infusions was increased as well; the majority of patients rated it as 5 prior to starting therapy vs. 8 after multiple infusions (p<0.0001). Change in perception of IV infusions varied based on the initial rating with over 90% of patients increasing their rating from 1-6 pts after undergoing infusions.

Conclusions: While this study is subject to a strong selection bias, we found that these patients lead busy/active lifestyles, see the time commitment of IV treatment as worthwhile, have a positive experience at the clinics and report significant improvements in their perception of IV infusion. Further studies on this topic are warranted.

P626
Histological improvement after induction therapy with infliximab provide prolonged clinical remission during maintenance therapy in children with Crohn disease.

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Background: Recently, so-called "deep remission" has become a conceptual, more "extended" goal that contribute to achievement of long-term clinical remission and may even alter the long-term natural history of the disease in selected patients. Since data on that issue are limited, especially in pediatric population, the aim of this study was to assess impact of histological healing during biological therapy for maintenance of Crohn disease (CD) remission.

Methods: 33 patients aged 16,7±4 years with moderate to severely active CD who had clinical response following induction therapy with infliximab (IFX) and continued with maintenance therapy during 1 year were included into the study. Colonoscopy and gastroscopy with samples collection were performed in all patients at baseline (week 0), after three injections of IFX (week 10), and after 1 year of maintenance therapy with IFX. Histological changes were evaluated with numerical scoring system (0-no inflamation; 1-nonactive inflamation; 2-cript distortion, abscesses; 3-active inflammation, ulcerations). Histological scorings at week 0 and week 10 were compared between 2 subgroups: patients with remission at week 52 present (n=26) vs. patients with no remission (n=7). Discriminant ability was assessed with ROC curve analysis.

Results: Neither histological scoring at week 0 nor at week 10 did not differ significantly between subgroup with remission at week 52 present vs. subgroup with no remission, whereas difference between scoring at week 0 and at week 10 was significantly higher in subgroup with remission. Area under ROC curve for this parameter (scoring week 0 - scoring week 10) was 0,76 and optimum cut-off point greater or equal 2 discriminate subgroups with sensivity 0,62 and specifity 1.

Conclusions: Histological improvement after induction therapy with at least 2 points provides prolonged clinical remission, whereas 40% patients with less histological improvement have CD flare during maintenance therapy with IFX.

P627
Correlation between adalimumab serum levels and remission after the induction phase in Crohn's Disease patients

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"Table 1. Area under the ROC curves (AUC) for adalimumab trough levels to predict response and remission at week 14"

	Weeks	AUC	Threshold concentrations	Sensitivity (%)	Specificity (%)
Remission	4	0.75	13 µg/mL	82	75
	8	0.75	9 µg/mL	68	75
	14	0.80	8 µg/mL	80	75
Response	4	0.89	9.4 µg/mL	89	100
	8	0.88	6.4 µg/mL	88	100
	14	0.94	7.6 µg/mL	88	100

Background: Detectable adalimumab trough levels have been associated with higher rates of clinical remission. However, the correlation between adalimumab trough levels and remission during the induction phase in Crohn's disease (CD)patients has not been studied so far

Aim: To evaluate the correlation between adalimumab levels and remission after the induction phase in CD patients. To evaluate the accuracy of adalimumab serum levels to predict short-term remission

Methods: CD patients with active disease (CDAI>150) naïve to anti-TNF treatment were included. Patients received 160/80mg adalimumab at weeks 0 and 2 and 40mg every-other-week thereafter. Remission was defined as a CDAI score < 150 and response as a decrease of >70 points after 14 weeks of treatment. Clinical evaluation was assessed and blood samples were drawn at baseline and weeks 4,8 and 14. Adalimumab and antibodies to adalimumab (ATA) were measured using a homogeneous mobility shift assay (HMSA; Prometheus Lab, San Diego, USA). Correlation between adalimumab trough levels during the induction phase and response at week 14 was calculated. Receiver operating characteristic (ROC) curves were constructed and the area under the ROC curve (AUC) was calculated. Determination of predictive adalimumab trough concentration thresholds were based on the choice of the corresponding specificity and sensitivity pair determined from the ROC curves

Results: Twenty-two patients were included (54% male, 91% ileal or ileocolonic involvement, 73% inflammatory behaviour, 23% previous surgery and 82% on concomitant immunosuppressants). At week 14, 80% of patients had remission, 10% partial response and 10% non-response. Patients that reached remission were younger than those who did not (37 vs. 54 years, p=0.03). Mean adalimumab trough levels at week 8 were higher among patients that achieved remission at week 14 compared with those who did not (12 vs. 7 µ g/mL, p=0.02). Mean adalimumab trough levels at weeks 4 and 14 were also higher among patients in remission at week 14, but the differences did not reach the statistical significance (week 4: 16 vs. 11 µ g/mL, p=0.19; and week 14: 13 vs. 8 µ g/mL, p=0.08). The AUC for adalimumab trough levels to predict remission and response at week 14 and the best thresholds are shown in table 1

Conclusions: CD patients that reached response and remission at week 14 showed higher adalimumab trough levels during the induction phase than those who did not. We could identify the threshold concentrations of adalimumab that predict response and remission with a high accuracy

P628
Anti-TNF treatment and renal cell carcinoma in patients with inflammatory bowel disease, rheumatoid arthritis and spondyloarthropathy: trigger or cure?

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Background: There is limited evidence on the risk of solid cancers such as renal cell carcinoma (RCC) in chronic inflammatory conditions treated with anti-TNF therapy. We studied the occurrence of RCC in patients with inflammatory bowel disease (IBD), as well as rheumatoid arthritis and spondyloarthropathy (REU) at a tertiary referral centre.

Methods: In this retrospective cohort study using a supervised automatic search of our electronic clinical database, we included all IBD and REU patients who were diagnosed with RCC between January 1990 and September 2014. Medical records were reviewed for demographic and clinical variables, including type and duration of anti-TNF treatment. Age at diagnosis of RCC, tumour stage and surgical treatment were compared between groups.

Results: The diagnosis of RCC was confirmed in 22/2538 (0.9%) anti-TNF naïve IBD patients and in 7/1847 (0.4%) IBD patients with anti-TNF exposure (p=0.049). IBD/RCC patients with anti-TNF had a significantly higher rate of prior immunosuppression (100% vs. 27%; p=0.001) and surgery (100% vs. 62%, p=0.042) compared to anti-TNF naïve IBD/RCC patients. In anti-TNF treated IBD patients, RCC was diagnosed at a younger age (median 46.0 (IQR 42.3-56.4) vs. 63.1 (51.6-71.8) years; p=0.034) and early surgery (within 1 month of diagnosis) (100% vs. 23%; p=0.0003) and partial nephrectomy (86% vs. 33%; p=0.013) were more common. In the REU group, 29 patients with RCC were identified with only one patient previously exposed to anti-TNF. Compared to IBD, symptomatic RCC was more common in REU patients (41% vs. 17%; p=0.043) and RCC was diagnosed at a significantly older age (70.0 (60.0-77.0) vs. 58.1 (46.0-67.3) years; p=0.008) and in advanced tumour stages (≥ T2 28% vs. 7%; p=0.037).

Conclusions: IBD/RCC patients with anti-TNF exposure were diagnosed at a younger age and undergoing early and nephron sparing surgery, inferring a better patient and tumour profile. Conversely, REU/RCC were diagnosed at a higher age and in more advanced stages with only one patient with anti-TNF. The higher rate of prior immunosuppression and surgery in IBD patients with anti-TNF indicates more active disease, requiring regular abdominal imaging which may lead to incidentally found low stage RCC. However, a potential treatment or disease related risk is not excluded and further long-term multicentre case-control studies are needed.

P629
Adherence - does patient involvement and satisfaction matter?

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Background: Adherence to treatment for inflammatory bowel diseases (IBD) is important to achieve remission of the disease. Previous studies report that approximately a third of patients are non-adherent to medical treatment. In Denmark, the National Health Service provides tax-supported health care for all inhabitants including refunds of a major part of the costs of all prescription drugs for IBD. This might be associated with high adherence. The aims of the present study were to investigate adherence rate and identify predictors of non-adherence for outpatients with IBD in a tertiary university hospital.

Methods: An anonymous electronic questionnaire was prospectively distributed to 20% of the IBD-cohort at Aarhus University Hospital, Denmark. Patients were recruited consecutively in the outpatient clinic. Patients could either complete the survey in the clinic or at home.

Results: Among 377 patients, 300 (80%) completed the survey. 117 (39%) were males; median age was 35 years (range 15-79 years); Type of IBD were equally distributed among Crohn's disease (CD) (46%) and ulcerative colitis (UC) (51%). A total of 268 patients (90%) ranked their overall adherence rate (medication, appointments kept, blood and stool sample collection) > 7 on a Likert scale (1-10; 10=best). Of those who received medication, 254 patients (93%) stated adherence to medical treatment greater than 80%. IBD diagnosis, gender and disease duration did not influence adherence. Young age and smoking were associated with non-adherence (p<0.05). All (100%) adherent patients reported that they informed the health care professionals about their actual intake of medication. However, the proportion was only 74% for non-adherent patients (p<0.01). Adherence rates between 78-99% were found when stratified by type of medication and disease activity. Of note, patients in remission on topical treatment had a lower adherence rate (60%) compared with patients with disease activity on topical treatment (p< 0.01). On Likert scales (1-10; 10=best) the following proportions reported a score > 7: 'satisfaction with treatment' (85%); 'continuity in the treatment' (72%); 'contact to the clinic' (76%); 'accessibility over the telephone' (60%); 'quality of the information provided by the clinic' (60%). Furthermore, 77% stated involvement in the decision making regarding the treatment plan.

Conclusions: Self reported adherence rates, patients' satisfaction and involvement in treatment plan were very high. This may indicate coherence between adherence and the quality of care provided. Apart from young age and smoking, no clear indicators of non-adherence could be identified. This was probably due to the high percentage of adherent patients in the present study.

M, male; F, female; CD, Crohn's disease; AS, ankylosing spondylitis; IFX, infliximab; ADA, adalimumab; ETA, etanercept; AZA, azathioprine; MTX, methotrexate; Cx, ciclosporine

N	Sex	Age IBD/REU diagnosis	Type of IBD/ REU	Age start anti-TNF	Use of anti-TNF	Time on anti-TNF (months)	Other immunosuppression	Age RCC diagnosis
1	M	46	CD	54	IFX	48	AZA	59
2	M	17	CD	50	IFX	30	AZA, MTX	55
3	F	22	CD	34	IFX, ADA	48, 41	AZA, MTX	43
4	M	23	CD	31	IFX, ADA	168, 3	AZA, MTX	46
5	M	30	CD	36	IFX, ADA	36, 48	AZA	42
6	M	27	CD	39	ADA	2	AZA	41
7	F	28	CD	43	IFX	10	AZA, Cx	58
8	M	24	AS	50	IFX, ETA	28, 38		55

P630
Efficacy of TNF -alpha therapy in Crohn's disease: A 5-year retrospective cohort study in an intermediate sized hospital

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Background: Meta-analysis and randomised controlled trials have demonstrated the efficacy and safety of anti-TNF-alpha antibody therapy (anti-TNF α), and this has been confirmed in cohort studies from tertiary care centres. Whether these results can be projected to daily clinical practice in smaller primary and secondary centres is not as well described. The aim of this study was to evaluate the effects and side effects of anti-TNF α in a non-selected population of Crohn's patients in a real life clinical setting.
Methods: We conducted a retrospective cohort study in an intermediate sized hospital. All patients with Crohn's disease who initiated treatment with infliximab or adalimumab at Koege Hospital, Denmark, between January 2009 and January 2014 were identified and their files were reviewed. Effect and safety of therapy (response, remission, and side effects) was based on physician's global assessment, symptoms and paraclinical findings in the patient files.
Results: Of the 142 patients included 105 were TNF α naïve. During the study period 37 of the 105 patients reinitiated or switched between infliximab or adalimumab therapy. Patient demographics were: average age 36 years, male 52%, disease duration: 5 years, bowel resection: 36%, concomitant immunosuppressive therapy at inclusion: 66%, a total of 46% did not tolerate thiopurines. The indications for anti-TNF α were luminal disease in 119 patients (84%) and fistulae in 23 (16%). After 6 weeks of treatment (induction) 87% had an initial response or were in remission. 125 patients were still on anti-TNF α after 12 month and 49% of patients were in steroid-free remission. Median time on anti-TNF α was 16 months and median time of follow-up was 25 months. Patients who received infliximab gained and maintained a mean of 3 kilograms during the first months of treatment. Side effects caused discontinuation in 24 % of patients who received infliximab treatment and in 9 % who received adalimumab treatment. Severe infections and anaphylactic reactions were the most frequent severe side effect associated with infliximab, severe infections the most frequent severe side effects associated with adalimumab.
Conclusions: In this real life clinical setting anti-TNF α induced steroid free remission in 50 % of patients with Crohn's disease at 12 month. Discontinuation of anti-TNF α due to side effects was higher than reported in randomised controlled trials.

P631
Mesalamine versus azathioprine for maintenance treatment after steroid-induced remission in pediatric ulcerative colitis

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Background: Guidelines for the treatment of Ulcerative Colitis (UC), both in adult and pediatric patients,recommend the use of salicylates as first-line maintenance treatment even in moderate-to-severe disease after steroidinduced remission. Our aim is to compare the efficacy of two maintenance strategies (mesalamine and azathioprine) for
pediatric UC after steroid-induced remission at diagnosis.
Methods: Patients with UC diagnosed in our center (January 2008-December 2013), who needed treatment with systemic steroids to induce remission were retrospectively studied. Patients receiving mesalamine and those receiving azathioprine (AZA) were compared.
Results: 16 patients were included. Seven patients received mesalamine (group 1) and 9 AZA (group 2). PUCAI at
diagnosis, extension, and duration of steroid treatment were comparable.
Group 1: Mean time until first relapse was 22 weeks. During the follow-up all the seven patients (100%) needed a change in maintenance treatment due to relapse of the disease.
Group 2: Mean time until first relapse was 30 weeks. During the follow-up 5 patients (55%) needed a change of
treatment; 1 patient was switched to 5ASA after toxicity attributable to AZA and 4 patients after relapse.
We found statistically significant differences in the number of patients with failure of initial treatment (100% in group 1, 55% in group 2, $p<0.04$).
Conclusions: Treatment with azathioprine is more effective than salicylates for maintaining the steroid-induced remission
in pediatric UC at diagnosis. The course of the disease in these patients is severe enough to determine the need for treatment escalation in 55% of the patients even on AZA since diagnosis.

P632
Thiopurine metabolite (TM) monitoring in Adolescent IBD (aIBD): Non- and poor adherence is common adolescent practice

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Background: Azathioprine (AZA)/6-Mercaptopurine (6-MP) are established treatments in IBD. Adherence and dose optimisation can be monitored by measurement of serum 6-Thioguanine (6-TGN) levels (therapeutic range 245-450pmol/8x108 RBC. We aimed to identify if adolescent patients were both receiving and taking an optimal dose of Thiopurine
Methods: 96 patients with 130 patient episodes were retrospectively identified over a 24 month period, 52 male; median age 19 years, range 14-23y, diagnosis of: Crohn's (n=68), Ulcerative Colitis (n=16), IBDU (n=2), OFG only (n=1, 82/93 (88%) were on AZA, 11/93 (12%) were on 6-MP
Results: TM were monitored for symptomatic patients 60/96 (63%), well patient/routine blood monitoring 19/96 (20%), adjustment

of dose due to weight gain (9%), side effects 3/96 (3%), others 5/96 (5%).
Thiopurine doses varied between 0.4-1mg/kg, median 0.8mg/kg in 6-MP and 0.8-2.7mg/kg, median 1.8mg/kg in Azathioprine, the lower doses being in TPMT heterozygotes.
6-TGN levels were divided into 6 groups (G): G1: levels of 0 (8/96; 8.3%)G2: < 100 (8/96; 8.3%)G3: 101-150 (12/96; 12.5%)G4: 151-244 (18/96; 18.7%)G5: 245-450 (37/96; 38.5%)G6: >451 (11/96; 11.4%).
30/96 (28%) of adolescent patient either did not take their medication at all (n=8, 8.3%) or skipped doses (n=22, 22.9%. Of 8 patient with 0 levels 6/8(75%) were unwell, 2/8(25%) were asymptomatic/best ever. In G4 compliance was checked and dose escalation was instigated. In G6 dose was reduced. In G5 24/37 (54%) patients were symptomatic, 6/37 (16%) were well, 4/7(11%) had gained weight, 2/37(5%) had side effects. Overall 48% (46/96 patients) were inadequately dosed. TPMT levels had poor correlation to 6-TGN levels, even in G6.
Conclusions: TM monitoring is highly useful in adolescents with IBD as it unequivocally identifies lack of adherence and is vital in optimising dose tailoring in a challenging group of patients with complex disease and weight variability.

P633
Does computerised cognitive behavioural therapy help people with Inflammatory Bowel Disease? A randomized controlled trial

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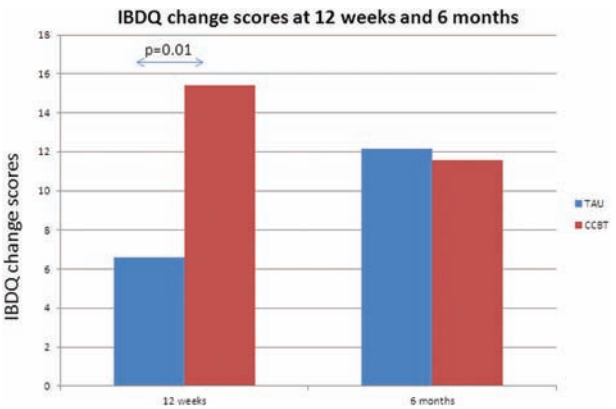
Background: Psychotherapy, especially cognitive behavioural therapy (CBT), may be a useful intervention for some inflammatory bowel disease (IBD) patients, especially those with psychiatric comorbidities [1] . However, CBT can be financially and practically difficult to access. These difficulties can be overcome by computerised CBT (CCBT) [2] . This is a randomized controlled trial of a CCBT intervention for IBD patients. It is hypothesised that those who complete an IBD-specific CCBT program will have improved health-related quality of life (HRQOL), anxiety, depression, stage of change, coping strategies, perceived stress, and IBD symptoms relative to people not allocated to the CCBT.
Methods: IBD patients were randomly allocated to CCBT (n=113) or treatment as usual (TAU; n=86). The IBD questionnaire (IBDQ) at twelve weeks after baseline was the primary outcome while generic HRQOL, anxiety, depression, stage of change, coping strategies, perceived stress, and IBD symptoms were the secondary outcomes. Outcomes were also measured at six months after baseline.
Results: Twenty-nine CCBT participants (25.7%) completed (i.e. downloaded >50% of the resources) the CCBT. IBDQ was significantly increased at twelve weeks in CCBT completers compared to TAU patients (F=6.38, p=0.01; Figure 1).
SF-12 mental (F=5.00, p=0.03) and the action stage of change (F=4.86, p=0.03) also improved significantly in the CCBT group compared to TAU patients at twelve weeks. These outcomes were no longer significant at six months. Forty participants completed the acceptability questionnaires about their perceptions of the program (35.4% response rate). The majority of questionnaire completers enjoyed the program (73.7%), felt it had relevance (87.2%), improved their understanding of IBD (79.5%), improved their physical and/or mental health (74.4%), and would recommend it to others with GI disorders (79.5%).
Conclusions: Improvements in IBDQ scores at twelve weeks after baseline were not maintained at six months. The high dropout rate from the CCBT was of concern and future research should aim to improve adherence rates. Nevertheless, there were positive reports from completers in terms of enjoyment, relevance and improved understanding and no negative effects were reported.



"IBDQ change scores at 12 weeks and 6 months"

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P634
What Are The Long Term Outcomes of Perianal Crohn's Fistulae Treated with Anti-TNF Therapies?

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Background: Fistulising perianal Crohn's disease (CD) is a challenging condition to treat and a multidisciplinary approach to treatment is frequently required. Little is known regarding the long-term efficacy of anti-TNF therapy for this group of patients. We evaluated the clinical and radiological outcomes and the effects of biological therapy on our cohort of patients.
Methods: A local database of 180 consecutive patients with Crohn's disease treated at our institution between 2005 and 2014 was established.

Results: Patients underwent Infliximab therapy (61%), Adalimumab therapy (6%) or switched between the two (33%) for the treatment of the perianal fistulas.
Clinical remission was noted in 47% of patients with a classification of a simple fistula, and 22% of those with a complex fistula (p<0.01). Radiological remission however was noted in 28% of patients with a simple fistula and 5% of those with a complex fistula (p<0.01)
After a median follow-up period of 52 months (range 1-163), 32% of patients were in clinical remission, 74% of patients had a clinical response to treatment and the recurrence rate after remission was 12%. Radiological remission was noted in 14% of patients, response in 62% of patients and recurrence of 4.7% over a median of 37 months (range 3-101) MRI follow-up.
The median time to clinical remission was 21 months (IQR 11-36), and time to radiological remission was 20 months (IQR 1-88). Whereas the median time to clinical response was 25 (IQR 18.8-31.2), and radiological response median time was 19 months (IQR 13-24). Factors influencing the time to clinical response were fistula duration (p=0.03), and the current use of immunomodulators (p=0.02).
Patients who did not have a Montreal classification of L1 disease were 2.68 times more likely to achieve clinical remission (CI=1.23-5.86, p=0.01), Having no proctitis at the start of biological therapy predicts a twofold increase in the likelihood of clinical remission in this group of patients (CI=1.01-6.18, p=0.04)
Conclusions: This is the largest single centre study using both clinical and radiological outcomes on perianal Crohn's fistulae. About three-quarters of patients had clinical response to biological therapy, whereas two-third had a radiological response. Twelve percent of the patients had a clinical recurrence after remission, whereas only 4.7% had radiological recurrence after remission on MRI scanning. A time delay is noted between clinical and radiological response to treatment. Response to anti-TNF therapy for fistulising perianal Crohn's disease should be monitored with regular MRI imaging as an adjunct to clinical follow-up.

P635
Mean platelet volume and neutrophil-to-lymphocyte ratio as new biomarkers of predicting response to infliximab therapy in Crohn's Disease patients

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Background: The loss of response to infliximab (IFX) in Crohn's disease (CD) is currently an important clinical problem. Therefore, searching for predictors of maintenance or loss of response to anti-tumor necrosis factor-alpha (anti-TNF-alpha) agents has become the aim of current studies in the field. Recently, the neutrophil-lymphocyte ratio (NLR) and mean platelet volume (MPV) have been proposed as new biomarkers of subclinical inflammatory process. Here we hypothesized that NLR or MPV may be used as cost-effective biomarkers of subclinical inflammation during 52-week IFX therapy in CD patients responding to induction regimen.
The study aimed at establishing whether NLR or MPV at baseline and pre-infusion at week 14 are good predictors of sustained response after week 14 in CD patients undergoing 52-week IFX therapy.
Methods: Thirty five adult patients with CD (20 women and 15 men; mean age 33 years), who responded to the induction regimen and underwent a 52-week course of treatment with IFX were evaluated at week 14 and enrolled to the study. The control group consisted of 12 healthy subjects. The association between NLR and MPV, baseline disease parameters and maintained clinical response or remission during IFX therapy was assessed.
Results: Ten patients (28%) have not reached full one year maintenance IFX treatment because of loss of response. The analysis showed a mean NLR of 3.54 and a mean MPV of 10.92 fL in our patients at baseline. Higher NLR at baseline (5.31 vs. 3.22 ± 1.28; p<0.05) and at week 14 (4.51 vs. 1.99; p=.006) were observed in patients with loss of response to IFX maintenance treatment than in those with sustained response. NLR lower than 4.00 at baseline predicted sustained response with 80% sensitivity and 80% specificity (p< 0.01). NLR lower than 3.5 at week 14 predicted sustained response with 72% sensitivity and 70% specificity (p<0.05). MPV at week 14 in CD patients with loss of response was significantly higher (11.37 fL vs. 10.21 fL; p<0.05) than in patients with sustained response. In patients with sustained response to maintenance IFX treatment higher Delta-MPV between baseline and week 14 was calculated (0.65 fL vs. 0.32 fL; p<0.05). MPV higher than 10.5 fL at week 14 predicts sustained response with 70% sensitivity and 69% specificity (p<0.05). Delta-MPV between baseline and week 14 higher than 0.4 fL predicts sustained response with 80% sensitivity and 73% specificity (p<0.01).
Conclusions: In CD patients with loss of response to IFX therapy higher NLR and lower MPV were observed. It can be suggested that NLR and MPV may serve as good predictors of sustained response to IFX maintenance treatment in CD patients as well as may allow selection of the most appropriate

P636
Which is the real life maintenance mesalazine dose in ulcerative colitis

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Background: Mesalazine (MSZ) is frequently used as maintenance therapy for ulcerative colitis (UC). However, the real life dose used by clinicians is still a mystery. In our study, we wanted to describe how MSZ is used in our practice, at which dose, and with what success (regarding adherence to therapy).
Methods: Transversal study, including all patients with UC and with MSZ maintenance therapy (at least for 6 months) seen in scheduled outpatient visits during September and October, 2014, in two IBD Units in Madrid, Spain. Patients receiving immunosuppresors or biologicals were excluded. Treatment adherence was measured by the Morisky-Green scale.

Results: We included 90 patients (mean age 52 ± 15 y; 52% females, 13.5% smokers). The mean disease duration was 10 ± 8 y. Topical MSZ was used in 35 cases (39%). Mean MSZ dose was 3 ± 2.4 g/d, for a mean of 38 ± 46 months. Doses <2 g/d were used in 13.3% of cases, from 2-2.9 g/d in 35.6%, from 3-3.9 in 23% and ≥ 4 g/d in the remaining 27.8%. A single daily dose was preferred in 45%, two doses in 36% and three doses in 19%. A different MSZ brand had been previously used in 40% of patients. Reasons for change were medical decision (n=21; 60%), side effects (n=7; 20%), patient's choice (n=5; 14.3%) or poor treatment compliance (n=2; 5.7%). During the year preceding the study, 55 patients were in remission (62%), whilst the remaining had suffered at least one flare. In 59 cases, the maintenance dose had been increased during a flare, and in 26 this higher dose had been kept for maintenance (40%, dose ≥ 4 g/d in 73%); in the remaining, the dose was lowered after a period of time (to 2 g/d in 50%). During the MSZ therapy, 8 patients were admitted (9%), 10 took drug holidays (90% due to patient's request, after a prolonged remission) and 10 (11%) suffered mild side effects (30% altered liver function tests). Therapy adherence was good in 83.3% of cases.

Conclusions: More than half of our UC patients take high MSZ doses (3-4 g/d) as maintenance therapy, with acceptable safety and good adherence. Variable doses are used in clinical practice, highlighting the need to tailor dose according to UC behavior. Almost half of all patients are prescribed a different commercial brand during therapy, and a similar percentage takes a single daily dose. Opting for a higher MSZ maintenance dose is a possible strategy for a satisfactory maintenance therapy.

P637
Anti-TNF alpha therapy in Inflammatory Bowel Disease - safety profile in elderly patients

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Background: Infliximab (IFX) and Adalimumab (ADA) are tumor necrosis factor α (TNF α) antagonists, which is a key cytokine in immune regulation and defense against infections and malignancies. The ageing process has been associated with immune system functional changes, which could increase susceptibility to adverse events (AE). Advanced age has been suggested as a risk factor for infectious complications among patients with Inflammatory Bowel Disease (IBD) treated with anti-TNF α agents; however, safety data regarding biological therapy in elderly patients with IBD is still limited. The aim of this study was to evaluate the AE of elderly patients with IBD treated with anti-TNF α agents.

Methods: A retrospective analysis was conducted in all IBD patients ≥ 60 years treated with anti-TNF α drugs between 2000 and 2013 at a tertiary referral center for IBD. The probability of a causal association between each AE and the drug was determined by using an imputability score based in chronologic and clinical criteria and then classified as "not related", "doubtful", "possible", "likely" or "definite".

Results: Twenty-three patients (15 females) were included - 12 with Ulcerative Colitis and 11 with Crohn's Disease. Twenty-one patients were treated with IFX and 8 with ADA (6 after switching from IFX) for a mean treatment time of 35 months, performing a total of 368 IFX and 493 ADA administrations. Ninety-three AE were recorded (mean of 0,8 AE/patient/year): 73 with IFX and 20 with ADA. There was at least one AE in 21 of the patients (91%). The most frequently reported events were infections (n=50, in 16 patients), episodes of serum sickness-like disease (n=16, in 7 patients) and infusion reactions (n=14, in 4 patients). The likelihood of association with the anti-TNF α was considered possible in 26%, likely in 11% and definite in 23% of the AE. Seventeen of the 93 AE were severe, 14 of which had an association that was at least possible with the drug. Nine events led to definitive discontinuation or drug switch and 10 events directly or indirectly led to IBD relapse or hospitalization. Only 1 event resulted in permanent disability and/or progressive disease. Mortality was null and there were no cases of tuberculosis infection.

Conclusions: In this series, the annual rate of AE related with the anti-TNF α therapy was low in elderly patients. The range and severity of events were similar to those previously described for younger individuals. Although serious AE were relatively rare, the majority of them showed a plausible correlation with the biological therapy. More comparison studies are required to determine the relative risks of biological therapy in this age group.

P638
Biologic therapy is safe and effective in inflammatory bowel disease (IBD) patients with previous cancer. Experience of a single tertiary IBD center

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Background: Immunomodulator and biologic therapy is a mainstay of treatment in IBD. However, these effective therapies confer an increased risk for malignancies, specifically lymphomas and non-melanoma skin cancer. Data concerning the safety of immunomodulation in IBD patients with previous cancer are vague. We aimed to evaluate the short and long term consequences of treating IBD patients with previous cancer with biologic therapies.

Methods: Case records from a single tertiary referral IBD Center were retrospectively reviewed. Records of patients with a new diagnosis of cancer which were treated with biologic therapies after cancer diagnosis within the study period were included. Outcome measures were survival, cancer recurrence, new cancer appearance and IBD activity at end of follow up using physician global assessment.

Results: In the period between November 2008- November 2014 eleven IBD patients (Male= 6 [54%], Crohn's disease= 7, ulcerative colitis=4) with a previous cancer were treated with biologic or immunomodulator and biologic combination therapy. Most patients (n=9) received immunomodulators/biologics in the past: thiopurines, methotrexate, and biologic therapies (63%, 45%, and 63%, respectively). Cancer types were: breast=3, squamous cell carcinoma (SCC)=3, colorectal cancer=2, carcinoid tumor=1, Hodgkins lymphoma=1, sarcoma=1. Mean age at cancer diagnosis was 52 ± 10.5 years. At cancer diagnosis mean disease duration was 16 ± 10.8 years.

Biologic therapy was either continued after cancer diagnosis (n=7) or started in the follow-up period (n=4), at an average of 28 ± 22 (range 6-59) months after cancer diagnosis. Five patients were concomitantly treated with immunomodulators (3 thiopurines, 2 methotrexate). Overall, a total of 16.3 patient years of biologic therapy, of which 6.1 years were combination therapies elapsed. One patient with dermatofibrosarcoma of the vulva had local recurrence 6 months after surgery. Since surgical margins were not free of tumor the role of biologic therapies on disease progression is unclear. A second patient with SCC (anal verrucous carcinoma) was diagnosed with facial basal cell carcinoma a year after SCC excision. Both patients received biologic (anti-TNF-alpha) monotherapy. No cases of mortality were noted. Seven patients had no or mild IBD activity during the follow up period while three experienced moderate to severe disease activity according to clinical indices and endoscopy.

Conclusions: Biologic monotherapy or in combination with an immunomodulators in IBD patients with a previous cancer seems to be safe and effective. Furthermore, it may be started soon after cancer diagnosis.

P639
The use of biological therapies in managing patients with IBD in Iraq.

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Background: Biologic therapies provide a distinct advantage in managing patients with inflammatory bowel disease (IBD). Their use in Iraq is limited due to lack of funding and unstable infrastructure in the health system. The present study aimed to explore the use of biologics therapies used in Iraq for managing patients with IBD.

Methods: An online survey with 20 questions relating to prescribing biologics therapies in managing patients with IBD was sent to 35 gastroenterology departmental leads in all regional centres in Iraq managing patients with IBD.

Results: Thirty responces (86%) were received; 80% of respondents were from University Teaching Hospitals, 20% worked in district general hospitals or Private Hospitals. Patients with IBD served ranged from 20 to 500 patients with IBD. All gastroenterologists were aware of the biologics therapies in IBD but only 10% had access to infliximab. Adalimumab was not routinely used. Patients buy infliximab privately as it is not available free in most public hospitals. No agreed IBD management standards exist on a national level. Access to modern endoscopes and biochemical blood markers of inflammation to monitor IBD was acceptable. Active or history of tuberculosis is the commonest contraindication to start biologics therapies. Written information about biologics and IBD is limited and the practice of informed consent falls short of UK standards. There is no national database to record and monitor patients with IBD having biologics treatment. Around 85% reported willingness to use biologics treatment if available in Iraq.

Conclusions: This is the first study of its kind to explore the use of biologics in Iraq. The study identified gaps in the access and use of biologics therapies in Iraq. Future clinical cohort studies are warranted to examine the long-term efficacy and safety of biologics therapies in Iraq.

P640
Smoking is associated with higher healthcare costs in IBD patients, primarily due to more frequent anti-TNFalpha use

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Background: Smoking effects the disease course of inflammatory bowel disease (IBD). We aimed to study the impact of smoking on IBD-specific healthcare costs, disease activity and quality of life among adults with IBD.

Methods: A large cohort of IBD patients were prospectively followed for two years by three-monthly questionnaires (the COIN-study). Smoking status of patients was obtained at baseline while cost items, disease activity and quality of life were assessed during follow-up. Healthcare costs, disease activity and quality of life were compared between smokers and non-smokers. Differences between Crohn's disease (CD) and ulcerative colitis (UC) were identified. In addition, risk factors for high healthcare costs were examined using logistic regression analyses, adjusted for potential confounders.

Results: In total, 3,030 patients (1,558 CD, 1,054 UC and 418 IBD-unspecified) were enrolled, of whom 486 patients (16%) were current smokers. Smoking CD patients more frequently had active disease or fistulas than non-smoking CD patients. Also, smoking CD patients and those who had stopped smoking after the diagnosis of CD had a higher number of flares in the past and in addition, had undergone abdominal surgery more frequently. In contrast, smoking UC patients appeared to have a lower number of flares in the past. After one year of follow up, smoking CD patients had significant higher disease activity scores (Short Crohn's Disease Activity Index: median 170 vs. 149, $p < 0.001$), whereas in UC, disease activity scores did not differ between smokers and non- smokers (Modified TrueLove & Witts Index: median 4 vs. 4, $p = 0.11$). Mean total direct health care costs after one year of follow-up were

45% higher in the smoking IBD population as compared to the non-smoking population (Euro: 6,020; 95% confidence interval (CI) 4,607 - 7,434 vs. 4,166; 95% CI 3,715 - 4,617, p <0.001), which was mainly explained by a higher percentage of TNFalpha inhibitor users (19.3% vs. 13.0%, p =0.001). When analysed separately, smoking CD and UC patients were still found to incur higher costs, although statistical significance was lost (CD: Euro 7,845 vs. 6,472, p =0.16; UC: 3,101 vs. 2,315, p =0.31). Multivariate analysis revealed smoking as an independent factor for high healthcare costs in IBD (adj. odds ratio 1.75; 95% CI 1.09 - 2.81). Moreover, the quality of life proved to be significantly worse in the smoking population, which applied to both CD as well as UC (median IBD- questionnaire: 170 vs. 184, p <0.001).

Conclusions: Mean healthcare costs are 45% higher in smoking IBD patients, primarily due to anti-TNFalpha use. The quality of life is decreased in both smoking CD as well as UC patients.

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Poster presentations

Epidemiology

P641
Does Ulcerative Colitis prevent the development of colonic diverticulosis?

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Background: Colonic diverticulosis (D) is common after 40 years of age in the western world. Advanced age, constipation, low-fiber diet, and connective tissue disorders are risk factors for D. A segmental colitis which shares some endoscopic and histologic features with IBD [Segmental Colitis Associated with Diverticulosis (SCAD)] has also been described in patients with diverticulosis. On the contrary, ulcerative colitis (UC) affects younger people and inflammation involves the rectosigmoid area in the vast majority of patients. Aim: To study the incidence of D in patients with UC

Methods: This was a prospective, single-center study. Between 2006 and 2013, 267 patients [141 males, mean age 36 years (range 17-75), median disease duration 7 years (range 0.6-34), 35 (25%) smokers], with UC[extensive (n=107), left sided (n=142) proctitis (n=18)] in clinical remission underwent colonoscopy to assess disease extent and/or epithelial dysplasia. 335 subjects, matched for age, gender, place of birth, inhabitance (rural or urban) and dietary habits who underwent colonoscopy for irritable bowel syndrome, iron deficiency, or colorectal cancer screening served as controls. The presence and distribution of diverticula was recorded. Exclusion criteria were known D, Crohn's disease or uninvestigated signs of complicated D (such as bleeding, bowel obstruction, diverticulitis, etc).

Results: Diverticula were detected only in 13/267 (4.9%) UC patients [7 with proctitis, and 6 with left-sided colitis (4 distal colitis)] but in 195/355 (55%) controls (p<0.0001). D in UC was detected in patients over 55 years of age, usually outside the area of distribution of UC. In the control group, diverticula were predominantly distributed in the left colon; 22/355 (6.2%) patients had SCAD and two of these 22 patients had rectal involvement. A significantly less proportion of UC patients were smokers.

Conclusions: In contrast to the general population, diverticula are rare in UC. Several factors may be accounted for this inverse association such as young age at UC onset, involvement of the left colon, non-smoking, and probably the production of pro-inflammatory cytokines (especially TNFa) which strengthen the enteric wall by inducing hyperplasia/hypertrophy of the muscle layers and changing the composition of connective tissue leading to 'primary' prevention of diverticulosis.

P642
Clinical impact of concomitant endometriosis among women with Inflammatory Bowel Disease: A case-control study

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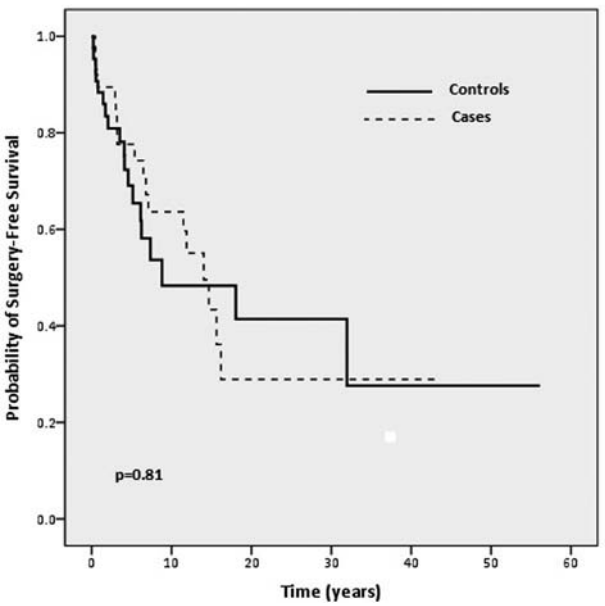
Background: Co-existence of intestinal endometriosis and inflammatory bowel disease (IBD) has been reported in case series. A recent study demonstrated an increased risk of IBD among women with endometriosis[1]. However, the clinical significance of concomitant endometriosis and IBD has not been studied. The aim of our study was to compare IBD phenotype at diagnosis and disease prognosis among IBD patients with and without endometriosis.

Methods: Women diagnosed with endometriosis and IBD were identified using ICD.9 codes at an academic medical center in New York City. Controls were frequency-matched by gender, age (±5 years), and IBD diagnosis. Primary outcomes included disease phenotype at diagnosis (for Crohn's disease [CD]: location and behavior according to Montreal Classification; for ulcerative colitis [UC]: disease extent according to Montreal classification), the need for immunomodulators (IM), anti-TNF agents and combination therapy, and the need of surgical management for refractory disease (for CD: at least 1 intestinal resection; for UC: ileal pouch-anal anastomosis). Multivariable logistic regression analysis was performed to compute odds ratios (ORs) and 95% confidence intervals (CIs), adjusted for IBD disease duration and race. The Kaplan-Meier method was used to compare event-free survival to surgery for refractory disease.

Results: Forty-nine cases with endometriosis and IBD (CD, N=28; UC, N=21) were matched to 49 controls (CD, N=27; UC, N= 22). Endometriosis was surgically verified in 38 (78%) of cases, among whom 7 (18%) involved the small or large intestines. There was no difference in disease phenotype at diagnosis (p>0.05 for all



"Figure 1: Kaplan-Meier estimates of time to surgery for refractory disease"

comparisons). Similar proportions of cases and controls required IM (OR 1.72; 95%CI, 0.66-4.54), anti-TNF (OR 2.04; 95%CI, 0.76-5.46), and combination therapy (OR 2.08, 95%CI, 0.56-7.22). Though a higher proportion of cases required abdominal surgery for any reason (67.3% vs 46.9% controls, p=0.04), there was no difference in need of surgery for refractory disease (46.9% vs 42.9% controls, p=0.69; OR 0.95; 95%CI, 0.38-2.39). Kaplan-Meier estimates of time to surgery for refractory disease (Figure 1) showed no difference among cases and controls (p=0.81 by log-rank test).

Conclusions: In this case-control study, we found no difference in IBD phenotype and disease course among women with and without endometriosis. These findings suggest that while endometriosis may increase risk for developing IBD, it may not have significant clinical impact on IBD prognosis.

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P643
Differences in Mucosal Distribution and Clinical Characteristics of Crohn's Disease in South Asians and Caucasians in the North of England

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Background: Inflammatory bowel diseases (IBD) are inflammatory conditions that affect the gastrointestinal tract and may have extra intestinal manifestations. The two main subtypes are Crohn's disease (CD) and ulcerative colitis (UC). The aetiology remains elusive but the current paradigm is of an aberrant immune response as a result of an environmental factor(s) in a genetically susceptible individual

The incidence of IBD has traditionally been higher in Caucasian populations in Europe, North America and Australia compared to other regions of the world.

There is now evidence of increasing incidence in all populations worldwide. Studies from the UK, North America, Malaysia and Singapore have observed a 2-3 times higher incidence of IBD in South Asian immigrant populations compared to local cohorts. However, few studies have described the disease phenotype and luminal distribution in the South Asian immigrant population.

Methods: Ethics approval was obtained ref: O5/Q1407/274. Patients were recruited prospectively in 11 centres in the North Of England. Inclusion criteria were diagnosis of CD and age > 16 years. Exclusion criteria were Diagnosis of IBDU or IDC and Age < 16 years. Information was collected from using a standard clinical proforma. Data was stored on and analysed on a FileMaker Pro database. Chi Squared analysis was used to compare groups.

Results: 554 patients were recruited, 128 South Asians (SA) and 426 Caucasians (CAU). Males were more likely affected in the SA cohort versus CAU , which had the opposite trend. South Asians were most likely to be diagnosed with Colonic disease (L2) vs. CAU (50% vs. 24%), which was highly statistically significant (p= 1 X 10-6). Differences in luminal distribution between groups (L1-L4) were statistically significant between groups. Also differences in disease behaviour (B1,B2) were statistically significant but was not for B3 disease. South Asians were less likely to be diagnosed >40 years of age (A3) versus CAU (p=0.02). No statistical difference in positive family history or EIM's between groups. South Asians were less likely to need surgery versus CAU (29% vs. 58%), which was highly statistically significant (p<0.001).

Conclusions: There are significant differences in luminal distribution, age of diagnosis and need for surgery between groups. The fact that South Asians are less likely to need surgery suggests a less severe phenotype compared to Caucasians. These differences may represent difference in disease pathogenesis in particular genetic susceptibility or environmental factors. This information will help inform current and future genotype/phenotype correlations.

P644
Epidemiology and characteristics of inflammatory bowel disease in a large population-based cohort in the Netherlands.

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Background: Results from population based studies in inflammatory bowel disease (IBD) will reveal information on the disease phenotype and may facilitate adequate treatment stratification. Aim of this study was to update prevalence and incidence rates of IBD in a population-based cohort covering 319,976 inhabitants. In addition, use of medical therapy and surgical procedures for IBD were assessed.

Methods: IBD patients living in the adherence area receiving medical care at 3 regional (non-academic) hospitals in the Netherlands between 1-1-2004 and 1-1-2010 were identified. Three independent hospital databases were used for case-finding. Cochrane-Armitage trend test was used to test change in prevalence over time. Montreal classification was used to report on IBD behavior and location. Data on medical and surgical treatment were obtained from medical records.

Results: Case-finding identified 2,466 possible IBD patients. In total, 1,461 IBD patients were included (40.7% male). 761 (52.1%) patients had ulcerative colitis (UC), 579 (39.6%) Crohn's disease (CD) and 121 (8.3%) IBD-unspecified (IBD-U). Point prevalence of IBD was 432.1 (CI 409.7-454.5) per 100,000 inhabitants on 1-1-2010 (UC: 225.6, CD 171.8, IBD-U 34.7). Prevalence increased significantly over time from 1-1-2004 to 1-1-2010 (X 2=49.4, p<0.0001). The mean annual incidence between 2004 and 2009 for IBD was 29.6 (CI 23.6-35.5) per 100,000 inhabitants per year (35.0 for UC, 20.2 for CD and 2.2 for IBD-U). Two peaks in the mean annual incidence rate were observed in UC patients in the age categories 40-49 and 70-79 years. In CD, an incidence peak was observed in young adolescent patients. Left-sided colitis was most commonly observed in UC patients (46.1%), whereas 23.7% had proctitis and 30.2% pancolitis. In the majority of CD patients ileocolonic involvement (L3)(36.3%) was observed. 30.4% had ileitis without colitis (L1), 32.2% had colitis (L2) and 1.1% had upper GI involvement. In CD patients, 53.9 % had nonstricturing, nonpenetrating behavior (B1). Stricturing, nonpenetrating behaviour (B2)was found in 21.4% of patients and penetrating in 24.7% (B3). A history of steroid use was significantly more common in CD as compared to UC patients (81.5% versus 62.9%, p<0.0001). Proctocolectomy was performed in 4.1% of UC patients after a median follow-up of

8.0 years (IQR 5.0-16.0). In CD patients an ileocecal resection was performed in 12.4%.

Conclusions: Point prevalence of IBD was 432.1 per 100,000 inhabitants and increased significantly over the study period. The mean incidence of IBD was 29.6 per 100,000 inhabitants per year. Whereas the incidence of CD was highest in lower age groups, two peaks in the incidence of UC were observed. Steroid use was significantly more common in CD patients.

P645
Perception of social and emotional impact of Ulcerative Colitis by Spanish patients - UC-life survey

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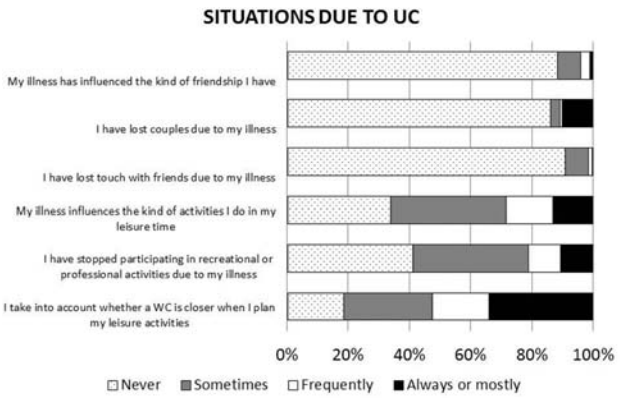
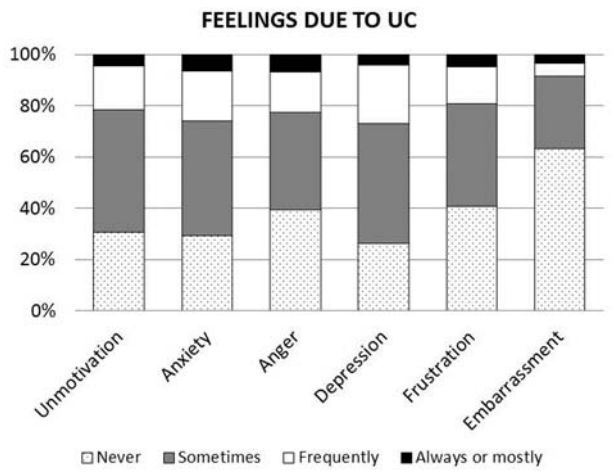
Background: Objectives. To describe the social and emotional impact of ulcerative colitis (UC) as perceived by patients followed in hospital clinics from Spain

Methods: UC-LIFE was a survey to UC patients. Each of the 39 participating hospital gastroenterologists handed the survey to 15 consecutive UC patients >18 years. Patients completed the survey at home and returned it by post-mail. The social and emotional aspects comprised a set of questions on the impact of UC on patient feelings, work and personal relationship, with "yes/no" answers and ranks of importance and from "never" to "always or nearly always".

Results: 585 patients received the survey and 436 returned it (response rate: 75%). Mean age was 46 years (SD: 13), 53% were men. Median duration of UC was 8 years (IQR: 4-15). Twenty-four percent of patients considered that UC prevented them from normal life always or most of the time; 41% of patients considered that UC determines the kind of job they perform; 55% referred sick-leaves because of UC; 38% of patients recognized that UC decreases their self-confidence and 26% pointed out that UC affects the vitality to take care of their children. Other aspects of life influenced by UC are described in figure 1



"Situations due to UC"



"Feelings due to UC"

Regarding the emotional impact of UC, a quarter of patients reported feeling depressed, anxious, angered or unmotivated frequently or most of the time because of UC (figure 2)

The main fear mentioned was the possibility of developing colon cancer, followed by the need of a colostomy and the main concern needing a hospitalization due to UC, followed by to the inability to reach their goals in life due to UC.

Conclusions: In this survey, patients described the high emotional and social impact that UC implies. Self-confidence, relationships, job and leisure activities are frequently affected. These aspects must be part of usual evaluation by treating physicians and their teams. All patients came from hospital clinics and the sample was non-randomized; thus the results must be interpreted in this context.

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P646
Outcome of Clostridium difficile Infection in Inflammatory Bowel Disease Patients Hospitalized due to an Exacerbation

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Background: Inflammatory bowel disease (IBD) is considered a risk factor for Clostridium difficile infection (CDI). Once infected, IBD patients are thought to be at increased risk for complications and mortality. However, most studies evaluated outcomes in hospitalized IBD patients including those not initially hospitalized for IBD exacerbation. We aimed to find the rate and clinical implications of CDI in IBD patients who were hospitalized due to IBD exacerbation in order to clarify whether these patients should be more aggressively treated and followed for CDI as has been previously suggested.

Methods: Clinical data were retrospectively retrieved from electronic patient files of all IBD patients (according to the ICD-9 codes) hospitalized in a tertiary referral center (the Tel Aviv Medical Center, Israel) between 1/7/2008 to 31/7/2013. Inclusion criteria included hospitalization due to diarrhea and being tested for CDI. Patients that were post total colectomy were excluded from the study.

Results: A total of 383 IBD patients [ulcerative colitis (UC):151; Crohn's disease (CD):225, and IBD-U:7] were tested for CDI during the study period. CDI was detected in 28 (7.3%) patients (7.3% UC; 7.6% CD). The mean age of patients with or without CDI was comparable (46±21 vs. 44±20 years, respectively). Patients with CDI were more frequently hospitalized during the 2 months prior to CDI (71% vs 29%, P<0.05), they were more likely to be treated by systemic steroids (50% vs 24%, P<0.05) and by proton pump inhibitors (54% vs 21%, P<0.05).
Patients with or without CDI had similar mean hospitalization duration (7.1 days), and there was no significant difference in mortality and in the number of subsequent hospitalizations during the year following CDI was noticed.
Conclusions: The rate of CDI in patients hospitalized due to IBD exacerbation is 7.3%, higher than the reported CDI rate of the general population. However, CDI may not impact patients' prognosis as previously thought.

P647
EBV and CMV status in children with IBD at diagnosis: a case control study

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Background: The cause of inflammatory bowel disease (IBD) remains to be established. Evidence has linked viral infections in childhood with the subsequent risk of developing IBD. Furthermore Epstein-Barr virus (EBV) and Cytomegalovirus (CMV) have both been implicated in re-activation of IBD
Methods: We report a case-control study of 20 newly diagnosed IBD children, naïve to treatment and enrolled between 2011 and 2013 and 20 matched controls, with the aim to assess the influence of EBV and CMV exposure on later development of IBD. Controls were children newly diagnosed with solid tumors and not exposed to chemotherapy, living in the same area and matched for age and sex. Clinical data and serology for EBV (VCA IgG and IgM, EBNA IgG) and CMV (IgG and IgM) were recorded.
Results: In children with IBD (mean age: 9.3 years, 9 with Crohn's disease [CD]) rate of previous exposure to EBV and CMV at diagnosis was 50 and 20 % respectively. In controls children (mean age: 9.2 years, 10 Ewing's Sarcoma, 3 neuroblastoma, 3 rhabdomyosarcoma, 2 teratoma, 2 brain tumors) seropositivity for both EBV and CMV was not different (65 and 35% respectively). In patients with IBD matched odds ratios for previous exposure to EBV and CMV were 0.33 (95% CI 0.1-0.9) and 0.5 (95% CI 0.32-1.01), respectively. Furthermore 4/8 IBD patients developed EBV infection after starting immunosuppressive treatments. No CMV infection or re-activation was recorded during the follow-up.
Conclusions: These findings provide no support for the hypothesis that exposure to EBV and CMV predisposes to the later development of IBD. Overall we found a 50% seropositivity for EBV in a newly diagnosed IBD population, comparable to previous reports [1] [2] and to our control population. Furthermore we described an high rate of IBD patients developing EBV infection after starting immunosuppressive treatment.

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P648
The epidemiology of microscopic colitis from 1997-2014 - a single centre study

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Background: Microscopic colitis (MC) is an increasingly recognized, frequent cause of chronic diarrhoea. Its epidemiology was described in several Western countries, however epidemiologic data from Eastern Europe is lacking. We aimed to investigate MC cases in our single centre cohort.
Methods: All cases of microscopic colitis diagnosed at colonoscopy over a 17-year period (January 1997 - August 2014) were retrieved at the Department of Pathology and retrospectively reviewed. The diagnostic criteria for lymphocytic colitis (LC) were ≥ 20 intraepithelial lymphocytes per 100 epithelial cells, and for collagenous colitis (CC) a collagenous layer of ≥ 10 µm. Several demographic and clinical parameters were analysed.
Results: 110 patients (91 patients with LC, and 19 patients with CC) were included in the study. 79 (71%) patients were female with a mean age of 52.0 years (SD±16.8) for LC and a mean age of 57.5 years (SD±17.0) for CC. Comparing the period 1997-2005 and 2006-2014, the incidence increased in both genders (30 females, 9 males vs. 49 females, 23 males). Chronic, watery diarrhoea was the most common symptom (74%). The diagnosis of LC would have been missed in 11% of cases, if only left-sided biopsies had been taken, whereas all cases (100%) of CC were diagnosed with distal colonic biopsies alone. Osteodensitometry was performed in only 20% of cases, however it was pathological in 64% of the cases: osteoporosis was diagnosed in 46% and osteopaenia in 18% of these cases. Among associated autoimmune diseases, coeliac disease was the most common with 9%, followed by hypothyroidism (7.3%). 31.5% of patients were taking any of the previously associated drugs (proton pump inhibitors, ACE inhibitors, beta blockers, calcium antagonists, statins, acetylsalicylic acid or antidepressants).
Conclusions: The incidence of MC is increasing in Hungary, but still below of that reported in Western countries. LC seems to be more common than CC, but this might be due to underdiagnosis. Our results should be further examined in multicentre studies.

P649
The incidence of glomerulonephritis in a population-based inception cohort of patients with Inflammatory Bowel Diseases

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Background: Glomerulonephritis (GN) was described to be related to inflammatory bowel diseases (IBD) in some case reports, but only

a few data are available on the incidence and prevalence of GN in population-based studies. Our aim was to explore the incidence of GN and its relationship with disease characteristics and medical therapy in a population-based inception cohort of IBD patients in the Veszprem province database between 1977 and 2012.

Methods: A total of 1708 incepted IBD patients were included (male/female: 879/829; CD: 648, age at onset: 29, IQR: 22-39; UC: 1060, age at onset: 36, IQR: 26-50 years) and followed-up until the 31st of December 2012 for a total of 21369 patient-years. Cases with histopathological diagnosis of GN were collected and included in the further analysis.

Results: GN was identified in a total of 6 IBD patients (CD (Crohn's disease)/UC (ulcerative colitis): 5/1, male/female: 5/1, median age at diagnosis: 27.5 (25-39) years). The incidence rate of GN was 0.28 per 1000 patient-years. All patients were administered 5-ASA (5-aminosalicylate) treatment. Total anytime 5-ASA exposure was 88.5 % in CD and 97.5 % in UC. The histopathological types of GN were IgA nephropathia, granulomatous nephritis, membranous glomerulonephritis, mesangio-capillaris glomerulonephritis and mesangio-proliferative glomerulonephritis.

Conclusions: A higher incidence of GN was observed compared to the findings of previous studies. The incidence was higher in males and in CD and a high use of 5-ASA was found.

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Age of onset is associated with disease seasonality in inflammatory bowel disease: A multi-center observational study by the Osaka Gut Forum

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Background: Although environmental factors are suggested to affect the pathogenesis of inflammatory bowel disease (IBD), disease seasonality in IBD has not been well investigated. We aimed to clarify the disease seasonality and investigate the underlying characteristics in IBD patients.

Methods: This was a multi-center observational study conducted by Osaka Gut Forum (OGF) comprising 20 institutions in Japan. A total of 1,078 IBD patients (303 Crohn's disease [CD], 775 ulcerative colitis [UC]) were enrolled. All patients were Japanese and data were collected using survey forms from doctors and questionnaires from patients from November 2013 to August 2014. Association between disease seasonality and patient characteristics was investigated. Statistical analysis was performed using Pearson's chi-square test, and odds ratio (OR) and 95% confidence interval [CI]) were analyzed.

Results: Disease onset was significantly more frequent in spring-summer compared with autumn-winter in IBD, especially in CD ($p = 0.037$ and 0.030, respectively), but UC patients did not show seasonality of disease onset. When the patients were divided into two groups by age of onset (A1/2 and A3 in Montreal classification), the proportion of patients with spring-summer onset was larger than that with autumn-winter onset in A1/2 group of IBD, especially of CD ($p = 0.014$ and $p = 0.019$, respectively), whereas A3 group did not show onset seasonality. Disease exacerbation was significantly more frequent in autumn-winter than in spring-summer in IBD, especially in UC ($p = 0.006$ and 0.016, respectively), but CD patients did not show seasonality of disease exacerbation. A1/2 group had significant dominance in autumn-winter exacerbation in IBD, especially in UC ($p = 0.013$ and $p = 0.038$, respectively), whereas A3 group did not show exacerbation seasonality in both CD and UC. Multivariate analysis showed that age onset of A1/2 was the independent factor of seasonality for disease onset and exacerbation in IBD (OR 1.33, 95% CI 1.01 - 1.75, $p = 0.042$ and OR 1.62, 95% CI 1.21 - 2.16, $p = 0.001$, respectively).

Conclusions: Seasonality of disease onset and exacerbation was observed in young-onset IBD patients, suggesting that young and elderly-onset patients might have different pathophysiological triggers for disease initiation and exacerbation.

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Complementary and alternative medicine (CAM) use in patients with inflammatory bowel disease - preliminary Results of a multicenter study of the Austrian IBD study group

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Background: CAM is frequently used in Western European countries, especially in chronic diseases such as inflammatory bowel diseases (IBD), with a frequency ranging from 20% to 50%. No recent data on CAM use are available for Austrian IBD patients. The aim of our study is to determine the frequency of CAM use in IBD patients in Austria as well as factors influencing CAM use.
Methods: In a cross-sectional study design, adult patients with IBD (Crohn's disease CD, ulcerative colitis UC, inflammatory bowel disease unclassified IBDU) attending outpatient clinics at 20 hospitals throughout Austria are eligible to complete a multi-item questionnaire. For study completion inclusion of 1500 subjects is planned. Surveyed data consist of demography, clinical variables and the use of CAM for IBD. Disease activity was determined by patient estimation. Due to the presentation of preliminary results of this ongoing study with low numbers of included patients until now, we describe only numeric results without performing further statistical analyses.
Results: Between June and November 2014 223 patients (141 with CD, 71 with UC, 3 with IBDU) with a mean age of 40.6 years (range 18-74 years) were included. Previous CAM use for IBD was reported by 71 CD patients (50.4%), 37 UC patients (52.1%) and 3 IBDU patients (100%). 56 out of 104 (53.9%) female patients and 57 out of 119 male patients (47.9%) reported CAM use. 22 out of 47 (46.8%) smokers used CAM compared to 48 out of 89 (54%) non-smokers. The frequency of CAM use according to disease activity was as follows: inactive 19 out of 34 (55,9%), mild active 40 out of 80 (50%), moderate active 34 out of 68 (50%), and highly active 18 out of 32 (56,3%).
Conclusions: CAM use for IBD is frequent in Austrian IBD patients. This was observed in CD patients as well as in UC patients.

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Treatment, evolution and associated risk factors of extraintestinal manifestations in patients with inflammatory bowel disease

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Background: Patients with inflammatory bowel disease (IBD) present affectation in other organs different from digestive system that may cause great morbidity. Although, many extraintestinal (EIMs) are directly related to intestinal activity, other have independent course and need specific treatments. Our aims were to evaluate the characteristics, treatments and evolution of EIMs in patients with IBD in our environment and to identify the risk factors associated to them
Methods: Restrospective, observational, case-control study. All patients with Crohn's disease (CD) and ulcerative colitis (UC) and EIMs were considered as case. On the other hand, patients with IBD without EIMs were controls
Results: 619 patients with IBD (327 CD, 265 UC, 27 indeterminate colitis) were included; mean age 45 ± 14 ys, 60% females, 24% smokers. 16.5% of patients showed at least one EMIs (n=102).The EIMs observed were: 40% of EIMs (n=50) musculoskeletal manifestations (26 arthritis, 13 ankylosing spondylitis, 9 sacroiliitis, 2 psoriatic arthritis), 40%(n=50) cutaneous manifestations (28 erythema nodosum, 14 aphthous stomatitis, 6 pyoderma gangrenosum, 1 Sweet's syndrome, 1 granulomatous dermatitis), 11.2%(n=14) ocular manifestations (7 uveitis and 7 episcleritis), 6.4%(n=8) vascular thrombosis and 2.4%(n=3) hepatobiliary disorders (2 primary sclerosing cholangitis and 1 autoimmune hepatitis).Arthropathies were treated with nonsteroidal anti-inflammatory drugs in 26% of cases, oral or intra-articular corticosteroids in 18%, methotrexate in 10%, anti-TNF drugs in 10% and salazopyrin in 8%. The treatment of cutaneous manifestations was mainly with corticosteroid (74%) and anti-TNF drugs (2%). Ocular manifestations were treated with topic corticosteroids in the 64.3% of patients and anti-TNF drugs in 7%. Globally, the efficacy of treatment used to treat EIMs was of 90% and only 13% of patients had recurrence of EIMs. The multivariate analysis showed that female gender was a significant risk factor to developed EIMs (p=0.012; OR=1.61; 95CI% 1.11-2.34). Also, the severity of IBD was associated with the development of EIMs, patients with severe IBD who needed immunosuppressant therapies alone (p=0.009; OR=1.65; 95CI% 1.13-2.4) or in combination with adalimumab (p=0.029; OR=2.28; 95CI% 1.09-4.78) had an increased risk of developing EIMs
Conclusions: The most frequent EIMs in our environment are musculoskeletal and cutaneous manifestations. Patients with female gender and patients with more therapeutics requirements (immunosuppressant or anti-TNF drugs) and therefore with more severe disease, have higher risk of developing EIMs. Individualized treatment of EIMs is effective in most of patients. The risk of EIMs recurrence is low in our series

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Increasing prevalence of paediatric Inflammatory Bowel Disease in Japan: Direct comparison with adult disease using national registry data

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Background: Background: An increased incidence and prevalence of paediatric inflammatory bowel disease (IBD) has been reported in Western countries; however, changes in the prevalence of paediatric IBD in Asian countries remain unclear. This study evaluated changes in the prevalence of IBD among Japanese adults and children between 2004 and 2011.
Methods: Methods: Age-standardized prevalence and male to female ratios among Japanese IBD patients were analysed using the Japanese national registry database of patients receiving public financial aid

for intractable diseases. Data for adults (aged ≥ 20 years) were compared to those for children (aged 0-19 years).

Results: In 2004, 24,112 patients with Crohn's disease (CD) and 82,576 with ulcerative colitis (UC) were registered. Among them, 1012 CD (4.2%) and 2679 UC (3.2%) patients were under 20 years of age. The age-standardized prevalences of CD and UC were 4.2/100,000 and 11.0/100,000 among children, respectively; the corresponding prevalences among adults were 22.7/100,000 and 78.4/100,000, respectively. In 2011, 1504 (4.1%) of the 36,225 CD and 3302 (2.4%) of the 136,845 UC patients were under 20 years of age. The age-standardized prevalences of paediatric CD and UC were 6.7/100,000 and 14.6/100,000, respectively; the corresponding adult prevalences were 33.5/100,000 and 128.9/100,000, respectively. The prevalence of paediatric CD increased by 60.0% between 2004 and 2011, and by 47.8% in the adult population (NS). During this period, the prevalence of UC increased by 64.4% among adults, and by 32.5% among children (P < 0.001). The male to female ratio among paediatric patients increased for both CD and UC (CD, 1.98 to 2.13; UC, 1.35 to 1.40).

Conclusions: Conclusion: The prevalence of Japanese children with IBD has increased rapidly in recent years, with a trend towards a CD-dominance of IBD in the paediatric population. Conversely, the increase is UC-dominant among adult patients. This discrepancy between paediatric and adult IBD trends may provide further insight.

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Relationship between use of complementary and alternative medicine (CAM) and health related quality of life (HRQoL) among patients with inflammatory bowel disease (IBD).

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Background: Use of complementary and alternative medicine (CAM) has been reported to be frequent among patients with inflammatory bowel disease (IBD). Patients report improvement of health-related quality of life (HRQoL) and well- being as one of the important reasons of CAM use. Few studies however, have assessed the potential association between CAM use and HRQoL in IBD. The aim of this study was to investigate associations between CAM use and HRQoL in IBD patients.

Methods: From 2011 to 2012 adult IBD outpatients from 14 hospitals in Norway were included. CAM use was assessed with the International-CAM-Questionnaire and HRQoL with the Short Form-36 (SF-36). In addition, socio-demographic and clinical data was collected, including the Harvey-Bradshaw Activity Index (HBI) in Crohn's disease (CD) and the Simple Clinical Colitis Activity Index (SCCAI) in ulcerative colitis (UC). Univariate analysis of variance (ANCOVA) was used to assess the association between CAM use and HRQoL, controlling for age, gender, educational level and disease activity.

Results: Two hundred and ninety-nine patients with an established IBD diagnosis completed the questionnaires, out of which 235 (78.6%) had evaluable questionnaires (UC n=106, 41% females, and CD n=129, 56% females). A higher proportion of the UC patients (52%) compared with CD patients (38%) used CAM, p=0.003. The SF-36 scores were significantly lower in CD patients compared to UC patients in 3 out of 8 dimensions. In UC, patients with disease activity (SCCAI score ≥ 3) had significantly lower SF-36 scores in 5 out of eight dimensions. In CD, patients with disease activity (HBI score ≥ 4) had significantly lower SF-36 scores in all dimensions. Furthermore, after controlling for gender, age, educational level and disease activity, the UC CAM users had significantly lower SF-36 scores in all dimensions, except from physical function, compared with patients not using CAM. In CD, no differences in SF-36 scores were found between CAM users and non-users.

Conclusions: UC patients using CAM reported lower SF-36 scores compared to non-users. Among CD patients, no difference between CAM users and non-users in SF-36 scores was found. The relationship between CAM use and HRQoL needs further investigation.

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Incidence and risk factors of Clostridium difficile infection in patients with inflammatory bowel disease

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Background: Clostridium difficile infection (CDI) increases mortality, incidence and disease severity in hospitalized patients worldwide. Recent changes in the epidemiology of CDI include the identification of patients with inflammatory bowel disease (IBD) as a group at risk in comparison to the general population. The aim of this study was to identify the incidence and risk factors for CDI among patients with inflammatory bowel disease.

Methods: We performed a case-control study including 78 patients diagnosed with IBD hospitalized at the Institute of Gastroenterology and Hepatology in Iasi, Romania, between January 2012-July 2014. Demographic data and clinical characteristics were reviewed. IBD patients who had positive results for C. difficile toxins A and B were matched by sex, age and type of IBD with IBD patients hospitalized in the same period of time who had negative C. difficile toxins.

Results: Both groups were comparable for baseline characteristics. Out of the 78 patients diagnosed with IBD included in the study, C. difficile was detected in 26 patients (33.33%). The annual incidence of CDI in patients with IBD increased from 2.01% in 2012 to 16% in 2014. There was no statistical difference regarding hospitalization days (10.42 ± 7.34 vs. 8.01 ± 6.14, p=0.129) between the two study groups. Risk factors for CDI in patients with IBD were: ulcerative colitis (OR=1.90, CI= 1.320-2.720; p=0.001), use of proton pump inhibitors (OR=1.57, CI= 1.133-2.032; p=0.012), previous antibiotic use (OR=2.3, CI=1.587-3.332; p<0.0001), and albumin<3g/dl (OR=1.78, CI=1.023-5.558; p=0.038). Immunosuppressive and anti TNF- α treatment were not risk factors for C. difficile development in patients with IBD.

Conclusions: CDI in patients with IBD is a serious infection and should be treated aggressively with close clinical follow-up. Ulcerative colitis, previous treatment with antibiotics and proton pump inhibitors represent risk factors for CDI development in patients with IBD.

P656
Otorhinolaryngologic manifestations in Inflammatory Bowel Disease - Pilot study

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Background: Extraintestinal manifestations are often found in inflammatory bowel disease (IBD), mainly affecting the skin, eyes, joints and the hepatobiliary and renal systems. Some sporadic cases of otorhinolaryngologic manifestations were reported in patients with IBD however the real incidence and prevalence of these disorders have not been described. The objective of this study is to determine the prevalence of otohinolaryngologic manifestations in patients with IBD and to evaluate a possible correlation with the activity/progression of the disease.

Methods: We performed a prospective study of patients with ulcerative colitis or Crohn's disease that were referred to Otorhinolaryngology consultation with structured clinical assessment. We excluded patients with other systemic autoimmune diseases, hearing pathology, acoustic trauma and history of ear surgery. We used the Montreal Classification for disease characterization and the Harvey-Bradshaw Index or the Montreal Classification for the Crohn's disease or ulcerative colitis activity, respectively. We consider the normal tympanometric values between 0.3-1.4 cc.

Results: We included 25 patients, 14 with ulcerative colitis and 11 with Crohn's disease. Thirteen females and twelve males with a mean age of 40 ± 11 years. The mean duration of the disease was 10 ± 7 years. It was observed that the compliance of the ear was increased in 48% of patients, with a mean of 2.0 ± 2.6 cc. It was established the presence of tinnitus in 7 patients (28%), laryngeal ulcers in 4 (16%), nasal crusts in 4 (16%) and anterior septal perforation in 3 (12%). No relationship was found between the findings and the type or activity of the disease, presence of autoantibodies, other extraintestinal manifestations and medication.

Conclusions: There is a significant disturbance in the function of the middle ear as well as an increased frequency of tinnitus compared to the general population (14%). Despite the limitations imposed by the sample size, these preliminary data suggest that audiologic assessment in patients with IBD should be performed routinely.

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IBD in migrant South Asians: systematic review of epidemiology and disease phenotype

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Background: The epidemiology of inflammatory bowel disease (IBD) differs between developed and developing countries. Migrants moving from low to high incidence countries exhibit the incidence of their adopted country and yet different incidence rates and phenotype are reported between migrants and non-migrants. As the UK has a large South Asian (SA) community, we carried out a systematic review to examine the relationship between SA ethnicity and IBD.

Methods: A structured keyword search in Pubmed and EMBASE was undertaken in accordance with PRISMA guidelines. Studies on incidence, prevalence and disease phenotype of SAs compared to Caucasians were eligible for inclusion.

"Table 1: The incidence and prevalence of IBD in South Asians (SA) compared to Caucasians. CD= Crohn's disease; UC = Ulcerative colitis"

Author, year country	Region	Time period	Disease	SA vs Caucasian (per 100,000)	
				Incidence	Prevalence
UK					
Fellows 1990	Derby	1966 - 1985	CD	4.39 vs 7.47	
Probert 1992	Leicester	1972 - 1989	UC	10.8 vs 5.3	
Probert 1992	East London	1970-79 1980-89	CD CD	1.2 vs 3.8 2.3 vs 3.8	
Jayanthi 1992	East London	1972-1989	UC	1.2 vs 6.2	
Jayanthi 1992	Leicester	1972-1980 1981-1989	CD CD	1.24 vs 3.47 3.73 vs 5.27	
Probert 1993	Leicester	1989	UC CD	- -	135 vs 90.8 75.8 vs 33.2
Mayberry 1999	Leicester	1991-1994	UC	17.2 vs 9.1	
Canada					
Pinsk 2007	Vancouver	1985-2005	UC CD	6.7 vs 0.9 6.41 vs 3.69	
Mangat 2011	British Columbia	2006	UC CD	6.8 vs 5.0 1.0 vs 7.9	

Table 2: Disease phenotype in South Asians (SA). * Goodhand, 2012, SA group Bangladeshis, CD= Crohn's disease; UC = Ulcerative colitis"

Author, year, country	Region	Time period	Disease	Disease phenotype (SA*% vs Caucasian%)
UK				
Benfield 1987	Birmingham	1968-1984	UC	Remission rates 50 vs 23
Walker, 2011	London	2008 – 2010	UC CD	Total colitis 63 vs 42 Penetrating 4.3 vs 14.4
Goodhand 2012*	London	2010	UC CD	Total colitis 60 vs 33 Perianal phenotype 16 vs 3
Mayberry 1999	Leicester	1991-1994	UC	Total colitis 36.3 vs 31.7
USA				
Li 2013	San Francisco	1994 - 2009	CD	Perianal phenotype 46 vs 13 Fistulas 15.4 vs 4.4

Results: Thirteen eligible publications were identified. Those reporting incidence suggest an increase over time in both groups. The incidence in 4/5 ulcerative colitis (UC) studies was higher in SA than Caucasians. (Table 1) Six out of seven Crohn's disease (CD) studies showed higher incidence in Caucasians than SA. Total colitis was more evident in SA in 4/5 UC studies. (Table 2) Disease was more severe in SA for UC and CD.

Conclusions: Our preliminary findings highlight differences in incidence and phenotype between SA and Caucasians in the UK, Canada and USA. Further prospective studies to describe the current epidemiology and explore underlying reasons are needed.

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Inflammatory Bowel Disease and the Risk of Other Autoimmune Diseases

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Background: An increased risk of autoimmune disease has been reported in patients with IBD. Using data from the Clinical Practice Research Datalink (CPRD) this study set out to further examine this relationship.

Methods: Patients with a first time IBD diagnosis were randomly matched to an equally sized IBD-free comparison group. Incidence rates for new onset autoimmune diseases were estimated. A nested case-control

analysis comprising IBD patients was conducted, using conditional logistic regression to assess whether IBD severity, duration, or treatment influences the risk of developing additional autoimmune diseases

Results: During follow-up 1,069 IBD and 585 IBD free patients developed an incident autoimmune disorder. An increased incidence of autoimmune disease was observed in IBD patients (IR 9.65, 95% CI 9.09-10.24) compared to the non-IBD comparison group (IR 5.22, 95% CI 4.82-5.66). In IBD patients, increased disease severity was associated with an increased risk of autoimmune disease development (OR 1.62, 95% CI 1.28-2.05). Current antibiotic use was also associated with an increased risk (AOR 1.72, 95% CI 1.07-2.78). A reduced risk of incident autoimmune diseases was observed for current long term users of aminosalicylates (AOR 0.72, 95% CI 0.57-0.91).

Conclusions: Individuals with IBD had an increased incidence of developing a subsequent autoimmune disease. Increased disease severity and current antibiotic use were associated with an increased relative risk of developing additional autoimmune diseases in IBD patients. While, long term current aminosaliylate use was associated with a reduced risk.

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Knowledge and attitude of patient toward Ulcerative Colitis and disease activity in Europe: The UC CARES (Ulcerative Colitis Condition, Attitude, Resources and Educational Study)

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Background: As ulcerative colitis (UC) is a chronic inflammatory disease, patients require regular follow-up with healthcare providers. Increasing knowledge in patients has been shown to improve the medication compliance and self-management of chronic diseases. [1][2] This study is to describe the knowledge of patient regarding moderate to severe UC and to assess the consistency of patient and physician's assessment of disease activity.

Methods: Biologic naïve patients with moderate to severe active UC (Mayo score >=6), aged >=18 years who received conventional therapies during the 12 months prior to the enrollment date were recruited from 46 hospitals across the following 11 European countries: Belgium, France, Germany, Greece, Italy, the Netherlands, Spain, Sweden, Switzerland, Turkey, and the United Kingdom. Patients who underwent colectomy procedure or ileo-anal Jpouch reconstruction were excluded. Medical charts for the 12 months prior to the enrollment date were reviewed to collect clinical data. Remission was defined as full Mayo score < =2 with no individual sub-score >1. Patients completed questionnaires by rating their knowledge about UC disease by 4-point Likert scale from 1 very knowledgeable to 4 no knowledge. A weighted kappa was calculated to assess the agreement of disease activity (mild, moderate, and severe) between patient and physician.

Results: A total of 250 patients were included in the final analysis. Patients' mean age was 46.6 years (SD =16.3) and 59% were male. The median duration of UC was 6.9 years (IQR 2.3-14.4). Extent of UC included 21.6% proctitis, 28.4% left-sided, and 49.6% extensive colitis. Eighty-four percent of the patients rated somewhat to very knowledgeable about their UC disease. 51% of the patients reported that UC was somewhat disruptive and 26% of them reported that UC was very disruptive. 40% of the patients perceived UC as disruptive when their UC was in remission and 91% of the patients perceived UC as disruptive when they were experiencing a flare-up. The percentage of agreement between patients and physicians regarding the disease severity was 65.7% with a weighted kappa of 0.62. About 63% of the patients reported seeking information about UC and/or various treatment options and 96% of the patients reported that doctor was the main source for those information.

Conclusions: The majority of patients had somewhat to very good knowledge about their UC diseases. UC is a disrupting disease which impacts patients' lives even in those with disease remission. There was a fair agreement regarding disease activity between patients and physicians. The doctor was the main source of medical information on UC treatment information to patients.

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Estimation of cardiovascular risk according to asymptomatic organ damage in subjects with inflammatory bowel disease

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Background: Inflammatory bowel disease (IBD) is associated with an increased cardiovascular risk that is not fully explained by traditional cardiovascular risk factors. We previously reported that IBD subjects have an increased arterial stiffness that can be reverted by anti TNF-alpha therapy. In this study, we aimed to evaluate the net reclassification of cardiovascular risk in IBD subjects and controls after the assessment of carotid-femoral pulse wave velocity (PWV), in accordance with the 2013 ESH/ESC Guidelines for the management of arterial hypertension.

Methods: The total cardiovascular risk was calculated in 80 IBD subjects and 80 controls matched for age and sex. Carotid-femoral PWV, a marker of asymptomatic organ damage, was measured with a sphygmocor device according with the current guidelines. Individuals with cardiovascular disease (coronary heart disease, congestive heart failure, stroke, transient ischemic attack, or intermittent claudication), diabetes,

Table 1. Classification of cardiovascular risk in IBD subjects

Other risk factors or asymptomatic organ damage	Blood Pressure (mm Hg)			
	Optimal SBP <120 and DBP <80	Normal SBP 120-129 or DBP 80-84	High-normal SBP 130-139 or DBP 85-89	Grade 1 hypertension SBP 140-159 or DBP 90-99
Subjects classified without asymptomatic organ damage (carotid-femoral PWV>10 m/s)				
1-2 RF	43	19	10	8
Subjects reclassified with asymptomatic organ damage (carotid-femoral PWV>10 m/s)				
1-2 RF	40	16	9	8
Carotid-femoral PWV>10 m/s	3	3	1	0

chronic kidney disease and dyslipidaemia were excluded. The risk factors considered in this analysis were the following: (a) male sex; (b) age ≥ 55 years in men and ≥ 65 years in women; (c) BMI ≥ 30 kg/m2.

Results: IBD patients, have higher carotid-femoral PWV compared with controls (7.9 ± 1.6 vs. 7.0 ± 1.1 m/s, respectively; P< 0.001). Results were confirmed after adjustment for age, gender, mean arterial pressure and heart rate. After inclusion of asymptomatic organ damage (carotid-femoral PWV >10 m/s), risk prediction was improved in 7 (8.8%) IBD subjects and only in 1 (1.3%) control subject, resulting in a reclassification of all these subjects from a low-to-moderate cardiovascular risk category to a moderate-to-high cardiovascular risk category.

Conclusions: Compared to controls, the measurement of carotid-femoral PWV produce a net reclassification of 7.5% of IBD subjects commonly considered in a low-to-moderate cardiovascular risk category.

P661
Different phenotypical characteristics in Romanian IBD patients with rural vs. urban residence: Results of a nationwide multicentric cohort

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Background: According to last population statistics, Romania has a population of over 20 million inhabitants out of which only 54% reside in urban areas. Different residential areas might indicate different environmental factors influencing phenotypical presentation of IBD patients in our country.

Methods: We have investigated phenotypical characteristics of Romanian IBD patients using the the IBDPROSPECT Referral Center Database, a web-accessed database implemented in our Country in order to facilitate collection of significant IBD epidemiological data Nationwide. A total of 1481 patients from 15 referral centers nationwide were included in the analysis during the time period 2006-2014. Only data at first presentation was analyzed.

Results: There were 73.8% of cases residing urban areas, with male predominance (53%). There was a significantly higher proportion of patients diagnosed with UC in rural vs urban areas - 63.7% vs 56.5% (p=0,03). Significantly more moderate to severe cases were from rural areas of residence - 62% vs 49.5% (p=0,0004). Similar differences in severity of flare were registered for both UC and CD cases, in subgroup analyses. No significant differences in rural vs urban residents were identified according to different phenotypical features of Montreal classification. Patients from rural areas presented with lower digestive hemorrhage more frequently - 20,4% vs 14% (p=0.006), however, extraintestinal manifestations were more frequently encountered in patients with urban residence - 16,7% vs 10,9% (p=0,01).

Conclusions: The analysis of our multicentric referral center cohort indicates that Romanian IBD patients residing in rural areas represent approximately 27%, have a higher incidence of UC and a more severe presentation of the disease.

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P662
Pain in IBD patients: very frequent and frequently insufficiently taken into account

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Background: Abdominal pain is a common symptom related to inflammatory bowel disease (IBD) and appears to be present in about 50-70% of IBD patients. Other pain localizations can be caused by extraintestinal manifestations (EIM) of IBD such as arthralgia/arthritis, ankylosing spondylitis, pyoderma gangraenosum, erythema nodosum and uveitis. Pain is also an important manifestation of inflammation. Inflammatory cytokines and mediators sensitize primary afferent neurons. However, inflammation does not fully explain pain in many IBD patients: about 20% of patients in clinical and endoscopic remission continue experiencing pain.

Methods: The patients of the Swiss IBD Cohort Study (SIBDCS) (n=2152) received a questionnaire regarding pain localization, impact of pain on daily life, how the surrounding responds to the patients' pain and how activities of daily life are influenced. Furthermore the questionnaire investigated the use of pain medication. Additionally, using prospectively collected data from the Swiss IBD cohort study, we compared the disease characteristics of the participating patients with the data of the questionnaire.

Results: Among a total of 1258 completed questionnaires (response rate 58.5%) the vast majority of patients reported having experienced pain during the course of the disease. Only 11.2% of the patients reported no pain. With regard to chronicity we found pain to be a longstanding problem with 17.8% of patients reporting pain since 2-5 years prior to the current assessment and even more than a third of patients (37.4%) reporting pain since more than 5 years. Almost one in six patients (14%) reported to experience pain every day. Pain medication could not sufficiently ameliorate pain.

Conclusions: Pain is an important factor of disease presentation of IBD. It is present in many more patients than generally assumed. Moreover, pain is a longstanding problem for the majority of the patients affected. Thus, an increased awareness is mandatory address this frequent complication in the course of IBD.

P663
Association of sleep quality and mucosal activity in IBD patients in clinical remission

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Background: There is emerging data indicating that sleep disturbances in IBD patients in clinical remission are related with increased risk to develop clinical relapse. It is also known that inflammatory processes can affect sleep pattern.

Aim of this prospective study was to investigate possible relationship between quality of sleep and mucosal activity.

Methods: 84 patients, 35 with ulcerative colitis (UC) and 49 with Crohn's disease (CD), in clinical remission defined by partial Mayo score ≤2 or CDAI< 150, completed the Pittsburgh Sleep Quality

	Sleep quality	Good	Poor	Total
Mucosal Activity				
Negative		35	13	48
Positive		10	26	36
Total		45	39	84

PSQI absolute value	Coef.	Std. Err.	P-value	95% C.I.	R2
Positive mucosal activity	2.67	0.68	<0.001	1.31–4.02	0.23
Sex (females)	1.93	0.67	0.005	0.59–3.28	

Index questionnaire (PSQI) [1] . As poor sleep quality was defined PSQI score >5. Mucosal activity was assessed either by ileocolonoscopy (51 patients) or by fecal calprotectine (32 patients). As negative mucosal activity was defined, in case of endoscopic assessment, an endoscopic Mayo score ≤1 in UC and SES-CD ≤ 3 in CD or Rutgeert's score <i2 (postoperatively in CD) and in case of fecal calprotectine assessment a value <50 µg/g. X2 with Yates correction and multivariate anova regression analysis using absolute values of PSQI as dependent variable were performed.

Results: X2 analysis resulted in X^2=16.8519 p<0.01 according to table 1. Results from multivariate anova regression analysis are shown in table 2.

Conclusions: Both analyses suggest that poor sleep quality in patients in clinical remission is related with positive mucosal activity determined by endoscopic mucosal lesions and/or increased faecal calprotectine levels. Positive mucosal activity is associated with higher values of PSQI (2.67 units higher) in comparison to negative mucosal activity.Women have higher PSQI scores than men by multivariate analysis

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P664
Use of smartphones by UC patients: A vehicle for communication and education

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Background: With the wide distribution and popularity of smartphones, most people can access the Internet anytime. Patients with Inflammatory bowel disease (IBD), Crohn's disease and ulcerative colitis (UC), should not be different. There are a range of application software (Apps) for Android or Apple to support the patients in different situations (preparing for colonoscopy, bathroom finder, teaching about IBD, online diary, reminder for adherence etc.). Previous studies have demonstrated that already using land-line telephones to follow up with patients improves adherence (1). To get a full picture on the availability of and access to smartphones dedicated data were collected in an UC patient survey.

Methods: Data Source: The study was conducted among a sample of 372 UC patients (204 in United Kingdom, 77 in Spain, 21 in Denmark, 34 in Finland, 28 in Sweden and 8 in Norway) from a qualified panel.

Period of data collection: The data collection took place from the 11th of December 2013 to the 10th of January 2014.

Implementation: The individuals from the sample received a link via email to an online questionnaire on a secured platform. The questionnaire asked about their UC history, their attitudes and behaviors towards UC and its management and their level of adherence to treatment. Socio-demographic characteristics and information on the possession of a smartphone were also collected.

Results: The socio-demographic and disease data (not shown here) are in line with other recent epidemiologic data of UC patients. Out of the 372 UC patients 267 used a smartphone (72%). 242 had a private one, 49 a business one. The highest observed ownership was in Finland and Spain (74 and 77%). 66% of women and 64% of men reported to possess a private smartphone. In the age group "up to 33 years" 93% reported ownership of a smartphone. In the age group "34-55 years" the figure was around 80% and only "above 55 years" the possession rate drops to 37%. In this group only 31% of women own a smartphone.

Conclusions: There can be a certain bias in the sample (computer and access to internet is at 80 to 90% in the countries of the sample) as participants needed internet access. Nevertheless the high availability of smartphones in both genders and across the age groups up to 55 years allows targeted communication between healthcare providers and patients. The functionality of smartphones also enables the use of special medical Apps. However, as with other tools, the access does not predict usage or the capabilities to use the relevant function of a smartphone or the features of Apps. Despite this 'caveat' healthcare providers should make the most out of the smartphone opportunity - especially in the young age group - to support/increase adherence(2).

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P665
Regional differences in health care of patients with IBD in Germany

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Background: The regional availability of specialized physicians is an important aspect in the discussion about the healthcare of patients with IBD. Principles of the optimal healthcare were defined in the course of the development of German IBD pathways and treatment guidelines. The association between physician density and healthcare is not yet clear. Most studies did not consider district type, which reflects population density and may also have an impact on healthcare. Our research question was, "Do specialist density and district type influence the healthcare of IBD patients in Germany?"

Methods: We combined a claims dataset from a German health insurance fund with population and physician data. Four main aspects

were investigated in our cohort study (derived from pathways and guidelines): regular specialist visits, drug therapies, surveillance colonoscopy, and IBD-related hospitalizations. Various regression analyses were performed.

Results: The study cohort was comprised of 21,771 individuals, including 9,282 patients with Crohn disease and 12,489 patients with ulcerative colitis. The patients who were living in districts with higher specialist densities were more likely to attend specialist visits on a regular basis. No difference in the frequencies of TNF-alpha inhibitor therapies was found. However, individuals from urban areas were more likely to receive a permanent immunosuppressive therapy with continuous specialist support. Age, sex, and IBD type also had significant effects.

Conclusions: The study results revealed that some aspects had positive effects on the probability of implementing healthcare in accordance with pathways and guidelines. However, no clear evidence of a general healthcare undersupply in rural areas was found.

P666
Changing disease patterns in Crohn's disease; experience from Malta

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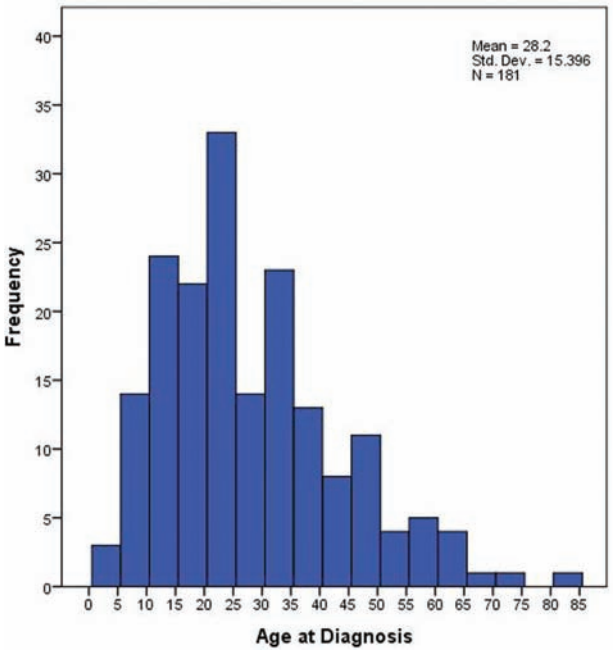
Background: In Malta the incidence of Crohn's disease (CD) has been estimated at 0.96/100,000 per year in males and 1.62/100,000 per year for females. These rates are amongst the lowest in Europe [1]. Nonetheless over recent years we have noticed changing disease patterns with increasing disease frequency amongst younger patients.

Methods: We conducted a cross-sectional survey looking at disease patterns, treatment and surgical outcomes of 181 Maltese patients with CD who came for routine follow up between January 2013 and July 2014.

Results: Gender distribution was similar, with a slight male preponderance (51.4%;n=93). Age at diagnosis was positively skewed towards younger age groups.

Older age at diagnosis was associated with a higher risk of surgery (p=0.18). This was especially true for those older than 50, 61.1% of whom required surgery (n=11;p=0.01). Gender was also associated with a greater need for surgery, males being twice as likely to undergo intervention (47.6% males, 23.9% females;p=0.47). Mean delay between diagnosis and initial surgery was similar for all groups. Disease behaviour and location were significantly associated with need for surgery, B3 and L3 disease predisposing towards intervention (p=approx 0 and 0.20 respectively). A significant proportion of newly diagnosed patients are those aged 10 and under (8.8%;n=16). Amongst this group only 1 patient required surgery. Out of the 5 patients under 16 who did require surgery, 3 had been previously diagnosed with UC and underwent



"Histogram demonstrating age distribution of Maltese patients with Crohn's disease followed up between January 2013 and July 2014"

panproctocolectomy and 1 was operated upon before a diagnosis of CD was suspected. All cases had perianal disease at presentation and had not undergone upper endoscopy. Biologic and thiopurine use was common (50.3% and 66.9% respectively). Those aged 50 and older at diagnosis were less likely to be treated with antiTNF agents (38.9%;n=7) compared to those younger than 50 (51.5%;n=84). On average biologics were started 5.6 years (95%CI +/- 1.3 years) after diagnosis and 2.8 years (95%CI +/- 1.9 years) after surgery.

Conclusions: CD is being increasingly diagnosed in younger patients. Surgery in this group is usually as a consequence of unrecognised disease and may be avoidable. Our data shows more aggressive disease behaviour with increasing age. In spite of the fact that those who are diagnosed with CD at an older age are more likely to require surgery, biologic agents are being used less frequently in this group. Additionally we are not able to explain the significant gender difference suggesting more severe disease in males.

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P667
The effects of azathioprine/6-mercaptopurine and TNF-alpha antagonist on surgery in Korean patients with Crohn's disease from the CONNECT cohort

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Background: The complications of Crohn's disease often should be treated through surgical intervention. The risk factors of complications have been studied largely. However, there are few data about the trend of medicines against Crohn's disease around surgery in Koreans. This study was designed to investigate the association between medicines and surgery in patients with Crohn's disease retrospectively.

Methods: The Crohn's Disease Clinical Network and Cohort (CONNECT) retrospective cohort was used in this study. Between 1982 and 2010, patients with confirmed Crohn's disease were enrolled. The effect of azathioprine/6-mercaptopurine (6-MP) and TNF-alpha antagonist on abdominal surgery and perianal surgery were analyzed by the logistic regression analysis adjusting age, sex, location (L), and behavior (B).

Results: A total of 1376 patients (M: 973, F: 403) were selected, and 622 patients (abdominal surgery: 338, perianal surgery: 284). In 412 patients with abdominal surgery or no surgery, a multivariate analysis revealed that preoperative use of azathioprine/6-MP and TNF-alpha antagonist had an odds ratio of 0.225 (95% confidence interval [CI]: 0.127-0.398, P<0.0001) and 0.797 (95% CI: 397-1.599, P=0.522) for abdominal surgery, respectively. In 393 patients with perianal surgery or no surgery, a multivariate analysis azathioprine/6MP, and TNF-alpha antagonist, revealed that preoperative use of azathioprine/6-MP and TNF-alpha antagonist had an odds ratio of 0.148 (95% CI: 0.078-0.282, P<0.0001) and 0.239 (95% CI: 0.086-0.664, P=0.006) for perianal surgery, respectively.

Conclusions: Azathioprine/6-MP is significantly associated with a reduced risk of abdominal surgery and perianal surgery, and TNF-alpha antagonist is significantly associated with a reduced risk of perianal surgery in Crohn's disease.

P668
Fertility in IBD women is comparable to fertility in non-IBD controls

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Background: As inflammatory bowel diseases (IBD) often arises in young people, questions about fertility and reproduction are common. Prior studies on infertility in IBD women are scarce and conflicting. The aim of this study was to compare subfertility between IBD women and non-IBD controls. Furthermore, we investigated the effect of several IBD associated factors on fertility.

Methods: All consecutive IBD women with a pregnancy wish from 2008-2014 were prospectively followed at the preconception outpatient clinic in the Erasmus University Medical Center Rotterdam. Data on patient characteristics, disease and obstetric/gynecologic history, paternal health, time to conception and pregnancy outcomes were recorded. The control group consisted of a random age-, and ethnicity-, matched sample from a large non-diseased birth cohort (Generation R) from the same geographical region. Primary aim was to compare subfertility rates between IBD women and non-diseased controls. Subfertility was defined as the inability to conceive within 12 months of unprotected intercourse and/or the need for fertility treatment to conceive. Secondary aim was to identify risk factors for subfertility in IBD women.

Results: A total of 333 cases in 227 IBD women (236 CD (70.9%), 87 UC (26.1%), 10 IBDU (3.0%)) and 804 non-diseased controls were included. Mean maternal age was 30.5 yrs (SD=4.4 yrs). There were no differences between the IBD and the control group in maternal and paternal BMI (p=0.55 and p=0.53, respectively) and smoking status (p=0.14 and p=0.06, respectively). Median time to conception was 2.4 months (IQR: 0.9-7.2) in the IBD group versus 3.0 months (IQR: 2.0-7.0) (p=0.001) in the control group. IBD was not significantly associated with subfertility when compared to controls (aOR: 1.39 (95% CI: 0.99-1.94, adjusted for maternal age, BMI, education and paternal smoking). IBD women more often underwent fertility treatment than controls (21 (10.1%) vs 30 (3.7%), p=0.001). Reasons for fertility treatment in the IBD group were of gynecologic or andrologic cause in 18 cases (85.7%). Diagnosis, previous bowel surgery, perianal disease activity, IBD medication type and the number of disease flares in the past year were not associated with subfertility in IBD women.

Conclusions: This study shows IBD is not associated with increased time to conception or subfertility. Fertility treatment was more common in IBD women, but this was not associated with IBD. Type of IBD, previous bowel surgery, perianal disease, IBD medication and disease activity were not associated with subfertility in IBD women.

P669
Inflammatory Bowel Disease is prevalent in Australia but rare in Indigenous Australians

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Background: The incidence of inflammatory bowel disease (IBD) has risen dramatically in Western countries since the 1950s,

with the highest rates observed in North America and Western Europe[1]. In Canada, there is a significantly lower incidence of IBD in rural Aboriginal communities[2]. Although this may be due to under-diagnosis, genetics and changing environmental exposures may also be factors. A lower risk of developing IBD has been reported in developing countries, rural communities, poor socioeconomic groups, overcrowded communities and in areas lacking clean or hot water[3]. These factors are found in rural Indigenous communities in the Northern Territory (NT) of Australia. The incidence of IBD in urban Australia is comparable to Western Europe [4] but limited data is available for Indigenous Australians (IA).

Methods: The Royal Darwin Hospital is the only tertiary referral centre in the NT and all IBD patients are referred to its Gastroenterology service. The hospital's database was searched for all patients who presented with IBD from 2007-14. Prospective data was collected from 2013. Population demographic data were drawn from the Australian Bureau of Statistics.

Results: In 2013, there were 212,651 individuals residing in the NT, including 64,560 IA. In 2007-2014, 279 patients with IBD were treated at the Royal Darwin Hospital, equating to a period prevalence of 131 per 10^5. The prevalences (per 10^5) of various types of IBD were: ulcerative colitis (UC) 62, Crohn's Disease (CD) 67 and indeterminant colitis 2. Notably, only 3 patients with IBD were IA (all of mixed race), meaning to a prevalence of 5 per 10^5 among IA. The specific prevalence among the non-IA population was 186 per 10^5. The NT population residing outside of the capital city comprised 76,406 individuals, of whom 49457 were IA. Of the 279 IBD patients, only 2 resided rurally (1 IA and 1 non-IA). Hence the period prevalence of IBD was 3 per 10^5 in the non-urban population and 203 per 10^5 in the urban population. In 2013 the incidence of IBD was 20 (UC 9, CD 11) per 10^5 with no cases in the IA population.

Conclusions: This is the first epidemiological study of IBD in Australia that includes IA. Mindful of the small samples in some subgroups, it suggests a high prevalence of IBD in the non IA urban population but a very low prevalence among IA and people living in non-urban areas. This may be due to genetic or environmental factors. For example, a previous study has shown differences in gut microbial profiles in IA compared to Caucasian controls[5] .

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P670
Perception about disease activity and treatment attributes in patients with Ulcerative Colitis from Spain - UC-life survey

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	Crohns Disease	Ulcerative Colitis	Indeterminant Colitis	IBD
Male	69	77	3	149 (53.4%)
Mean age at diagnosis	32.3 (10-71)	33.2 (5-71)	32.9 (26-54)	32.3 (5-71)
Smoker	29	15	0	44 (16%)
Ex Smoker	58	41	0	99 (35.5%)
5 ASA	48	115	3	166 (60%)
Thiopurine	76	35	0	111 (40%)
Biologics	49	2	1	52 (18.6%)
Previous surgery	49	8	0	57 (20%)
Deaths	2	4	0	6 (2.2%)

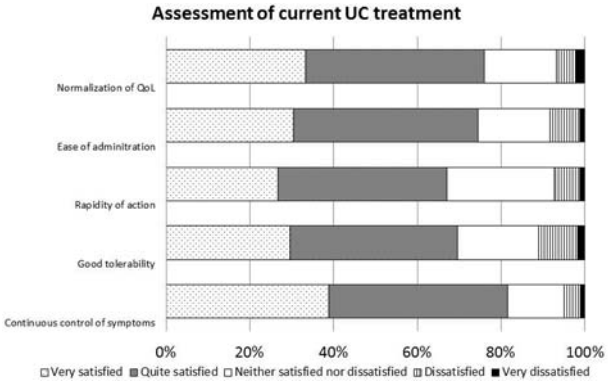
Demographic data of IBD patients in NT

Ethnicity	Number of patients	Population at risk
Asian	3 (1%)	10,200
Caucasian	245 (88%)	119686
Indigenous Australians	3 (1%)	64560
Indian subcontinent	14 (5%)	2531
Mediterranean	10 (3.6%)	7310
Other	3 (1%)	

Prevalence of IBD based on ethnic background

"Attributes of therapy. Ranking of Importance"

	RANK OF IMPORTANCE (1=most important; 5=less important)				
ATTRIBUTES OF THERAPIES	1	2	3	4	5
Continuous control of symptoms	44.6%	21.4%	16.4%	9.8%	7.9%
Good tolerability	15.8%	28.7%	29.0%	19.3%	8.0%
Rapidity of action	12.7%	24.3%	21.4%	26.8%	14.9%
Ease of administration	4.9%	6.0%	13.6%	23.9%	51.6%
Normalization of quality of life	36.5%	17.2%	17.2%	15.6%	13.5%



"Assesment of current UC Treatment"

Background: Objectives.To describe the perception about disease burden, preferred treatment attributes and satisfaction with treatment of patients with ulcerative colitis (UC) followed in hospital clinics from Spain.

Methods: UC-LIFE was a survey to UC patients. Each of the 39 participating hospital gastroenterologists handed the survey to 15 consecutive UC patients >18 years. Patients completed the survey at home and returned it by post-mail. Patients were asked to describe the disease behavior during the previous year responding to closed questions, and to describe their expectations and satisfaction degree with the treatment by ranking several attributes.

Results: 585 patients received the survey and 436 returned it (response rate: 75%). Mean age was 46 years (SD: 13), 53% were men. Median duration of UC was 8 years (IQR: 4-15). UC was perceived as mild by 57.3%, moderate by 35.9% and severe by 6.8% of the patients. During the previous year 50.5% patients reported an exacerbation (mean duration perceived: 6 weeks) and 19%, 31% and 47% respectively reported a hospital admission, emergency room visit or a non-scheduled visit due to UC activity. The most important attributes of therapies for patients were continuous control of symptoms (44.6%) and normalization of the quality of life (QoL) (36.5%); others were less frequently mentioned (table)

. Satisfaction with current treatments was as follows: very satisfied (38.8%), satisfied (40.0%), neutral (16.9%), dissatisfied (3.6%), very dissatisfied (0.7%). The percentages of satisfaction with the above mentioned attributes were similar (figure)

Conclusions: About 50% of patients reported UC activity during the previous year, and 43% perceived UC currently as moderate or severe. However, the degree of satisfaction with the current therapies is high. Continuous control of symptoms and normalization of QoL are the attributes considered as most important by patients. All patients came from hospital clinics and the sample was non-randomized; thus the results must be interpreted in this context.

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P671
The 5 year incidence of post-operative clinical recurrence following ileocolonic resection for terminal ileal Crohn's disease

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Background: Post-operative clinical recurrence following ileocolonic resection for Crohn's disease is common. It can occur in up to 55% of patients within 5 years [1]. Current predictors include smoking, redo surgery and penetrating disease [2]. The aims of this study were to determine the 5 year incidence and predictors of post-operative clinical recurrence following ileocolonic resection in terminal ileal Crohn's disease.

Methods: The clinical records of patients who underwent ileocolonic resection for Crohn's disease over a six year timeframe (1st January 2005 to 31st December 2010) were reviewed. Post-operative clinical recurrence was defined as an initiation or change in medical therapy for recurrent symptoms, with endoscopic or radiological evidence of active Crohn's disease. Life table analysis was used to determine the 5 year incidence of post-operative clinical recurrence. The Kaplan-Meier model and Log Rank test was used to determine predictors of post-operative clinical recurrence (P values < 0.05 were considered significant).

Results: There were 175 ileocolonic surgical procedures [142 one-stage and 33 two-stage procedures (13 stoma reversals and 20 stoma formations)] performed on 163 patients. Long-term follow-up data were obtained on 142 patients. Six patients received biologics preoperatively and continued biologics postoperatively. Three additional patients received biologics postoperatively. Life table analysis demonstrated 48.2% of patients with post-operative clinical recurrence at 5 years.

Kaplan-Meier analyses demonstrated redo surgery [P = 0.016], ileocolonic (Montreal L3) disease [P = 0.049], and the presence of postoperative intra-abdominal septic complications (IASCs) [P = 0.043] were associated with post-operative clinical recurrence.

Conclusions: The marginal improvement in the 5 year incidence of postoperative clinical recurrence may be indicative of a drive for multidisciplinary care as well as improved medical regiments. A risk stratification model is necessary to target high risk patients. This model may also need to include patients who develop postoperative IASCs, redo surgery and ileocolonic disease.

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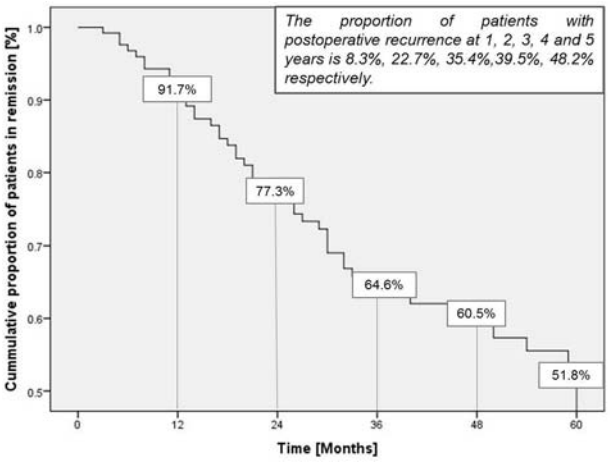

"Figure 1- Life table analysis demonstrating the proportion of patients in remission. Each drop in the curve represents a patient developing clinical recurrence"

P672
The impact of ethnicity on the prevalence and length of hospital stay in patients with Crohn's Disease

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Background: Crohn's disease (CD) has a UK prevalence of 145 per 100,000 of the population [R1] . We aimed to explore the impact of ethnicity on the length of hospital stay (LOS) in patients with CD.

Methods: Anonymous data of adult patients admitted to 7 hospitals within the North West of England between 2000 and 2013 were obtained and processed using the ACALM (Algorithm for Co-morbidity, Associations, Length of stay and Mortality) study protocol. ACALM uses the ICD-10 and OPCS-4 coding systems to identify patients [R2] [R3] . The impact of ethnicity on prevalence and LOS was analysed using SPSS.

Ethnicity	n(%)	Mean Age (years)	M:F Ratio	%admitted as emergency	%with co-morbidity	Mean Length of Stay (days)	ODDs ratio for length of stay*
All groups	3,439 (100.0)	47.25	1:1.2	77.8	17.1	4.6	-
Caucasian	3,012 (87.6)	48.01	1:1.3	78.5	17.9	4.5	1
South Asian	155 (4.5)	36.7	1.3:1	74.2	10.3	3.3	0.993 (0.987–0.999)**
Afro-Caribbean	43 (1.3)	39.43	1:1.2	55.8	7.0	3.3	0.994 (0.974-1.014)
Oriental	9 (0.3)	47.57	2:1	55.6	11.1	2.6	0.969 (0.859-1.093)
Mixed	23 (0.7)	28.83	1:1.3	73.9	4.3	4.8	1.010 (0.981-1.040)
Other	44 (1.3)	37.2	1.2:1	75.0	2.3	2.9	0.988 (0.943-1.036)
Unknown	153 (4.4)	50.83	1.1:1	76.5	22.2	8.0	1.013 (1.004-1.022)**

*adjusted for age, sex, co-morbidity, ** statistically significant, p<0.05

"Characteristics of admissions for patients with Crohn's Disease"

Results: Of 929,465 patient admissions, 3,439 (0.37%) were coded for CD. Females accounted for 55.5% of CD admissions. Patients were more likely to be admitted as an emergency (77.8%). CD was most common in Caucasian patients (87.6%) who were also more likely to have co-morbidities (17.9%). Logistic regression analysis accounting for variations in age, gender and co-morbidities revealed that LOS in patients with CD was significantly shorter in South Asian patients. Table 1 describes the sample demographics and LOS

Conclusions: CD is more prevalent in the Caucasian population, with ethnic variations in the LOS. The significantly shorter LOS in the South Asian population may be due to stronger family support facilitating discharge. Further understanding of such disparities is essential in the planning and development of healthcare services in regions with large multi-ethnic populations.

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P673
Annual Incidence of IBD in Otago, New Zealand: An 18-year Epidemiological Analysis

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Background: The incidence of Inflammatory Bowel Disease (IBD) continues to increase in some regions of the world, while in others it plateaus or even declines. It has been previously shown that New Zealand has one of the world's highest IBD incidence rates, but changes over time have not been investigated. The aims of this study were to determine the annual incidence of IBD, Crohn's Disease (CD) and Ulcerative Colitis (UC) in the Otago region, New Zealand from 1996 to 2013 and to examine changes in demographics and disease presentation at diagnosis over the 18-year study period.

Methods: All patients in Otago who had at least one ICD-10 code for IBD (K50.X and 555.X for CD, K51.X and 556.X for UC, and K52.3 and 558.9 for IBDU) during the period 1996-2013 were identified. A diagnosis of IBD according to accepted criteria, the date of diagnosis, demographic information, phenotypic data, according to the Montreal classification and treatment details were extracted from individual patients' electronic and paper records. Age standardised annual incidence rates of CD, UC, and IBD-Unclassified (IBDU) were calculated and trends over time assessed.

This study was approved by the University of Otago Human Ethics Committee.

Results: 442 Otago residents had confirmed IBD diagnosed during 1996-2013, of which 52% had CD, 40% UC and 8% IBDU. The median age at diagnosis for IBD was 35 (CD 31; UC 41) and the vast majority (97.1%) of new diagnoses were in patients with European ancestry, with a disproportionately low amount of cases in indigenous populations (IBD Maori 1.8% of all cases; Pacific Islanders 0.2% of all cases). The overall incidence over this time period for IBD was 13.4/100,000 (UC 4.46/100,000; CD 6.59/100,000) and the average annual age-adjusted IBD incidence rate increased by 0.27 cases per 100,000 people per year (p=0.095). The lowest incidence was recorded in 2006 for IBD with 6.4/100,000 people (CD 1.7/100,000; UC 2.6/100,000) and the peak incidence for IBD was 23.8/100,000 people in 2012 (CD 15.3/100,000; UC 5.7/100,000). Besides disease location in CD (increase in ileocolonic disease presentation L3, p=0.02), there were no significant changes in disease presentation over the 18 years (all p ≥0.19).

Conclusions: This study highlights the significant annual fluctuation of disease incidence and over the past 18 years there has been a slight but non-significant increase in IBD incidence. The average annual incidence for IBD remains one of the highest in the world. While the proportion of ileocolonic CD has increased, all other phenotypic measures for CD and UC have remained the same over the past two decades. In a nation with mixed ethnicities, IBD is more prevalent in those of European descent.

P674
Differences in Mucosal Distribution and Clinical Characteristics of Ulcerative Colitis in South Asians and Caucasians in the North of England

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Background: Inflammatory bowel diseases (IBD) are inflammatory conditions that affect the gastrointestinal tract and may have extra intestinal manifestations. The two main subtypes are Crohn's disease (CD) and ulcerative colitis (UC). The aetiology remains elusive but the current paradigm is of an aberrant immune response as a result of an environmental factor(s) in a genetically susceptible individual. The incidence of IBD has traditionally been higher in Caucasian populations. There is now evidence of increasing incidence in all populations. Studies from the UK and North America have observed a 2-3 times higher incidence of IBD in South Asian immigrant populations compared to local cohorts. However, few studies have described the disease phenotype and luminal distribution in this population.

Methods: Ethics approval was obtained ref: O5/Q1407/274. Patients were recruited prospectively in 11 centres in the North Of England. Inclusion criteria were diagnosis of UC and age > 16 years. Exclusion criteria were diagnosis of IBDU or IDC and Age < 16 years. Information was collected from using a standard clinical proforma. Data was stored on and analysed on a FileMaker Pro database. Chi Squared analysis was used to compare groups.

Results: In total 721 patients were recruited, 186 South Asians (SA) and 535 Caucasians (CAU). In the South Asian cohort males were more likely to be affected compared to Caucasians. South Asians had a younger average age of diagnosis 30 vs. 40 for Caucasians. There were differences in luminal distribution with South Asians more likely to have Extensive Colitis (45% vs. 26%) or Left sided colitis (42% vs. 22%) and Caucasians more likely to have Proctitis (13% vs. 52%). The differences in mucosal distribution between groups were highly statistically significant (p<0.001). There was no statistical difference in family history between groups with 21% of South Asians vs. 27% for Caucasians. There was no statistical difference in need for colectomy between groups (5% for SA vs. 3% for Caucasians). Also there was no statistical difference in the presence of EIM's 6% for SA vs. 5% for Caucasians.

Conclusions: There are significant differences in mucosal distribution and age of diagnosis between groups. South Asians had a younger age of onset and more extensive colitis, but the relatively low rate of colectomy and EIM's which suggest a less severe disease phenotype. In addition the younger age of onset and extensive disease in South Asians may influence risk of colorectal cancer in the future. These differences may represent differences in disease pathogenesis in particular genetic susceptibility or environmental factors. This information will help inform current and future genotype/phenotype correlations.

P675
Natural history of paediatric IBD around transition to adult services: a regional cohort study

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Background: Effective transition of young people with paediatric-onset IBD (PIBD) is essential, but there is a paucity of data in this area. We aimed to describe PIBD patient transition in SE Scotland (SES) through natural history (disease activity, therapy escalation and service utilisation) both at the point of transfer and post-transition.

Methods: Our prospective PIBD database provided all patients discharged from our regional service since 01/01/09. This retrospective cohort study is of patients leaving due to transition (graduation from paediatric to adult IBD services through a transition process, a transition event [single joint clinic] or transfer) until 30/09/13, with follow-up (FU) data collected at a minimum of 1yr post-transition; disease location/severity was assessed by Montreal classification/Physician Global Assessment (PGA).

Results: 83 patients transitioned (60 CD, 13 UC and 10 IBDU) with median age at transition of 18.0yrs (IQR 17.6, 18.4). 82% (68/83) of patients were in steroid-free remission (SFR) at transfer and 5% (4/83) had moderate-severe disease (MSD). 72% (43/60) of CD patients had ileocolonic involvement (L3) and 55% (33/60) pan-enteric disease (L3+L4); 74% (17/23) of UC/IBDU patients had extensive disease (E3). 78% (65/83) had exposure to thiopurines, 47% (39/83) to methotrexate (MTX) and 25% (21/83) to anti-TNF therapy in paediatric services; only 19% (16/83) had never had immunosuppression. 10% (8/83) had major IBD-related surgery prior to transfer and 3 patients (4%) had pan-treatment refractory IBD (primary non-response, complete loss of response or non-recoverable intolerance to all of thiopurines, MTX, infliximab and adalimumab). Median follow-up post transition was 2.7yrs (IQR 1.6, 4.0). At last adult FU 6 patients had transferred out of SES and 3 had defaulted from clinic. 85% (63/74) of those remaining

were in SFR; 8% (6/74) had MSD. The rates of ileocolonic CD (L3) and pan-enteric CD (L3+L4) had already increased to 75% (40/53) and 60% (32/53) respectively; 67% (14/21) of UC/IBDU patients had extensive disease (E3). 13% (2/16) patients had their first thiopurine exposure, 3% (1/37) their first MTX exposure and 19% (10/54) their first anti-TNF exposure in adult services. 12% (9/74) had major IBD-related surgery in adult services; the pan-treatment refractory IBD rate increased to 14% (10/73). One patient died of metastatic cholangiocarcinoma 3.5 yrs post transition.

Conclusions: PIBD patients have significant disease at transfer to adult services with 25% having required anti-TNF therapy and 81% at least one immunosuppressant. Progression of disease severity continues; 19% of patients required their first anti-TNF agent in adult services and the rate of pan-treatment refractory IBD more than trebled to 14%.

P676
Influence of alexithymia on the clinical course of Inflammatory Bowel Disease (IBD)

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Background: Alexithymia is a personality trait characterized by difficulty to perceive and express emotions. Previous studies have reported a high prevalence of alexithymia in IBD patients, but its influence on the clinical course of the disease is unknown. The aim of this study was to assess the influence of alexithymia on the clinical course of IBD patients.

Methods: A prospective observational cohort study was designed. Crohn's disease (CD) and Ulcerative Colitis (UC) patients older than 18 years of age were included. Alexithymia was evaluated using the Toronto scale (TAS-26). This scale is a self-report instrument consisting of 26 items with a response format of a five-point scale (range 26 to 130). Alexithymia was defined as a total score of > 73 points. In order to assess the clinical course of IBD, all unscheduled or emergency visits and hospitalisations related with IBD were recorded over a 18-month follow-up time. The influence of alexithymia on clinical course was analysed by logistic regression analysis.

Results: 470 patients were included; 219 (46.6%) male, mean age 44 years, range 18 to 85 years, 60.8% with UC and 39.2% with CD. The overall prevalence of alexithymia was 67.4%. Mean emergency or unscheduled visits was 1.08 (SD 1.50, range 0-14) and mean hospitalizations of 0.38 (SD 1.04, range 0-9). Higher alexithymia scores at baseline were not associated with more emergency visits (B=0.06; 95%CI 0.93-1.21; p=0.364) nor more hospitalizations (B=-0.02; 95% CI 0.82-1.18;p=0.838).

Conclusions: Alexithymia is highly prevalent in IBD patients but it has no influence on the number of emergency visits and hospitalizations.

P677
Hormonal contraceptive use is not associated with increased disease activity in IBD women - Results from an online survey

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Background: The effect of hormonal contraception (HC) on disease activity in women with inflammatory bowel disease (IBD) is still unclear. The primary aim of this study was to assess the effect of HC on IBD activity. Secondary aims included (1) the efficacy of oral hormonal contraceptives (OHC) in IBD women in terms of unplanned pregnancies and (2) the occurrence of venous thromboembolism (VTE) in IBD women using HC.

Methods: We conducted an online survey between October 2014 and November 2014 at the patient panel of the Dutch IBD patient association (CCUVN). IBD women between 15 and 45 years of age were eligible. Data on demographics, disease characteristics, contraception use, disease activity and the occurrence of VTE were collected. Past year prednisone use, hospital admittance for IBD, inflammation at endoscopy were used to assess disease activity.

Results: The survey was completed by 194 out of 282 (69% response) women (122 CD (62.9%), 67 UC (34.6%), 5 IBDU (2.6%)). Median age was 32 yrs (IQR: 26-38) and median disease duration 5 yrs (IQR: 2-10). In the past year 142 women (73.2%) used any form of contraceptives (44 (31.0%) barrier contraceptives, 72 (50.7%) OHC and 37 (26.1%) other HC or intrauterine device). Between HC users and non-HC users in the past year, there was no difference in prednisone use (19 (9.8%) vs 33 (17.0%), p=0.32), hospital admittance for IBD flares (13 (6.7%) vs 19 (9.8%), p=0.85) or inflammation seen at endoscopy (24 (12.4%) vs 41 (21.1%), p=0.66) in the past year.

"Table 1: Childless females and males within the SIBDCS who actively tried to conceive."

	CD Females	CD Males	UC/IC Females	UC/IC Males	Total IBD Females	Total IBD Males
Number of patients	39 (52.7)	36 (58.1)	35 (47.3)	26 (41.9)	74	62
Age at diagnosis (median; IQR, range)	21, 18-24 8-39	24; 20-29 4-45	28, 22-31 17-44	27; 23-34 13-51	23, 19-30 8-44	25; 21-31 4-51
Age when trying to conceive (median; IQR, range)	29, 24-34 17-51*	27; 30-41 24-54	34, 31-39 21-45*	35; 31-44 21-64	31, 27-36 17-51	36; 31-42 21-64
Disease duration when trying to conceive (median; IQR, range)	8, 3-11 0-26	10; 7-16 0-28	6, 3-9 0-20	7; 4-13 0-25	6, 3-10 0-26	8; 5-15 0-28
BMI (median; IQR, range)	20.9, 18.6-22.7 15.6-31.1	23.7; 23.1-25.2 18.2-36.2	21.5, 19.6-25.2 18.7-34.5	24.3; 23.1-25.6 21.7-29.3	21.0, 19.3-23.1 15.6-34.5	24.1; 23.1-25.5 18.2-36.2
Current therapy when trying to conceive						
5-ASA	6 (15.4)	5 (13.9)	26 (74.3)	22 (84.6)	32 (32.2)	27 (43.6)
Steroids	15 (35.9)	5 (13.9)	6 (17.1)	7 (26.9)	20 (27.0)	12 (19.4)
Antibiotics	1 (2.6)	1 (2.8)	0 (0.0)	0 (0.0)	1 (1.4)	1 (1.6)
Immunomodulators	14 (35.9)	11 (30.6)	15 (42.9)	9 (34.6)	29 (39.2)	20 (32.3)
Anti-TNF Agents	15 (38.5)	17 (47.2)	4 (11.4)	4 (15.4)	19 (25.7)	21 (33.9)
History of surgery						
Intestinal surgery	9 (23.1)	19 (52.8)	0 (0.0)	0 (0.0)	9 (12.2)	19 (30.7)
Fistula/Abscess surgery	9 (23.1)	11 (30.6)	1 (2.9)	0 (0.0)	10 13 .5)	11 (17.7)

"Table 2. Kaplan-Meier failure estimates. Probability of partners of males with IBD of getting pregnant, according to age < 35 vs. > 35 years"

	CD Females	CD Males	UC/IC Females	UC/IC Males	Total IBD Females	Total IBD Males
Number of patients	39 (52.7)	36 (58.1)	35 (47.3)	26 (41.9)	74	62
Age at diagnosis (median; IQR, range)	21, 18-24 8-39	24; 20-29 4-45	28, 22-31 17-44	27; 23-34 13-51	23, 19-30 8-44	25; 21-31 4-51
Age when trying to conceive (median; IQR, range)	29, 24-34 17-51*	27; 30-41 24-54	34, 31-39 21-45*	35; 31-44 21-64	31, 27-36 17-51	36; 31-42 21-64
Disease duration when trying to conceive (median; IQR, range)	8, 3-11 0-26	10; 7-16 0-28	6, 3-9 0-20	7; 4-13 0-25	6, 3-10 0-26	8; 5-15 0-28
BMI (median; IQR, range)	20.9, 18.6-22.7 15.6-31.1	23.7; 23.1-25.2 18.2-36.2	21.5, 19.6-25.2 18.7-34.5	24.3; 23.1-25.6 21.7-29.3	21.0, 19.3-23.1 15.6-34.5	24.1; 23.1-25.5 18.2-36.2
Current therapy when trying to conceive						
5-ASA	6 (15.4)	5 (13.9)	26 (74.3)	22 (84.6)	32 (32.2)	27 (43.6)
Steroids	15 (35.9)	5 (13.9)	6 (17.1)	7 (26.9)	20 (27.0)	12 (19.4)
Antibiotics	1 (2.6)	1 (2.8)	0 (0.0)	0 (0.0)	1 (1.4)	1 (1.6)
Immunomodulators	14 (35.9)	11 (30.6)	15 (42.9)	9 (34.6)	29 (39.2)	20 (32.3)
Anti-TNF Agents	15 (38.5)	17 (47.2)	4 (11.4)	4 (15.4)	19 (25.7)	21 (33.9)
History of surgery						
Intestinal surgery	9 (23.1)	19 (52.8)	0 (0.0)	0 (0.0)	9 (12.2)	19 (30.7)
Fistula/Abscess surgery	9 (23.1)	11 (30.6)	1 (2.9)	0 (0.0)	10 13 .5)	11 (17.7)

Abdominal complaints during menses less often occurred in IBD women using HC versus non-HC users (53 (27.3%)vs 93 (47.9%), p=0.04). Out of the past year OHC users, 18 (25%) reported use of extra barrier contraceptives in times of active disease. Six women (3.6%) reported an unplanned pregnancy ever despite OHC use. These conceptions did not occur in periods of self-reported active disease. VTE occurred in 9 (4.6%) women of which 3 women had confirmed underlying thrombophilia. VTE without thrombophilia was not significantly associated with ever OHC use (p=1.00). VTE occurred in times of active disease in 4 women (66.7%).

Conclusions: This study shows HC is not associated with increased risk of disease activity over the course of one year. Furthermore, unplanned pregnancies despite OHC use in this study were not associated with IBD disease activity at time of conception. VTE was not associated with ever OHC use in this study. However, to adequately assess the efficacy and safety of HC in IBD women a controlled study will be needed to put these data into perspective.

P678
Childlessness in IBD patients - Analysis of data from the prospective multicentre Swiss IBD Cohort Study

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Background: The impact of inflammatory bowel disease (IBD) and its treatment on fertility and pregnancy is an important clinical consideration in patients of reproductive age. Overall, the rate of infertility in women with IBD has been reported to vary between 7% and 12%. Main objectives were to analyse the rate of childlessness of female and male IBD patients with unfulfilled wish to conceive within the Swiss Inflammatory Bowel Disease Cohort Study (SIBDCS), one of the largest prospective multicentre IBD cohorts.

Methods: We analysed data from the SIBDCS with currently more than 3000 patients with Crohn's disease (CD), ulcerative colitis (UC), or indeterminate colitis (IC), respectively. We included only females with IBD diagnosed at the age <35 years and with age at enrolment <45 years (limitation of childbearing age), with at least two-year follow-up. Also, childless males who actively tried to conceive were analysed by means of descriptive statistics.

Results: As of August 2014, a total of 1412 females were included into the SIBDC (843 CD, 539 UC, 30 IC), with 629 female patients (386 CD, 227 UC, 16 IC) fulfilling inclusion criteria. 266/629 (42%) females had either given birth to at least one child, or were pregnant at last follow-up. There were 363 (58%) females without any children. Of those, 122 childless females have at least once reported to actively have tried to conceive. 74/122 (39 CD; 35 UC/IC) completed at least one follow-up (Table 1). In our cohort, 11.7% of females with IBD (10.1% of CD, 14.4% UC/IC) at childbearing age who were diagnosed with IBD <35 years, tried to conceive without success during follow-up. Among the subgroup of childless females, 20.4% tried to conceive.

Regarding males, 89 patients have at least once mentioned to actively try to conceive. Of those, 62 (36 CD; 26 UC) had available follow-up questionnaires (Table 1). Table 2 shows the Kaplan Meier diagram regarding the probability of the male IBD patient's partner to get pregnant, according to the male patient' s age < 35 vs. >35 years.

Conclusions: In the SIBDCS nearly 12% of females with IBD in childbearing age and diagnosed with IBD < 35 y, tried to conceive without success during follow-up. This data matches with reported data in IBD literature.

P679
Can we trust on patient's infectious history? A prospective study on the agreement between medical history, vaccination record and serology.

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Background: Current therapy for inflammatory bowel disease (IBD) often involves immunomodulators and with these, potential for infection increases. In Portugal there is no study concerning the immune status of IBD patients. The primary aims of this study were to assess the immune status and the agreement between recall of infection, recall of vaccination, vaccination registry and infection serology in IBD patients and to determine the risk of cervical neoplasia in female individuals.

Methods: Prospective study including patients attending the IBD clinic of a tertiary referral hospital. We evaluated the following infections:

hepatitis A virus (HAV), hepatitis B virus (HBV), varicella-zoster virus (VZV), tuberculosis, human papilloma virus (HPV), influenza virus and Streptococcus pneumoniae. Patients were asked to recall past infections and/or vaccination by these agents and to bring the vaccination record in order to assess the agreement with serology. Female patients were screened for HPV infection risk factors and invited for a cervical cancer screening by liquid based cytology (LBC).
Results: 139 patients (68 ulcerative colitis and 71 Crohn´s disease), with 86 female patients, were included and 55.4% were considered immunocompromised. Regarding HAV and HBV infections, 78.4% and 33.1% were immune. For tuberculosis infection, 13% had a positive Mantoux or IGRA result. There was no (p=0.152), poor (kappa=0.18) and no (p=0.184) agreement between recall of disease and serology for HAV, HBV and tuberculosis, respectively. Concerning correlation between recall of vaccination and vaccination registry for HAV, HBV and tuberculosis, we found no (kappa=-0.118), slight (kappa=0.378) and substantial (kappa=0.765) agreement, respectively. The most prevalent risk factor for HPV infection was immunosuppression (51.2%), followed by the use of birth control pill for a period over five years (26.7%). A total of 44 patients underwent LBC: 40 (90.9%) had a normal result; 3 (6.8%) presented atypical squamous cells of undetermined significance and 1 (2.3%) had low-grade squamous intraepithelial lesions. There was no association between abnormal LBC and any risk factor for HPV infection, type or length of IBD. The rates of VZV, Influenza and Pneumococcal vaccinations were 0%, 24.5% and 5.8%.
Conclusions: Assessing immune status by vaccination record and serologic analysis should always be considered in IBD patients due to poor or no agreement between recall of infection or vaccination and serology. Efforts should be conducted to increase the rate of Influenza and Pneumococcal vaccinations. Conclusions about a possible connection between IBD or immunosuppression with abnormal LBC were not possible because of the small sample.

P680
Post-operative clinical recurrence of Crohn's Disease in clinical practice in Spain. Practicrohn, a retrospective study

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Background: Preventive strategies for post-operative Crohn's disease (CD) are not well established. Our aim was to describe the clinical management of CD after ileocolonic surgery and the incidence of clinical recurrence in clinical practice, after a follow-up of up to 5 years.
Methods: PRACTICROHN is a retrospective study on CD patients aged ≥ 18 years-old who underwent ileocolonic or ileorectal resection between January 2007 and December 2010 from 26 Spanish hospitals. Patient's data before and up to 5 years after surgery were collected from clinical records. We excluded patients that were prescribed an anti-TNF for post-operative recurrence prevention. Clinical recurrence was defined as presence of abdominal pain, diarrhea, perianal complication, abdominal mass or symptoms suggestive of active CD. The chi-square test was used to analize the 5-year cumulative incidence of clinical recurrence, Kaplan-Meier method was used to assess time to clinical recurrence and a log-rank test was performed to obtain the statistical significance.
Results: 191 patients were included (mean age 46 ± 13 years, 49% men). Of these, 93 (48.7%) were smokers at CD diagnosis and 69 out of 93 (74.2%) kept on smoking after surgery. Median time from CD diagnosis to surgery was 7.4 years (IQR 25-75: 0.9-11.2). Reasons for surgery were: penetrating complication (27.2%), intestinal stenosis (44.5%), stenosing + penetrating complication(13.6%), refractoriness to medical treatment (4.2%) and others (10.5%). Only 39.7% started primary medical prevention of postoperative recurrence (immunomodulators (IMM) 27.6%, antibiotics 11%), whilst 61.3% received no preventive treatment. The probability of clinical recurrence at 1, 3 and 5 years was 32.5%, 51.3% and 59.2%, respectively. Smoking did not affect the 5-year probability of clinical recurrence. The 5-year cumulative probability of clinical recurrence was lower in those who received IMM as preventive therapy (42.2%) than in those with no preventive therapy (68.0%) p=0.0034. Comparison of survival curves (log rank) showed that preventive treatment with IMM were associated with lower clinical recurrence and a longer time to clinical recurrence (1042 days; from 676 to >1825) vs no treatment (617 days; from 335 to 1006) p= 0.043. Recurrence in those receiving antibiotics was 50.0% (p=NS). During 5-year follow-up, 19 patients (9.9%) needed surgical reintervention with no associated risk factors.
Conclusions: More than half the patients developed clinical recurrence after CD surgery, being lower in those patients with post-operative recurrence prevention with IMM. Although IMM preventive treatment reduced the risk and time to clinical recurrence, the 5-year incidence of clinical recurrence despite IMM was also considerably high.

P681
Incidence of endoscopically and histologically confirmed ileal ulceration in a sequential cohort of patients undergoing screening colonoscopy as part of the UK Bowel Cancer Screening Programme

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Background: The incidence of ileal ulceration in patients presenting for colonoscopy within the UK Bowel Cancer Screening Programme (BCSP) is unknown. Terminal ileal intubation is not a prerequisite of the programme and usually not performed on a systematic basis. Anecdotally we became aware that ileal ulceration was a surprisingly common finding. We therefore decided to prospectively evaluate the incidence of ileal ulceration in sequential patients presenting for colonoscopy through the BCSP.
Methods: All sequential patients being endoscoped by a single BCSP colonoscopist over a 28 month period from July 2012 were prospectively audited. All patients had been referred for colonoscopy on account of positive faecal occult blood samples performed as part of the UK BCSP. Terminal ileal intubation was planned at the outset in all cases. If ileal ulceration was seen it was photographed and biopsied. Current symptoms, past medical and drug history was recorded in all cases. Histology was reported by BCSP pathologists, with all cases of ileal ulceration subsequently reviewed by a specialist gastrointestinal pathologist.
Results: 354 sequential colonoscopies were undertaken by a single BCSP colonoscopist (JNG) during the study period. Terminal ileal intubation was achieved in 327/354 (92.4%) of cases. Endoscopic evidence of terminal ileal ulceration was found in 28/327 (8.6%) of

cases where the ileum was intubated. Ulceration was confirmed on biopsy in 24/327 (7.3%) cases. 2/24 cases had previously diagnosed Crohn's disease (1 on active follow-up, the other historical) and a further 5/24 patients were taking regular NSAIDS. The remaining 17/327 (5.2%) with both endoscopic and histological evidence of terminal ileal ulceration had no known risk factors.

Conclusions: In this study endoscopically and histologically confirmed ileal ulceration was a common finding occurring in 7.3% of cases. This is the first study to document these findings prospectively in a sequential cohort of BCSP patients where intubation of the terminal ileum was attempted in a systematic manner. The incidence is dramatically higher than that previously reported in non-BCSP cohorts. Some cases can be attributed to drug use with the remainder appearing likely to be either physiological or potentially represent Crohn's disease. The clinical relevance of these findings is currently unknown though it is pertinent that many patients in this cohort either had symptoms or had been previously been investigated for IBS or a change in bowel habit.

P682
Elderly onset inflammatory bowel disease is a risk factor for gastric cancer development

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Background: In inflammatory bowel diseases (IBD), both chronic inflammation and medication-induced immunosuppression increase the risk of (extra-)intestinal malignancy development. An increased risk for gastric cancer (GC) was previously suggested, particularly for patients with Crohn's disease (CD).

At present it is unclear whether chronic inflammation and/or impaired immunosurveillance play a role in the GC development in IBD. Furthermore, it is unknown whether the clinical course of GC in IBD is different from the general population.

The aim of this study is to compare the clinical course of GC in IBD with the general GC population and to explore potential risk factors for the development of GC in IBD patients.

Methods: From the Dutch Pathology Registry we identified all patients with IBD and GC in The Netherlands between January 2004 and December 2008. Only adenocarcinomas were included. To identify risk factors for GC in IBD, we performed a nested case-control study with controls from the IBD South Limburg Cohort (IBDSL), a population-based IBD cohort. Data about GC incidence and outcomes in the general population were obtained from the regional Eindhoven Cancer Registry (ECR).

For relative risk (RR) determination two strategies were applied to estimate the Dutch IBD population: first a national report of the Dutch National Institute for Public Health and Environment based on general practitioner registrations and secondly epidemiological data from the European Crohn's and Colitis Organisation.

For statistical analyses a Chi-square test for categorical data was used. Variables with a p value of <.1 in univariate analyses were included in a multivariate logistic regression analysis with backward elimination to determine risk factors.

Results: We identified 59 patients with confirmed diagnoses of IBD and GC. We found that IBD patients with GC were significantly older at IBD diagnosis than IBD controls (mean age 57.9 year versus 43.1; $p < 0.01$). Ulcerative colitis (UC) was more frequent in the GC group versus IBD controls (69.5 % versus 51.4 %; $p < 0.01$).

In the ECR, 1339 non-IBD patients with GC were identified. No differences in age at diagnosis, gender, tumor location, tumor differentiation and survival were observed between the IBD patients and the general population.

The Dutch IBD population was estimated between 57,100 and 83,148 patients, resulting in a RR for gastric cancer development for IBD of 1.3-1.8 (UC 1.5-2.5; CD 0.6-1.2).

Conclusions: Elderly onset IBD seems a risk factor for development of GC in IBD patients. The clinical course of GC was not different between patients with and without IBD. The increased RR to develop GC in IBD can be mainly attributed to the increased RR in UC patients.

P683
C.difficile colonisation or infection does not appear to increase the risk of a diagnosis of IBD in the subsequent 2 years

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Background: Epidemiological studies have shown that gastroenteritis[1] and infection with Campylobacter or Salmonella species increase the chance of subsequent diagnosis of IBD[2]. About 1% patients with Campylobacter/Salmonella have a later diagnosis of IBD, 37% within a 1 year; the risk is higher if the infection causes admission[2]. To assess whether C.difficile colonisation (CDC) or infection (CDI) confer a risk for later IBD, we have examined all cases of CDC and CDI in non-IBD patients at our hospital during the year ending April 2013.

Methods: The microbiology database (Barts Health NHS Trust) was retrospectively searched for all stool samples testing positive for CDC and/or CDI during the year to April 2013. CDC was defined as the presence of the C.difficile-specific enzyme (glutamate dehydrogenase) and CDI as the presence of toxin B. Follow up data to see if these patients went on to be diagnosed with IBD from date of sample to end October 2014 was gathered from electronic patient records.

Results: 2486 stool samples were analysed for CDC/CDI. 11% (271) samples from patients with known IBD were excluded. Overall, 12% (273/2215) samples showed CDC and 3% (71/2215) CDI. Median (range) ages were 61.2 (1.1- 98.3) years for CDC and 60.7 (1.1-90.8) years for CDI (p=ns). 15% (265/2006) inpatient samples and 7% (8/109) of outpatient samples were CDC-positive (p=ns) with inpatient and outpatient CDI rates being 3% (67/2006) and 4% (4/109) respectively (p=ns). None of the CDC or CDI patients went on to be diagnosed with IBD within the follow up period of 2 (1.5-2.5) years (median (range)).

Conclusions: In our cohort of 273 infected patients, CDC/CDI did not result in a diagnosis of IBD in any patients after a median of 2 years follow up. Any increased risk of IBD after CDC or CDI is likely to be small.

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P684
Patient clinical characteristics at diagnosis of Ulcerative Colitis

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Background: A nationwide study on the clinical features and course of ulcerative colitis (UC) in Spain is lacking. We aim to describe the socio-demographic and clinical characteristics of the UC disease present at diagnosis in the patients attending a gastroenterology unit in Spain.

Methods: A retrospective, multicenter, cross-sectional study was conducted (EPICURE study). At 58 selected gastroenterology units, adult patients with confirmed UC at any stage or extent of disease were randomly invited to participate. Data concerning the UC at diagnosis were collected during a single routine follow-up visit. Descriptive univariate analyses of data were performed.

Results: A total of 568 UC patients were recruited. A 55% of patients were male. Median age at diagnosis was 36 years [Q1, Q3: 28, 47]; Median age for female patients (33 years; [Q1, Q3: 25, 44]) was lower than for males (40 years [Q1, Q3: 30, 50]) (p<0.0001). Before being diagnosed with UC patients had been presenting symptoms for a median of 3 months [Q1, Q3: 1, 6].

Data on extension of UC at diagnosis was available in 93.9% of patients being left sided colitis the most common (38.2%; n=217) followed by extensive UC (32.4%; n=184) and proctitis (23.1%; n=131). Median values for Mayo Total and Partial scores were 7.0 [Q1, Q3: 6.0, 9.0] and 6.0 [Q1, Q3: 4.5, 9.0], respectively. Type of UC extent of disease at diagnosis was significantly associated with severity of disease as per Mayo Total (6 for proctitis [n=85], 7 for left sided [n=160] and 8 for extensive UC [n=141]; p<0.0001) and Partial (5 for proctitis [n=24], 6 for left sided [n=20] and 6 for extensive UC [n=15]; p=0.0277) median scores. According to the Mayo score, 30.8% (n=175), 54.9% (n=312) and 12.7% (n=72) of patients presented mild, moderate or severe UC disease, respectively. Regarding smoking habits, 288 (50.7%), 129 (22.7%) and 149 (26.2%) patients were never, current and former smokers, respectively.

The most frequent diagnostic imaging procedures were colonoscopy or rectosigmoidoscopy in 448 (78.9%) and 134 (23.6%) patients, respectively, and endoscopy in 293 (51.6%) patients. MRI was done in 1.4% of patients. Histological exam was available in 499 (87.8%) patients with findings suggestive of UC in 88.8% (n=443). Tuberculosis screening was performed at diagnosis by Chest X-ray in 130 (22.9%), Mantoux test in 67 (11.8%) and Booster test in 33 (5.8%) patients.

Conclusions: Overall, clinical characteristics at diagnosis of UC patients in our cohort are consistent with most studies in Europe. A male preponderance was seen. Most patients were former/never smokers at diagnosis. The extent of disease was significantly associated with Mayo disease severity at diagnosis.

P685
Characteristics of non-responders to self-reported questionnaires in a large Inflammatory Bowel Disease cohort study

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Background: A major threat to the validity of longitudinal cohort studies is non-response to follow-up, which can lead to erroneous conclusions. The profile of chronic diseases non-respondents is therefore important, but rarely assessed. The objective of this study was to evaluate the number and profile of non-respondents to self-reported questionnaires among patients included in the Swiss Inflammatory Bowel Disease Cohort.

Methods: In this study, we included all patients enrolled between 1st November 2006 and 30th June 2011. Patients who returned their questionnaires and those who did not were compared according to age, sex, socio-demographic, clinical and psychosocial characteristics. Odds ratio for non-response to initial and one-year follow-up were calculated using logistic regression. Missing values of socio-demographic and psychosocial variables were imputed using multivariate chained equations before assessing non-response to follow-up questionnaires.

Results: Among 1945 IBD patients who received the inclusion questionnaire, 340 (17.2%) did not respond (18.8% Crohn's disease [CD], 15.6% ulcerative colitis [UC]). In CD patients, complicated disease (penetrating disease behaviour [OR=2.95; p< 0.001], perianal involvement [OR=1.74; p=0.003]) was the main risk factor of non-response, whereas longer disease duration (>16 years) prevented UC and CD patients from being non-responders. Out of 1605 patients who received the first follow-up patient questionnaire, 323 (24.0%) did not respond (26.0% CD, 21.4% UC). Main risk factors of non-response to the follow-up questionnaire among CD patients were complicated disease (penetrating [OR=3.72; p<0.001], stricturing [OR=2.43; p<0.001], perianal involvement [OR=2.72; p<0.001]), mild or moderate depression (OR=2.27; p<0.001 resp. OR=1.83; p=0.048), or recent disease activity (OR=1.58; p=0.015). Being aged more than 30 (OR=0.45; p<0.001), taking immunomodulator (OR=0.64; p=0.007) or biological therapy (OR=0.47; p<0.001), having already had surgery and being higher educated prevented CD patients from being non-responders to the follow-up questionnaire. History of resection surgery (OR=0.35; p=0.019), taking immunomodulator therapy (OR=0.44; p<0.001), being married (OR=0.58; p=0.005) or having a positive social support (OR=0.97; p=0.040) were preventive factors for non-response to follow-up among UC patients.

Conclusions: Our study showed that characteristics of non-responders highly differed between UC and CD. The risk of non-response to repetitive solicitations (longitudinal versus transversal study) seemed to decrease with age. Assessing non-respondents' characteristics is important to document potential bias in longitudinal studies.

P686
Clostridium difficile infection in inflammatory bowel disease and non-inflammatory bowel disease patients

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Background: During the last decades the incidence and severity of Clostridium difficile infection (CDI) has increased throughout the world both in general population and in other subgroups like inflammatory bowel disease (IBD) patients. The aim of this study was to investigate the differences between CDI in IBD and non-IBD patients.
Methods: We conducted a case-control study including 78 patients diagnosed with CDI hospitalized at the Institute of Gastroenterology and Hepatology in Iasi, Romania, between January 2012-July 2014. Demographic data and clinical characteristics were reviewed for all patients.
Results: A total of 78 patients were diagnosed with CDI, of whom 26 patients (33.33%) had concomitant IBD. The non-IBD patients were older than the IBD patients (60.92 ± 17.48 vs 50.96 ± 18.16, p=0.022) and co-morbidities were more common in the non-IBD study group (OR=2.22, CI=1.33-3.69; p<0.0001). There was no differences between the two groups regarding previous antibiotic treatment. The use of proton pump inhibitors was more frequent in the IBD patients than in the non-IBD subjects (OR=6.09, CI=2.31-16.04; p<0.0001). The duration of hospital stay was similar in both study groups.
Conclusions: Patients with IBD were significantly younger and with less co-morbidities than the non-IBD patients. IBD itself may be an independent risk factor for CDI in IBD patients.

P687
Work disability in IBD: prevalence, severity and predictive factors.

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Background: Patients with inflammatory bowel disease (IBD) may develop work disability. However, data on disability's true prevalence are scarce. The aim of the present study was to evaluate the prevalence and severity of disability and its predicting factors in a well-characterized community-based IBD population.
Methods: All patients included in the community-based IBD register of the Complejo Asistencial de Burgos were contacted. After full information, the patients gave signed informed consent and fulfilled a set of standardized questionnaires including demographic data, data on the characteristics and activity of disease and whether they have a recognized degree of disability and/or a disability grant. In addition, the patients fulfilled the IBDQ-9 and EuroQol questionnaires for quality of life. Statistical analysis was performed using SPSS 21 (IBM Corporation, Chicago, IL).
Results: Two hundred ninety-two patients -151 Crohn's diseases (CD), 141 ulcerative colitis (UC), 137 female, mean age: 45 ± 11 years) were included in the study. Mean time from the diagnosis of IBD was 10.6 ± 11 years. Most patients were in remission or had moderate symptoms at inclusion. Harvey-Bradshaw and modified Mayo score were 4.1 and 2.2 for CD and UC respectively. Fifty percent were on immunosuppressant drugs (mainly thiopurines) and 15% received anti-TNF. Twelve patients (6.1%) had a work- disability grant; eight of them (2.7%) were considered to be unable to perform any kind of work. In all but two the main cause of the disability was exclusively the IBD. In addition, the Spanish National Health Service acknowledged a certain degree of disability to 93 (32%) patients. Over a 100% scale, 73 (26%) had a moderate disability degree (mayor or equal 33%-<55%) and 16 (6%) a severe disability (mayor or equal 55%). Univariate analysis showed that age and time of evolution of the disease, having CD, perianal disease, incontinence, the use of an anti-TNF drug, having one o more surgeries or intestinal resections and having an ostomy were the major predictors of having any degree of disability. For severe disease requiring a disability grant, major predictors were having extensive disease, incontinence, use of a biological drug, previous surgery or resection and ostomy.
Conclusions: Work disability is frequent in IBD although only a minority develops severe disability requiring a pension. Disability increases with the time of evolution of the disease. Major sources of disability are persistent activity of the disease and surgical long-term complications.

P688
The SOLE Survey: Disease related concerns of a large cohort of Italian patients with active Crohn's Disease

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	Baseline	Last visit	p
Financial difficulties	52,1	45,5	<0,001
Pain or suffering	64,9	57,5	<0,001
Achieve full potential	65,9	56,6	<0,001
Loss of bowel control	60,6	52,1	<0,001
Being a burden on others	60,4	54,5	<0,001
Feeling out of control	43,3	39,7	0,010
Feeling dirty	29,1	34,5	<0,001
Unpleasant odors	46,0	41,7	0,020
Energy level	63,1	54,7	<0,001
Body feelings	46,7	39,7	<0,001
Intimacy	39,3	35,2	0,013
Access to quality care	51,9	47,2	0,006
Uncertain nature of disease	60,0	56,2	0,015
Effects of medication	59,2	52,1	<0,001

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Background: A large Survey on Quality Of Life in Crohn's PatiEnts (SOLE) was conducted in 38 Italian IBD centres on adults with active moderate-to-severe Crohn's disease (Harvey-Bradshaw Index [HBI] ≥ 8), with the aim to assess health-related quality of life (QoL) over a 12-month period. Namely, patients' perception of their experience and discomfort, as a number of social, cultural and psychological factors, was gathered. Here we report the final results on patients' disease-related worries and its correlation with demographic and clinical variables.

Methods: Disease-related worries were measured at baseline and at 3, 6, and 12 months by the Rating Form of Inflammatory Bowel Disease Patient Concerns (RFIPC). Results were correlated with demographic and clinical variables with multilevel mixed effect linear regression models.

Results: 552 patients with active CD (51% males, mean age 41.3 ± 13 yr, range 18-84) were recruited.

Mean HBI was 10.3 (SD 3.2) at baseline, dropped to 5.6 (3.2) at the first follow-up visit and to 4.4 (3.2) at the last visit. Accordingly, all associated symptoms (nausea, vomit, weight loss, anemia, asthenia, fever) showed at least a 50% decrease at last visit.

Mean RFIPC was 47.5 (21.9; range 0-100) at baseline and progressively declined to 44.5 (21.8) at 12 months; the decrease was statistically significant both at the 6 and at the 12 months visit (p=0.026 and p<0.01). Higher worries were having an ostomy bag and undergoing surgery (68.6 and 67.9 at baseline, with no significant reduction at 12 months). Significant changes in RFIPC scores from baseline are shown in table 1. Variables significantly associated with a higher global RFIPC score based on a linear regression model included disease activity (p<0.001), age older than 41y.o. (p=0.0016), and being a smoker (p<0.001). Patient's with high treatment adherence (defined as Medication Adherence Rating Score [MARS] ***25) had lower mean RFIPC scores at all study visits compared to those with low adherence (<0.001).

Conclusions: Our survey underlines that major worries among CD patients are having an ostomy bag and undergoing surgery. Moreover, major worries are significantly associated with the degree of disease activity and low adherence to treatment.

P689
Inflammatory Bowel Disease and psychological status: Determinants and social consequences

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Background: High levels of anxiety are reported in inflammatory bowel disease (IBD) and causes could be multiple.

The aim of our study is to evaluated the presence of anxiety and the role of therapy in IBD patients.

Methods: From 1/6/2014 to 31/8/2014, 220 consecutive patients (73 affected by Ulcerative colitis (UC) and 147 by Crohn's disease (MC) with mean age of 47 years (range 16-78), in therapy with Anti TNF alfa and immunosuppressor were studied with Visual Analouge Scale (VAS) and State-Trait Anxiety Inventory (STAI) questionnaire. Anxiety was defined when State Anxiety > Trait Anxiety.

Activity inflammatory index (HBI, MTWSI), quality of life (S-IBDQ), work productivity (WPAI) and adherence to therapy (Morisky scale) were valueted to identify the possible determinants for anxiety. 40 peers patients in therapy with mesalazine (24 with CU; 16 with MC) were enrolled in the same period, as controll group.

Results: The 32,4% of patients refered anxiety. In the multivariate analysis the determinants of anxiety for STAI were: single state versus married (50% vs 36%, p= 0.003, OR= 2.21, CI 1.31-3.72) and CU vs MC (45,9% vs 31,7%, p=0.03, OR 1.83, CI 1.08-3.11). The Analouge Scale was correlated only with disease activity (p=0.0005, beta= 1.47) either for UC and MC. Anxiety was correlated directly with a lower WPAI (p=0.0001) and lower S-IBDQ (Correlation coefficient -0,62, p<0.0001), while the adherence wasn't associated with anxiety. (p=0.90). No differences emerged between patients in Anti TNFalfa therapy versus mesalazine either for VAS (p=0.59) and for STAI (p=0.84).

Conclusions: Anxiety is frequent in IBD patients, particurlarly in single, in active disease e in patients with UC. The anxiety isn't affected by the type of therapy, instead quality of life and work productivity are negatively influenced by the psychological status.

P690
Current views and concerns of European UC patients based on an online survey

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Background: Ulcerative colitis (UC) affects many aspects of a patient's life. UC substantially impairs patients' health-related quality of life which includes both the physical symptoms of UC and possibly also major psychosocial and emotional consequences (1). The consequences are dependent on the individual coping capabilities and personality. Detailed data has been collected in the past. Like in other areas insights, attitudes and concerns are subject to dynamic, continuous change. As an individual long-term prognosis is not possible, the population derived data (in conjunction with socio-demographic variables like gender, level of education, socioeconomic status, and age) are guiding the overall treatment and communication strategy of healthcare providers (HCP).

Methods: Data Source: The study was conducted among a sample of 372 UC patients (204 in United Kingdom, 77 in Spain, 21 in Denmark, 34 in Finland, 28 in Sweden and 8 in Norway) from a qualified panel.

Period of data collection: The data collection took place from the 11th of December 2013 to the 10th of January 2014.

Implementation: The individuals from the sample received a link, via email, to an online questionnaire on a secure platform. The questionnaire asked about their UC history, their attitudes and behaviors towards UC and its management and their level of adherence to treatment. Socio-demographic characteristics (gender, age, geographic location) and medical history were also collected.

Results: Out of 20 pre-defined descriptors, participants ranked 5 to describe their feelings. The patients ranked as their No. 1 feeling: Uncomfortable (18%); Fed up (13%); Bothered (8%); Powerless (8%); Depressed (7%).

The 5 most common feelings were: Uncomfortable (43%); Fed up (13%); Stressed (33%); Exhausted (28%); Frustrated (28%).

The 3 least common feelings were: Defeated (9%); Despaired (8%); Rejected (4%).

A majority of the UC patients fear the following: UC leads to serious complications (74%), is painful (67%) and is recurrent (66%).

More than a quarter of the patients are convinced that neither relatives/friends (31%) nor their physician (29%) take their disease seriously. 8% have low confidence in the healthcare professionals treating them and 10% are unsatisfied with their medical care.

Conclusions: Despite the clear burden of disease most patients cope quite well. There is a certain lack of trust in the diagnostic and treatment capabilities of their healthcare providers, expressed by almost 10% of the patients. The likely reasons are frustration about the course of disease and the futility of previous medication. Patients' belief "that their disease is not taken seriously" by physicians needs further research. Some concerns and believes should be addressed by an education program.

References:

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P691
Budget impact analysis of introducing biosimilar infliximab for the treatment of gastro intestinal disorders in five European countries

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Background: Biosimilar infliximab has been approved by EMA for the management of inflammatory autoimmune disorders, including Crohn's disease and ulcerative colitis (UC), based on quality, safety and efficacy profiles comparable to those of infliximab. The aim of this study was to evaluate the one-year budget impact of introducing biosimilar infliximab in the management of Crohn's disease and UC from the healthcare system perspective.
Methods: An Excel-based budget impact model with a one-year time horizon was developed. The numbers of patients eligible for infliximab were calculated based on disease incidence and prevalence rates in Germany, Italy, Belgium, the Netherlands and the UK. The price of biosimilar infliximab was not yet known; therefore three discount scenarios versus infliximab (10%, 20%, and 30%) were applied. For patients currently treated with infliximab (switch population), the biosimilar infliximab market share was assumed to be 25% in all scenarios, whereas it was assumed to be 50% in all scenarios for newly diagnosed patients. We calculated the numbers of additional patients that could potentially be treated with biosimilar infliximab, if the projected savings due to the introduction of biosimilar infliximab were used: Savings made in the naïve and switch patient groups were to be used to treat additional treatment-naïve and switch patients, respectively.
Results: For treatment-naïve and switch patients combined, the projected net budget savings over one year due to the introduction of biosimilar infliximab ranged from € 0.7 million (Italy) to € 17.9 million (Germany) for Crohn's disease, and from € 0.3 million (UK) to € 6.3 million (Germany) for UC, depending on the discount rate applied. For treatment-naïve patients, the corresponding projected savings range from € 48,000 (Italy) to € 1.8 million (Germany) for Crohn's disease and from € 42,000 (UK) to € 1.1 million (Netherlands) for UC. For the switch population, the corresponding projected savings range from € 0.7 million (Italy) to € 16.1 million (Germany) for Crohn's disease and from € 0.3 million (UK) to € 5.3 million (Germany) for UC. If these projected savings were used to treat additional patients with biosimilar infliximab, 64 (Italy) to 1,358 (Germany) additional patients with Crohn's disease and 30 (UK) to 472 (Germany) additional patients with UC could potentially be treated with biosimilar infliximab.
Conclusions: The introduction of biosimilar infliximab as a treatment option for patients with Crohn's disease or UC could achieve substantial cost savings for healthcare systems. These savings could be used to treat additional patients. The net budget impact was highly sensitive to market uptake rates and the price discount applied.

P692
Therapeutic management of Ulcerative Colitis at gastroenterology units in Spain

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Background: Management of ulcerative colitis (UC) disease depends on the severity of disease and other factors. The therapeutic approaches for UC may vary from country to country or even from site to site. We aim to describe the therapeutic management of UC at Gastroenterology Units (GE) in Spain.
Methods: Adult patients with confirmed UC were randomly included in the retrospective, multicentre, cross-sectional EPICURE study. Data concerning current therapeutic management and at UC diagnosis were collected during a single routine follow-up visit. A descriptive analysis of data was done.
Results: A total of 568 UC patients (55% males; median age: 47 years) were recruited in 58 GE units. At study start, 82.8% (470/568) of patients were receiving 5-ASA, 29.9% immunomodulators (IM; azathioprine or mercaptopurine), 13.4% were on biologicals (in combination with IM in 40 of 76 patients) and 7.8% were receiving steroids. Nevertheless, 5.8% of patients were not receiving treatment.
Treatment of patients in remission at study start (n=497) was 5-ASAs (82.9%), IM (27.8%), biologicals (12.5%) and steroids (4.0%); 6.4% of patients in remission were not receiving treatment. Most patients with active UC at study were on 5 ASAs for mild (87.2%), moderate (76.9%) or severe (60.0%) disease. Some patients with mild disease were on IM (43.6%), steroids (20.5%) or biologicals (20.5%). About half percent of patients with moderate disease were on steroids (50.0%) or IM (53.8%). A large proportion of patients with severe disease were on steroids (60.0%) or biologicals (40.0%). A median of 0 (Q1, Q3: 0, 6), 3 (Q1, Q3: 1, 7) and 7 (Q1, Q3: 4, 13) years elapsed from UC diagnosis until starting 5-ASA, IM, and biological therapy, respectively. In case of a relapse, mesalamine was frequently used for mild or moderate flare and steroids for severe flare.
Around 20% (n=133) of patients reported to have some UC treatment related complaint being digestive intolerance (27.4%), leucopenia (17.7%), opportunistic infections (14.2%), bone marrow aplasia (8.9%), hepatotoxicity (7.8%) and pancreatitis (5.3%) the most frequent.
Conclusions: Most UC diagnosed patients are treated with 5ASAs. IM were commonly (~ 50%) used in mild or moderate disease, steroids in moderate or severe disease and biologicals in severe disease. Mesalamine is commonly used for mild or moderate flares and steroids for severe ones.

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Poster presentations

Genetics

P693
Thiopurine-induced leucopenia and hair loss were inevitable in Japanese IBD patients homozygous for NUDT15 R139C : a case series

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Background: Azathioprine (AZA) and its close analog 6-mercaptopurine (6-MP) are thiopurines widely used in the treatment of patients with inflammatory bowel diseases (IBD). Almost 10% of patients with IBD develop side effects during thiopurine treatment. The most potentially serious side effect is leucopenia. In a recent report, NUDT15 R139C was strongly associated with thiopurine-induced leucopenia in Koreans. However, there have been no reports that investigated the association between side effects including leucopenia and R139C in Japanese. Here we investigated the side effects of thiopurine-treated Japanese IBD patients who were homozygous for NUDT15 R139C.
Methods: A total of 300 Japanese IBD patients at Tohoku University Hospital who had histories of thiopurine treatment were examined. Written informed consent was obtained from all patients. NUDT15 R139C genotyping was performed using TaqMan assay. We investigated leucopenia and severe hair loss as serious adverse effects of thiopurine treatment from medical records. Leucopenia was graded by the common toxicity criteria, and severe hair loss was defined as objective hair loss, patients (especially women) may need for wearing wigs.
Results: Five patients (four male, one female), aged 22-47 years, were homozygous for R139C. Four patients required thiopurine treatment due to Crohn's disease and the remaining patient due to IBD unclassified. The average dose of AZA was 0.93mg/kg/day (0.36-2.0). Three patients developed grade 4 leucopenia (WBC count of <1000 cells/mm3) and the remaining developed grade 3 leucopenia (WBC count of <2000 cells/mm3) within 8 weeks of commencing thiopurine therapy. Additionally, all of these patients developed severe hair loss. Although they recovered from the leucopenia and hair loss, four of five patients were treated with granulocyte-colony stimulating factor.
Conclusions: It was remarkable that all the Japanese patients who were homozygous for R139C developed severe leucopenia and hair loss within 8 week. The genotype frequency of R139C homozygous is approximately 1 % in Japanese. It is not frequent but not ignorable, considering the severity of leucopenia and the cosmetic problem of hair loss. Based on our case series, we should perform NUDT15 genotyping before starting thiopurine treatment and avoid thiopurine treatment in patients homozygous for NUDT15 R139C.

P694
A functional variant of SLC26A3 in association with Ulcerative Colitis down regulates SLC26A3 expression

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Background: Our recent genome-wide association study has identified that rs2108225, located at 9 kb upstream of SLC26A3 gene, is associated with the susceptibility to ulcerative colitis (UC) in a Japanese population. The present study aimed to identify a functional variant in this locus.
Methods: We first carried out a re-sequencing of this locus using 94 UC cases to determine other misidentified causal variants. After fine-mapping, we investigated possible association of the identified single nucleotide polymorphisms (SNPs) and UC by single-marker and haplotype analyses using 752 UC cases and 2068 controls. Allelic difference in binding affinity to nuclear proteins of each SNP was evaluated by electrophoretic mobility shift assay (EMSA) and luciferase reporter assay. We also performed a chromatin immunoprecipitation (ChIP) assay to analyze the difference in binding affinity to the specific transcription factor.
Results: We identified 24 newly identified SNPs by re-sequencing and genotyped a total of 99 SNPs in this locus. The strongest signal was observed at rs6466189 ($P = 7.51 \times 10\text{-}6$), which was absolutely linked with rs2108225 and other seven SNPs ($r2>0.95$, respectively), in single-marker analysis. Haplotype analysis failed to identify any haplotype showing stronger association with UC than the nine SNPs. EMSA and reporter assay showed different binding affinity to nuclear proteins in rs7785790, causing the difference in transcriptional activity. In ChIP assay, such a difference in transcription relative to rs7785790 was caused by the negative transcription factor YY1, which suppressed the transcriptional activity by binding to the susceptible A allele.
Conclusions: The present study suggests that the functional variant rs7785790 affects the transcription of SLC26A3 by altering the binding affinity to YY1. Lower expression of SLC26A3 in the colonic mucosa might be associated with the susceptibility to UC.

P695
A mutation in CTLA4 associated with early-onset Crohn's disease and autoimmunity

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Background: Host genetics regulate the susceptibility to inflammatory bowel disease (IBD). While the genetic basis of IBD is incompletely understood, rare Mendelian forms of IBD have been identified and provide critical insight into disease pathogenesis.
Methods: Exome sequencing and functional studies were applied to delineate the pathogenesis of disease in a family with early-onset Crohn's disease (CD) and autoimmunity.
Results: We describe two half-siblings with severe, early-onset CD manifesting at the age of 7 and 13 years, who exhibited a complex immune-mediated syndrome consisting of intestinal inflammation, type I diabetes, demyelinating encephalopathy, fibrosing lung disease, and hematologic alterations. Exome sequencing of the two half-siblings, their mother and their fathers revealed a mutation shared by the siblings and the mother in the gene encoding cytotoxic T-lymphocyte associated protein 4 (CTLA-4), a co-inhibitory protein expressed by T cells, whose deficiency in mice and antibody-mediated blockade in humans is associated with intestinal inflammation and autoimmunity. CTL-4 Y60C affected an evolutionarily conserved residue in the immunoglobulin domain of CTLA-4, which was associated with reduced CTLA-4 dimerization, impaired cell surface expression, and abrogated binding of one of its ligands, the co-stimulatory protein CD80. Phenotypic and functional analyses of peripheral blood mononuclear cells of the affected son demonstrated an expanded CD4+ memory T cell population as well as increased T cell proliferation *in vitro*. The mother of the affected half-siblings shared the CTLA4 mutation and exhibited an expansion of CD4+ memory T cells but was asymptomatic. In studies to identify potential genetic modifiers explaining incomplete disease penetrance, exome sequencing revealed homozygosity of the mother for a common *IL10* variant associated with increased IL-10 secretion (allele G of marker rs3024496), while both affected children were heterozygous for this variant.
Conclusions: Together, these results demonstrate that mutations in *CTLA4* can provide the basis for Mendelian forms of early-onset CD. Incomplete penetrance of intestinal inflammation and autoimmunity in carriers of this *CTLA4* mutation suggests the presence of additional genetic and/or environmental modifiers.

P696
HLA-DRB1 is involved in the development of antibodies to infliximab in Inflammatory Bowel Disease

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Background: Loss of response is one of the biggest obstacles of maintenance treatment with infliximab (IFX) in patients with inflammatory bowel diseases (IBD). One of the factors driving loss of response, is the formation of antibodies to infliximab (ATI). Little is known about host factors that determine immune responses to IFX but genetic factors may play a crucial role.
Methods: We hypothesized that the formation of ATI is associated with specific HLA class II alleles. We retrospectively identified 76 IBD patients (44 CD, 32 UC) who developed ATI (=cases) during maintenance therapy and matched them with 116 IBD controls (64 CD, 52 UC). Controls required at least two years of maintenance therapy with at least six IFX trough level (TL) measurements and never detectable ATI. ATI and TL were measured with an in-house-developed and clinically validated ELISA. HLA-DRB1 allele groups were typed using PCR with sequence specific primers (Prometheus Laboratories Inc.). Patient and therapy factors and the number of allele carriers for the different DRB1 alleles were compared between cases and controls. Stepwise logistic regression was performed to identify independent predictors of ATI formation.
Results: At IFX start, a loading dose (at weeks 0-2-6) and a higher albumin level were protective for ATI formation ($P<0.05$, Chi^2 and Mann Whitney test). When considering the total number of DRB1 alleles, we found that 13% of the alleles in cases were DRB1*03 positive compared to 4% in the control group (P=0.02 (adjusted for multiple testing with FDR); OR=3.7, 95% CI 1.6-8.7). This association was independent of disease type, use of a loading dose or concomitant immunomodulator use ($P<0.01$; Cochran Mantel Haenszel). In a multiple logistic regression model, the presence of DRB1*03, absence of a loading dose or IFX monotherapy were independent significant predictors of ATI formation with OR (95%CI) of 6.7 (2.3-19.5), 2.9 (1.4-6.3) and 2.02 (1.0-4.2) respectively.
Conclusions: We demonstrate that ATI formation is influenced by the HLA-DRB1 locus in patients with IBD. This locus has already been associated with formation of antibodies to interferon beta therapy in multiple sclerosis and the DRB1*03 allele with formation of anti-Ro/La antibodies in lupus. Our results therefore further implicate a causal role for this allele group in immunogenicity. We also demonstrated that low serum albumin and absence of a loading dose are involved in ATI formation. Low albumin has previously been linked to ATI formation and might be a surrogate marker for disease burden and an aggravated immune response. The absence of a loading dose has not been previously implicated in ATI formation. Although this loading dose is now applied widely, we feel our findings are clinically important.

P697
Human-leukocyte antigen type is associated with duration on infliximab therapy in patients with antibodies to infliximab

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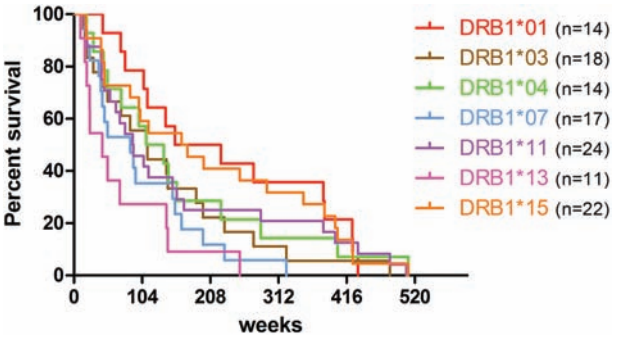

"Figure 1: Survival analysis for the different DRB1 alleles (only those with a frequency > 5%, heterozygous allele carriers were counted twice, homozygous only once) and total time on IFX"

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Background: The contribution of antibodies to infliximab (ATI) to loss of response (LOR) in patients with IBD is well established. It was also shown that ATI may be transient and that infliximab (IFX) discontinuation is not always necessary in this occasion. The variables that influence discontinuation of IFX in patients who have developed ATI are unknown. The HLA system, responsible for processing antigens, might play an important role.

Methods: We hypothesized that HLA class II alleles influence the duration on IFX therapy in patients who develop ATI. We retrospectively identified 74 IBD (42 CD, 32 UC) patients who developed ATI during maintenance IFX. Of these, 61 (82%) discontinued IFX therapy because of LOR or side effects and 13 (18%) were still receiving IFX at the end of follow-up. All patients were anti-TNF naïve before start of IFX. A total of 1889 serial serum samples were measured for ATI with an improved bridging ELISA using monoclonal antibody MA-IFX10F9 as calibrator. For each patient, the highest ATI concentration measured, was used to create ATI quartiles. HLA-DRB1 was genotyped with sequence specific primers (Prometheus Laboratories Inc.). Patient and therapy variables (e.g. presence of IFX dose optimization, immunomodulator rescue), ATI quartiles and DRB1 alleles were included as possible confounders influencing total time on IFX using Cox proportional hazard regression.

Results: The median time on IFX was 100 weeks (IQR 52 - 217) and did not differ significantly depending on ATI quartile (P=0.19, Kruskal-Wallis test). However, patients from quartile 4 showed a significant shorter time on IFX (median 72 weeks) compared to the other quartiles combined (median 111 weeks, P=0.049). We observed clear differences in time on IFX depending on the DRB1 allele with medians ranging from 43 weeks for DRB1*13 to 169 weeks for DRB1*15 (P=0.019, Log-rank test (Figure 1)).

Cox proportional hazard regression identified albumin at start of IFX, ATI in quartile 4, presence of DRB1*11 and presence of DRB1*15 as independent predictors (P<0.05) of total time on IFX with hazard ratios (95% CI) of 0.34 (0.19–0.59), 3.3 (1.6–6.9), 0.45 (0.23–0.9) and 0.35 (0.16–0.77) respectively.

Conclusions: In patients who develop ATI, besides the magnitude of the titer, a higher concentration of albumin at start and the HLA-DRB1 genotype prolong the time patients will remain on IFX. The concomitant use of immunomodulators did not affect time on IFX in this study. These results clearly warrant further investigation in prospectively designed studies.

P698
Methylomic profiling in Inflammatory Bowel Disease: New insights into disease pathogenesis and activity

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Background: The precise aetiology of IBD is not known. However, both environmental and genetic factors contribute and epigenetic regulation e.g. DNA methylation may integrate these factors. The goal of this study is to identify site-specific DNA methylation changes associated with IBD and disease activity.

Methods: One hundred and fifty patients (88 Crohn's disease, 83 male, median age 34 years, disease duration 6.7 years) with histologically confirmed IBD attending a university teaching hospital donated a blood sample from which peripheral blood mononuclear cells were isolated. Genomic DNA (500ng) was bisulfite converted using the EZ-96 DNA Methylation Kit. DNA methylation was quantified using the Illumina Infinium HumanMethylation450 BeadChip array with data normalisation and pre-processing performed using WateRmelon. The final analyses included 430821 probes and 188 (149 IBD cases, 39 controls) samples passed our stringent quality control filter. Statistical analysis was performed using R 3.1.1. Linear regression was used to examine differences in DNA methylation scores and p values were adjusted for multiple testing according to the false discovery rate procedure. Pathway analysis of genes associated with the 100 top-ranked DMPs identified in the IBD cases versus control analysis and the 100 top-ranked DMPs identified in the active versus inactive disease analysis was performed using Ingenuity Pathway Analysis. Gene expression was quantified using Real time quantitative PCR.

Results: A total of 22,556 probes were significantly differentially methylated between IBD cases and controls, after adjustment for multiple testing. Network analysis of genes associated with the 100 top-ranked DMPs highlighted significant enrichment for pathways associated with immunological disease, including notch signalling and histidine degradation. DMPs associated with disease activity were significantly enriched for pathways associated with inflammatory and antimicrobial response, including IL-6 and TGF-beta signalling. Traf-6 and Peli-1, both hypermethylated in IBD versus controls, were identified as targets for validation. Gene expression (n=50) was significantly reduced in IBD for both Traf-6 (p=0.008) and Peli-1 (p=0.006).

Conclusions: DNA methylation profiles of differed significantly between IBD patients and controls and with disease activity. Moreover, Traf-6 and Peli1 mRNA was significantly reduced in IBD cases compared to controls. Our data provide new insights into potential pathways and molecules which are targets of aberrant DNA methylation and may contribute to the pathogenesis and activity of IBD.

P699
Genetic and clinical characterization of 56 multiple-affected IBD families

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Background: Inflammatory bowel disease (IBD) pathogenesis comprises genetic, environmental and immunological factors. 163 genetic loci have been associated with the risk of IBD. Multiple-affected families (≥ 3 first-degree relatives affected) may have a higher genetic risk burden. We characterized these families clinically and genetically to find to what extent the 163 loci are associated with IBD in these families.

Methods: We included 62 multiplex families affected by Crohn's disease (CD), ulcerative colitis (UC) or IBD unclassified (IBD-U). We collected demographic (sex, smoking) and clinical data (age at diagnosis, disease location and behavior). We genotyped affected and unaffected members with Immunochip for the 163 loci. We analyzed serum samples for the Prometheus serology panel (ASCAA, ASCAG, CBir1, Fla2, FlaX, OmpC, ANCA).

Results: Among our families, 39 were CD, 2 UC, 17 CD/UC and 4 CD/IBD-U. They comprised in total 190 CD, 38 UC, 6 IBD-U and 307 healthy relatives. The average age at diagnosis was 25 years for CD (IQR 20-34) and 31 for UC (IQR 26-39). CD members of a same family showed high concordance in smoking habit (72%), age at diagnosis (87%), disease location (74%) and behavior (69%). The difference in average number of risk alleles (RA) between affected and unaffected members was not significant, nor between affected members and 2612 unrelated cases. Quartile analysis of the number of risk alleles showed that patients were most represented in Q4 and unaffected in Q1 (p=2.61x10-03). Of the 163 loci, 18 SNPs were nominally significant for the parenTDT test. The most significant (p=2.08x10-03) was rs2155219, located in 11q13 between C11orf30 and LRRC32. NOD2 frameshift mutation was also significantly associated with Crohn's disease (p=0.045). We found no enrichment of particular disease-associated pathways in any of the families. The serology panel was disease-dependent rather than family-dependent, with low intraclass correlation coefficients within families (0.06-0.21), suggesting that these antibodies increase with inflammation. Sensitivity, specificity, PPV and NPV for a diagnostic prediction of IBD vs non-IBD were 85.6%, 75.9%, 85% and 76.8%, respectively.

Conclusions: This is the largest cohort of multiple-affected IBD families studied to date. We found a high degree of concordance among CD patients of a same family in clinical features. We found nominal significance for disease association with 18 of the known IBD susceptibility loci but they do not explain much of genetic risk in these families. Exome sequencing on families with a low genetic risk score could identify additional risk loci. Serology markers could be useful to diagnose disease rather than to predict it.

P700
Genetic polymorphisms in IBD determine response to treatment

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Background: The role of single nucleotide polymorphisms (SNPs) associated with inflammatory bowel disease (IBD) is gaining interest. We previously observed that patients (pts) carrying an NCF4 risk allele are more exposed to prednisone and are highly steroid

	5-ASA	Steroids	Immunomodulators	Anti-TNF
IRGM (rs13361189, C)			↓Side eff 6MP (0.051) OR 0.28, CI 0.08-1.01	***↓Non resp IFX (0.045) OR 2.42, CI 1.02-5.73*** ↓Use ADA (0.057) OR 0.65, CI 0.42-1.01
ATG16L1 (rs2241880, G)			***↓Use Cyclosporin (0.003) OR 0.32. CI 0.15-0.67*** ↑Use MTX (0.091) OR 1.64 .CI 0.92- 2.92	***↑Use ADA (<0.0001) OR 3.14, CI 1.73-5.70***
NOD2 (rs2066844,T rs2066845, C rs2066847, C)		***↑Use Budesonide (0.02) OR 1.81, CI 1.10-2.96*** ↑Loss resp Predn (0.06) OR 1.86, CI 0.97-3.56		↓Use IFX (0.095) OR 0.708, CI 0.47-1.06
CCR6 (rs2301436, G)	***↓Side eff 5-ASA (0.03) OR 0.52, CI 0.28-0.95***	***↓Side eff Pred (0.003) OR 0.52, CI 0.33-0.80***	***↑Side eff MTX (0.03) OR 2.71, CI 1.08-6.82***	
STAT3 (rs744166, T)	↑Non resp 5-ASA (0.08) OR 3.13, CI 0.89-11.05)			***↑Side eff IFX (0.006) OR 2.22, CI 1.25-3.93 ↑Non resp IFX (0.02) OR 0.38, CI 0.17-0.86***
LRRK2 (rs11175593, T)			***↑ Use 6MP (0.02) OR 2.53, CI 1.18-5.46***	
XBP1 (rs35873774, C)	↓Side eff 5-ASA (0.07) OR 0.16, CI 0.02-1.19	↑Side eff budesonide (0.07) OR 2.43, CI 0.94-6.29)	↓Use AZT (0.06) OR 0.54, CI 0.28-1.04) ***↑Use MTX (0.005) OR 2.28, CI1.28-4.08***	***↑Non resp IFX (0.02), OR 3.74, CI, 1.28-10.87 ↑Non resp ADA (0.02) OR 4.49 CI 1.24-16.34***
IL23R (rs11465804, G)	↓Use 5-ASA (0.096) OR 0.52, CI 0.24- 1.12 ↑ non resp 5-ASA (0.09) OR 3.15 CI 0.85-11.60	***↑Non resp Predn(0.02) OR 4.20, CI 1.28-13.83***		↓Use ADA (0.06) OR 0.47, CI 0.22-1.04

"Table 1. IBD-risk gene (SNP, allele) against response to treatment (p-values). Pred: prednisone, MTX: methotrexate, ADA: Adalimumab, IFX: Infliximab, resp: response, side eff: side effects, OR: odds ratio, CI: confidence interval"

dependent, indicating divergent use of treatment in different genetic risk groups. As treatment strategies in IBD are aimed towards a more personalized approach in the future, we wondered whether other IBD-associated SNPs are able to predict response to treatment as well.

Methods: Data on treatment use and primary response, loss of response and side effects to treatments were retrieved for all IBD patients from whom DNA was available in our center. rs13361189 (IRGM), rs2066844, rs2066845, rs2066847 (NOD2), rs35873774 (XBBP1), rs11175593 (LRRK2), rs11465804 (IL23R), rs2301436 (CCR6) and rs744166 (STAT3) SNP status were determined (KBiosciences, UK). Correlations were calculated using logistic regression analysis. This study was approved by the medical ethical board.

Results: : Of the 583 pts, 46% were men. 71.2 % suffered from Crohn's disease, 27.3% from Ulcerative colitis and 1.5% from IBD-unclassified. SNP status was associated with response to treatment, especially towards the higher end of the treatment pyramid ( ). The most significant associations included a threefold increased use of Adalimumab and a decreased use of cyclosporine in patients carrying the ATG16L1 risk allele. In patients carrying the protective XBP1 allele a twofold increase in the use of Methotrexate was found, as well as a fourfold risk of primary non-response to Adalimumab. Furthermore, patients carrying the CCR6 risk allele showed a twofold decrease of prednisone side-effects, whereas STAT3 risk allele carriers had a twofold increase of side effects on Infliximab.

Conclusions: Genetic polymorphisms in known IBD-associated genes correlate with response to treatment, suggesting that genetic make-up of IBD patients may in future help physicians decide on personalized treatment strategies. Further investigation will need to elucidate the implications of these findings and asses the significance of patients genetic profile on differences in disease severity, disease phenotype and/or disease duration.

P701
The contribution of genetics in differentiating inflammatory bowel disease type unclassified

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Background: A definitive diagnosis of Crohn's disease (CD) or ulcerative colitis (UC) in patients who initially present with inflammatory bowel disease type unclassified (IBDU) remains challenging. Most often, a combination of clinical (presence of rectal sparing without local therapy; ileal disease/backwash ileitis; perianal abscess; segmental colitis; stenotic disease), histopathological and sometimes serology is used in clinic. We investigated if the combination of clinic, pathology, serology and genetics would improve differential diagnosis in these patients.

Methods: We retrospectively identified 60 patients diagnosed with IBDU. On the basis of histopathology, 21 of these were later reclassified as CD, 22 as UC and 17 remained IBDU at the end of follow-up (with a median follow-up time of 12.6 yrs). For each patient a clinical score ranging from 0-5 (sum of the clinical factors mentioned above) was calculated and a serum samples were analyzed for pANCA and several antimicrobial antibodies (ASCA IgA, ASCA IgG, CBir1, OmpC, Fla2 and FlaX (Prometheus Laboratories Inc.)). All antimicrobial antibodies were divided into quartiles and quartile sum scores (QSS) were calculated for each patient. We also genotyped patients for the 163 IBD loci through immunochip and calculated a genetic risk score (GRS) for specific CD vs UC loci (higher values more indicative for CD and lower for UC). All markers were compared between the different groups.

Results: The median time (IQR) to definitive diagnosis was longer in the CD patients (9.6 (4.9-12.9) yrs) than in the UC patients (2.1 (0.8-8.8) yrs, P=0.003). Both the clinical score and QSS could clearly distinguish the CD group from the UC and IBDU group (P=0.03 and P=0.04, Kruskall-Wallis test) but not the UC from the IBDU group. The GRS and pANCA status did not differ between groups (P>0.45). Logistic regression identified the clinical score and QSS to be independent predictors for diagnosing CD (P<0.01) with OR (95% CI) of 2.7 (1.3-5.7) and 1.3 (1.1-1.5) respectively and the accuracy of this prediction increased (AUC of 0.7 to 0.78 in ROC) when both were combined. A similar approach for the UC patients could only identify the clinical score as a predictor (P=0.01) with an OR of 0.4 (0.2-0.8).

Conclusions: In patients with IBD-unclassified, a combination of clinical factors and antimicrobial antibodies is superior for determining evolution to CD. The current validated genetic risk panel of 163 susceptibility loci does not have an added value in making this distinction. This is probably due to the fact that there is a significant overlap between CD and UC-risk alleles and the fact that only very few genes are specific for CD or UC.

P702
Influences of XDH genotype on thiopurine-induced leukopenia in Korean patients with Crohn's disease determined by gene-gene interactions

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Background: Thiopurine therapy, commonly utilized in inflammatory bowel disease, can be complicated by life-threatening leukopenia. Although the impact of genetic variation in the thiopurine S-methyltransferase (TPMT) gene on toxicity has been well emonstrated, only about a quarter of inflammatory bowel disease patients with thiopurine-induced leukopenia carry a TPMT mutation. As xanthine dehydrogenase (XDH) is the second major contributor to azathioprine breakdown besides TPMT, we conducted an association analysis in Crohn's disease (CD) population in order to identify association between XDH variation and thiopurine-induced leukopenia by gene-gene interaction.

Methods: A total of 978 of Korean CD patients treated with thiopurines were recruited from CD registry database of a tertiary referral center. The association between two XDH variants (G172R, N1109T) and thiopurine-induced leukopenia was analyzed in case

with early leukopenia (n=66), case with late leukopenia (n=280) and control without leukopenia (n=632). Three nonsynonymous SNPs, NUDT15 (R139C), SUCLA2 (S199T) and TPMT (T240C) were selected for epistasis analysis with XDH variants.

Results: There was no significant association for two variants of XDH and thiopurine- induced early and late leukopenia. In the epistasis analysis, only XDH (N1109T) * SUCLA2 (S199T) showed statistically significant association with early leukopenia [odds ratio (OR) = 0.16; P= 0.02]. After genotype stratification, positive association on the background of SUCLA2 wild type (199S) for XDH (1109T) G allele with thiopurine-induced early leukopenia (OR = 4.38; P= 0.01) was detected.

Conclusions: The present study has shown that genes were associated with thiopurine-induced leukopenia can act in a complex interactive manner. Further studies to explore the mechanisms of combination of XDH (N1109T) and SUCLA2 (S199T) in thiopurine-induced leukopenia are warranted.

P703
Genome-wide DNA methylation changes in Ulcerative Colitis patients

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Background: Inflammatory bowel disease (IBDs), including Crohn's disease (CD) and Ulcerative colitis (UC), are emerging globally to understand its pathogenesis. The biological cause of IBD still remains unclear but evidence is accumulating that complex interactions between the genome and the gut microbiota of the host and environmental factors. Regarding the interaction between environmental and genome, epigenetic mechanism and more specifically DNA methylation seem to be of great importance.

Methods: We employed high-throughput microarray-based method for genome-wide DNA methylation profile using Illumina Infinium HumanMethylation450 BeadChip arrays. For this analysis, we used eight UC samples and three normal control colonic tissues from patients and obtained genomic DNA from biopsies. Differential methylated signal in UC were analyzed using bioinformatics tools. We also validated our candidate genes in an independent UC sample panel by MSP or bisulfite sequencing analyses.

Results: We have identified new 70 hypermethylated genes in UC samples compared with normal controls. Surprisingly, these genes are already highly methylated in colon cancer cell lines. More interestingly, new 12 (STC2, TTC33, MYO1E, USH2A, C9orf3, FOXP2, ALOXE3, AGTR1, KLK11, PECI,HSPB6, and HS3ST3B1) out of 70 genes are hypermethylated in UC patient samples and colon cancer patients. We report first here that these genes are hypermethylated in UC patients. In addition, since we have two different groups of UC samples based on disease duration, differential methylation pattern identified clinical correlation loci in our UC samples. With our candidate hypermethylated genes in UC samples, several biological pathways are involved each other.

Conclusions: Our genome-wide approach could contribute to identify UC specifically hypermethylated genes therefore these genes could be great use of prognostic biomarker for this disease and also to understand biological pathogenesis of IBD disease.

P704
RNA sequencing shows transcriptomic changes in affected and unaffected mucosa of Crohn's disease patients compared to normal colonic mucosa of healthy controls.

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Background: Background: Crohn's disease is chronic inflammatory bowel diseases caused by dysregulated mucosal immune responses to the gut microbiota in genetically susceptible individuals. So far, over 140 susceptibility loci to CD have been identified through genome-wide association studies and meta-analyses, however it has not fully explained the heritability of CD. Because a phenotypic character of CD is an abrupt transition between unaffected normal-looking mucosa and affected ulcerative mucosa, so-called skip lesions, the evaluation of transcriptome in affected and unaffected mucosa of CD patients may give a direct evidence for pathogenesis of CD. The aim was to investigate the transcriptomic changes in affected and unaffected mucosa of Crohn's disease patients compared to normal colonic mucosa of healthy controls by using RNA sequencing.

Methods: We conducted a pilot case-control study of RNA expression profile using RNA sequencing of affected ulcerative and unaffected normal-looking intestinal mucosa of 13 CD patients compared to normal colonic mucosa of age/sex matched 13 healthy controls. Mucosal total RNA was isolated and purified, and next-generation pair-end sequencing was performed. After normalization between samples, differentially expressed genes were selected using DESeq R package.

Results: Forty four genes were differentially expressed in affected vs. unaffected CD mucosa ($p<0.01$), 1,158 genes in affected CD mucosa vs. normal control mucosa ($p<0.01$), and 182 genes in unaffected CD mucosa vs. normal control mucosa ($p<0.01$). Nineteen genes were overlapped on Venn Diagram. Fifteen genes were up-regulated sequentially in affected, unaffected CD mucosa, and normal control mucosa (ANGPT2, CHN1, CPXM1, CPZ, CXCL1, FCN3, GJC1, HSD11B1, LZTS1, MEOX1, MMP12, PLA1A, SERPINE1, SGIP1, and TRPC4). Four genes were down-regulated sequentially in normal control mucosa, affected, and unaffected CD mucosa (FAM189A1, PDE6A, SLC38A4, and HMGCS2). Pathway analysis revealed that identified genes were associated with collagen degradation, collagen biosynthesis and modifying enzymes, integrin cell surface interactions, extracellular matrix organization, degradation of the extracellular matrix, validated targets of C-MYC transcriptional activation, collagen formation, and leukocyte transendothelial migration.

Conclusions: RNA-Seq analysis of affected, unaffected CD mucosa, and normal colonic mucosa show transcriptome changes that provide the rationale for validation studies to explore the role of mucosal factors in the pathogenesis of CD.

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P705
Identification of 10 regions associated with IBD in a non- Caucasian Moroccan Population

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Background: We aimed to investigate the 163 known loci and top SNP associated with inflammatory Bowel Disease (IBD) in a non-Caucasian Moroccan IBD cohort.

Methods: We genotyped 549 non- Caucasian Moroccan individuals with 285 IBD patients (211 Crohn's disease (CD), 63 Ulcerative colitis (UC) and 11 Indeterminate colitis (IC)) and 264 controls on custom designed Immunochips from ILLUMINA®. We considered the 163 loci and top SNPs associated with IBD in Caucasian individuals and negative controls matched for the minor allele frequencies (MAF). After quality controls, association analysis was done using PLINK and population stratification was corrected using the first five principal components as covariates. Simulation tests with random groups of SNP (outside the 163 loci and matched for MAF) and regions (outside the 163 IBD loci and matched for the number of independent tests) were used to test the significance of the results.

Results: We identified 10 regions significantly associated with IBD and UC (Table1).

Surprisingly, none of NOD2 variants were found to be associated with IBD moroccan population. Increasing the sample size of the used cohort will definitively help to detect more IBD loci/SNPs associated with Moroccan IBD.

Conclusions: This is the first genetic study conducted in a large population of Moroccan IBD patients. Ten loci/top SNP were significantly associated with IBD and UC. Interestingly, none of the NOD2 variants were found to be associated to CD/UC and Moroccan IBD.

P706
Metallothioneins are downregulated in ileal mucosa of familial diarrhea syndrome patients susceptible to Crohn's disease.

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"Table 1: ten top SNP/loci significantly associated with IBD and UC"

Chr	Position of top SNP/loci	dbSNP	Disease	MAF	pvalues	Key genes
11	1.62-2.12	rs907611	IBD	0,2453	0,00099	TNNI2,LSP1
1	200.62-201.12	rs7554511	IBD	0,1982	0,00199	KIF21B
6	167.12-167.62	rs1819333	IBD	0.492	0,00499	CCR6,RPS6KA2,RNASET2
1	67.4-67.95	rs11465804	IBD	0,1663	0,01198	IL23R
7	31.02-31.52	rs9264942	UC	0,3798	0,0198	HLA-C,PSORS1C1,NFKBIL1,MICB
6	107.18-107.72	rs4380874	IBD	0.489	0,01998	DLD
16	11.12-11.95	rs529866	UC	0,08566	0,0209	SOCS1,LITAF,RMI2
9	138.99-139.64	rs10781499	IBD	0,08566	0,0297	CARD9,PMPCA,SDCCAG3,INPP5E
2	241.31-241.83	rs3749171	UC	0,0978	0,03796	GPR35
9	4.73-5.23	rs10758669	IBD	0,3483	0,04195	JAK2

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Background: Familial GUCY2C diarrhea syndrome (FGDS) is a rare dominantly inherited disease first described in a large Norwegian family (n=34). It is caused by an activating mutation in the gene encoding guanylate cyclase C [1] , the intestinal receptor for heat stable E.coli toxin, guanylins and the new drug linaclotide. Patients with FGDS have early onset chronic mild diarrhea and symptoms resembling IBS, but also increased susceptibility to ileal Crohn's disease (CD) (7 patients) and distal small bowel obstruction (9 patients). The aim of the present study was to compare global gene expression in ileal biopsies from FGDS patients, unrelated CD patients and healthy controls. In addition, we assessed whether CD genetic risk variants [2] segregate with ileitis in the FGDS patients.

Methods: Global gene expression was examined in ileal biopsies from 11 FGDS patients, (3 with CD), 6 unrelated CD patients, and 16 healthy controls (age 22-57), using Illumina Human HT-12 v4 Expression Bead Chip. Histology of the biopsy site was normal in all but one FGDS patient.

We genotyped 140 CD risk variants [2] using the Immunochip (Illumina Infinium) array and sequenced the NOD2 gene in 23 FGDS-patients above 30 years of age (7 with CD). A polygenic risk-score was calculated for each subject.

Results: A moderate number of genes were differentially expressed between FGDS patients and healthy controls. Of special interest were nine metallothioneins (MT1A, MT1E, MT1F, MT1G, MT1H, MT1M, MT1X, MT2A and MTE), which were 1.5-3 fold downregulated in FGDS patients. Gene ontology analyses showed significant enrichment for metallothionein-related terms. There were no significant differences in expression of metallothioneins in the unrelated CD patients compared to controls.

The polygenic risk score did not differ between FGDS patients with and without CD, and none of the 140 CD risk variants segregated perfectly with CD in this family. However, 6 of the 7 FGDS patients with CD carried NOD2 risk variants (JW1, R702W, R703C). The two most severely affected patients were homozygous for JW1. Three of 17 FGDS patients without CD were heterozygous for NOD2 risk variants.

Conclusions: Metallothioneins were significantly downregulated in non-inflamed terminal ileum of FGDS patients, but not in unrelated CD patients compared to controls. Downregulation of metallothioneins have previously been reported in IBD. Lower levels of these zinc binding proteins may interfere with NOD2-stimulated bacterial clearance and autophagy [3] . Further studies are warranted to investigate the role of these mechanisms in the susceptibility to CD in FGDS patients.

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P707
Gene expression of AKAP12 in the colonic mucosa is a marker associated with disease extension in patients with Ulcerative Colitis

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Background: Ulcerative colitis (UC) is a subtype of inflammatory bowel disease that affects the colonic mucosa layer. The gene of A-kinase anchor protein 12 (AKAP12) regulates cell cycle progression, cell motility, and morphology through its multiple scaffolding domains. The AKAP12 also acts in the suppression of oncogenic proliferation and chemotaxis. The up-regulation of AKAP12 causes cell flattening, reorganization of the actin cytoskeleton, and the production of focal adhesion structures. No previous studies have evaluated the role of AKAP12 expression in UC patients. The aim was to determine the gene expression of AKAP12 in patients with UC and to evaluate its association with clinical outcomes.

Methods: We included a total of 80 patients with confirmed diagnosis of UC and 30 controls without endoscopic and histological of any inflammation. The relative quantification of the gene expression was performed by real time PCR for AKAP12: forward: 5'- ccgctaagctgatctcctgt 3' and reverse 3'- catcttcagagtctctctgtccaa 5' and the glyceraldehyde-3-phosphate dehydrogenase (GAPDH): reverese 3'-agccacatcgctcagacac and forward 5'-gcccaatacgaccaaatcc, a housekeeping gene was analyzed for normalization. Statistical analysis was performed using the program SPSS ver. 17. A statistical significance was considered as P value <0.05.

Results: The extent of disease was evaluated using total colonoscopy, and biopsies were taken from rectum segments. The Montreal classification was used to define the extent of UC: 36.6% had pancolitis (E3); 33% had left-sided colitis (E2); and 39.4% had proctitis (E1). The AKAP12 gene expression was significant increased in the colonic mucosa from patients with active UC as compared with UC in remission and the control group (P=.01 and P=0.03 respectively). The up-regulation of AKAP12 was associated with the presence of pancolitis in patients with UC (P= 0.04, OR=12, 95% CI: 1.29-18.37).

Conclusions: The up-regulation of AKAP12 gene was found in patients with active UC and this gene was associated with pancolitis in UC. This is the first report about the role of AKAP12 in patients with UC suggesting that AKAP12 might play a role as molecular marker of disease extent.

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Poster presentations

Microbiology

P708
What causes recurrence of Crohn's Disease after intestinal resection? A prospective evaluation of microbiota, smoking and anti-TNF therapy. Results from the POCER study

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Background: The intestinal microbiota is the antigenic drive in Crohn's. It is also likely to be responsible for disease recurrence after intestinal resection. We aimed to identify microbiota predictive of, or associated with, disease recurrence, remission, smoking and adalimumab therapy.
Methods: 141 mucosal samples from 34 Crohn's disease patients were obtained at surgical resection (baseline) and from the ileum and anastomosis at colonoscopy 6 and/or 18 months post-operatively. 28 control samples were obtained; 12 colonic samples from healthy patients with a normal colon (healthy controls) and 16 ileal and anastomosis samples from 8 patients who had previously undergone right hemicolectomy for colon cancer (surgical controls). Endoscopic recurrence in Crohn's patients was assessed using the Rutgeerts score. Mucosal 16s ribosomal profiling was performed using the MiSeq Illumina platform.
Results: Crohn's disease was associated with reduced bacterial diversity when compared to healthy controls but not surgical controls (Shannon Diversity Index; t-test: p=0.012 and p=0.552 respectively). Bacterial composition (beta diversity) differed significantly between Crohn's disease and both healthy (p=0.024) and surgical (p=0.038) controls, and changed within Crohn's patients over time, but did not differ significantly between those with and without endoscopic recurrence. However significant taxonomic differences between recurrence and remission included increased Proteus (p=0.019) and decreased genera from the Firmicutes phylum including Faecalibacterium (p=0.004). No significant differences were observed in alpha or beta diversity between smokers vs. non-smokers and between adalimumab treatment vs. no adalimumab treatment. Smoking was associated with significantly elevated levels of Proteus (p=0.013) and lower levels of Phascolarctobacterium (p=0.028) and Faecalibacterium (p=0.029). Low abundance of Faecalibacterium and smoking were both independently associated with recurrence (OR 5.5 (CI 1.8-17) p=0.002 and OR 3.3 (CI 1-11) p=0.049) respectively.
Conclusions: Crohn's disease is associated with a microbial signature distinct from health. Surgical resection alone may be responsible for some, but not all, of the taxonomic differences observed in patients following intestinal resection in Crohn's disease. Microbial factors, such as the presence of Faecalibacterium, and smoking may influence post-operative Crohn's disease recurrence through independent mechanisms. The mechanism by which anti-TNF therapy prevents recurrence post-operatively does not appear to have a microbial basis.

P709
Association between genotypes of Bacteroidetes in fecal samples from patients with Crohn's disease and its assessment using an experimental mouse model

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Background: The pathogenesis of inflammatory bowel disease (IBD) involves an imbalance of the gut microbiota generating an inappropiate activation of the mucosal immune system in genetically predisposed individuals. The human commensal microbiota contains a large number of Bacteroidetes species that may cause inflammation in animal models. The aim of this study was to detect and evaluate the influence of different Bacteroidetes genotypes on the activity of Crohn disease (CD) patients. In addition, the effect of these bacteria isolated from CD patients on gut inflammation was evaluated in mice.
Methods: We performed a case control study on the intestinal bacteria of the phylum Bacteroidetes from faeces of CD and healthy controls (HC) using a polymerase chain reaction (PCR) designed to detect human-specific genetic markers targeting Bacteroidetes-like 16S rRNA genes in fecal DNA samples. The PCR products from the 16S rRNA genes were digested with HinfI, PciI, DpnII and AciI enzymes and restriction fragment length polymorphism (RFLP) were determined. RFLP and sequencing analysis indicated that a total of 6 bacterial genotypes do exist: N1, C1, C2, C3, C4 and C5 (of which N1 genotype is probably a strain of Bacteroides dorei and C1, and maybe C2, strains of B. vulgatus). The relationship between CD activity (CDAI>150) and microbiota was evaluated. Microbiota from CD patients were transplanted into mice gut to evaluate their ability to induce inflammation. Results are shown in percentages.
Results: 11 CD patients (8 with active CD -aCD- (CDAI>150), and 3 with inactive CD -iCD-), and 11 HC were included. The predominant Bacteroidetes genotype in feces from HC and iCD was N1 (present in 100% of samples), whereas this genotype was found in only 28% of patients with aCD. 18% aCD patients showed the C1 genotype, 9% the C1 and C3 genotypes together, 18% the C4 genotype, and 27% the C1 and C4 genotypes together. The transplant of bacteria from CD patients to mice led to large bowel inflammation, and the stool of the transplanted mice consisted in 30% C4 genotype and had a high level of Bacteroidetes cluster in comparison with the mice transplanted with bacteria from HC.
Conclusions: The fecal microbiota of CD patients is different from those of HC in that they present a wide variety of Bacteroidetes cluster genotypes. The C4 genotype by itself, or together with the C1

genotype, seems to be intimately related to the activity of the disease. These results were also confirmed in transplanted mice.

P710
Microbiota dynamics in paediatric Crohn's disease from active disease upon achieving clinical remission

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Background: In Crohn's disease (CD), genetic and environmental factors like alterations in intestinal microbiota composition, are considered to play a crucial etiological role. However, data on paediatric cases is limited and conflicting. Here we aimed to describe the intestinal microbiota composition in a cohort of children with newly diagnosed CD, from active disease up to three months following initiation of therapy.
Methods: Faecal samples were collected from children aged up to 18 years and suspected for CD, prior to bowel cleansing (baseline) and at week 1, 3, 6 and 18 following initiation of therapy. All patients were treated according to standard care guidelines. CD-patients were offered 6 weeks exclusive enteral nutrition (EEN) and in case of EEN-reluctance, failure or intolerance, corticosteroids were prescribed. As maintenance therapy thiopurines were prescribed. Disease activity was assessed by Global Physician Assessment (GPA) score, substantiated by fecal calprotectin and CRP. As control group, healthy children were invited to collect faecal samples at similar time-intervals as the study-group. Faecal samples were analysed by IS-pro (interspace 16-23S, PCR-based microbiome detection technique.
Results: Faecal microbiota profiles of 60 children with newly diagnosed CD (median 14 years; IQR 2.6) over time were compared to 60 healthy controls (median 8 years; IQR 3.3). 95% of CD patients were in clinical remission at t6. At baseline, Shannon diversity index in CD cases was higher for the phylum Proteobacteria, compared to controls (p0.041), next to a higher total abundance (p0.001). At baseline, total abundance of phylum Bacteroidetes was lower in CD compared to controls (p0.07). Upon achieving clinical remission, microbiota profiles seemed to resemble profiles healthy controls. Notably, microbiota profiles of CD patients, from baseline to 6 weeks follow-up, showed shifts towards composition of healthy controls.
Conclusions: Significant differences in intestinal microbiota were observed in a large cohort of paediatric CD patients and controls, mainly within phylum Proteobacteria, both in stability and diversity. From active disease upon achieving clinical remission, microbiota profiles of CD subjects showed microbial shifts towards healthy state. Observed microbiota alterations in CD, from active disease upon achieving clinical remission, could lead to development of novel, personalized, microbiota-targeted strategies.

P711
Metabolic dysbiosis concept and its biomarkers in ulcerative colitis and celiac disease

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Background: Specific features of intestinal dysbiosis in UC may include an increased proportion of Actinobacteria and Proteobacteria. Furthermore UC patients show an increase of Enterococcus and Fusobacterium varium, a loss of butyrate-producing bacteria (BPB) and a decrease in Akkermansia muciniphila.
CD patients show a significantly reduced Gram-positive to Gram-negative bacteria ratio, a loss of Bifidobacterium, Clostridium histolyticum, C. lituseburense and Faecalibacterium prausnitzii, an increase of Bacteroides-Prevotella group and an increased abundance of Bacteroides fragilis.
Such changes we call the "microbiological" dysbiosis, unlike "metabolic" dysbiosis (a novel term that we introduce) that is primarily characterized by metabolic abnormalities (e.g. serum, urinary or fecal) in the host due to changes in intestinal microbial metabolism. Metabolic dysbiosis is not necessarily accompanied by appreciable quantitative and/or qualitative changes in microbiota composition.
We aimed to identify the signs of intestinal dysbiosis (both microbiological and metabolic) in patients with UC and CD.
Methods: Serum metabolomic profiles and fecal samples were collected from 24 patients with mild-moderate active UC, 37 CD patients, and 28 healthy controls (HC).
Gas chromatography-mass spectrometry (GC-MS) to determine serum metabolomic profiles and quantitative real-time PCR (qRT-PCR) to assess of fecal microbiota composition were used.
Results: We found signs of both types of dysbiosis in UC and CD patients. Microbiological dysbiosis in UC and CD was characterized by a higher ratio of Bacteroides fragilis to Faecalibacterium prausnitzii and depletion of butyrate-producing bacteria. The degree of change differed between UC and CD groups. There was no significant difference in the abundance of individual species between groups.
Metabolic dysbiosis in both disorders is characterized by significant changes in serum organic acids of a microbial origin. In serum of UC patients, phenylacetic acid (PAA), 4-hydroxyphenylacetic acid (4-HPAA), 3-indolylacetic acid (IAA), succinic acid (SA) and fumaric acid (FA) were most prominently increased, whereas 3-phenylpropionic acid (PPA) was significantly decreased. Serum of CD patients showed significant increases in IAA, 3-indolepropionic acid (IPA), benzoic acid (BA), SA and FA.
Oral butyrate plus inulin was effective in an improvement of symptoms, serum metabolomic profiles and gut microbiota in both conditions.
Conclusions: An increased ratio of B. fragilis to F. prausnitzii and a decrease of BPB may be available biomarkers for intestinal dysbiosis in UC and CD.
Metabolic dysbiosis in UC and CD is characterized by changes in serum organic acids. Some of them may be useful biomarkers of chronic intestinal inflammation.

P712
Rapid identification of Bacteroidetes in biopsies of inflammatory bowel disease (IBD) patients.

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Background: The exact role of gut microbiota on the etiopathogenesis of IBD, both Crohn's disease (CD) and ulcerative colitis (UC), is not well known. Most studies of human gut microbiota rely on the non-invasive collection of stool samples. However, the analysis of the fecal microbiota may not reflect the role of the mucosa-associated microbes which live in close proximity to the intestinal epithelium and that are in contact with the cells of the innate immune system directly involved in the inflammatory response. The aim of this study was to investigate the genotypes of Bacteroidetes microbiota from colon biopsies of IBD patients and to determine their relationship with the endoscopic activity of the disease.

Methods: A prospective case-control study was designed. Colon biopsies from consecutive IBD patients and healthy controls (HC) (healthy subjects undergoing colonoscopy for colon cancer screening and having a healthy colon mucosa) were included. Inactive UC was defined as a Mayo endoscopic subscore of 0. Inactive CD was defined as a SES-CD score ≤ 2. Microbiota was characterized by using a restriction fragment length polymorphism (RFLP) analysis on PCR products targeting the 16SrRNA genes of Bacteroidetes digested with HinfI, PciI, DpnII and AciI. Results are shown as percentages.

Results: 29 consecutive IBD patients (22 UC and 7 CD) and 15 HC were included. 8 patients presented with inactive UC (iUC) and 14 with active UC (aUC). All 7 CD patients presented with endoscopic activity (aCD). A total of 7 genotypes of Bacteroidetes called N1 and C1-C6 (of which N1 genotype is probably a strain of Bacteroides dorei and C1, and maybe C2, strains of B. vulgatus) were detected in all the biopsy samples analyzed. The number of genotypes present in biopsies from IBD patients was higher than that in HC, in whom only the N1 (66%) and C1 (34%) genotypes appear. While the presence of N1 genotypes was relatively constant in patients with active and inactive IBD, the percentage of C1 genotype in patients with aUC and aCD were very low (<5%) compared to controls. The C4 genotype never appeared in control samples and it was present in only 2% of iUC biopsies, whereas it was present in 15% and 16% of patients with aUC and aCD respectively. The C2, C5 y C6 genotypes appeared sporadically in biopsies of IBD with percentages of 1% in iUC (C2), 3% in aUC and 1% in aCD (C5), and 1% in iUC and aCD (C6), but never in HC.

Conclusions: Bacteroidetes genotypes in colon biopsies differ between IBD patients and HC. These genotypes, and especially the C4 genotype, are highly specific for active IBD and further studies on their role on IBD pathogenesis are required.

P713
Clinical remission induced by exclusive enteral nutrition (EEN) in pediatric Crohn's disease is associated with microbiome metabolic changes toward altered xenobiotic biodegradation and metabolism

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Background: Exclusive enteral nutrition (EEN) is a first-line induction therapy in pediatric Crohn's disease (CD). Though unclear, the mode of action of EEN is proposed to involve changes in gut microbiome structure and function. Characterization of the microbiome in IBD has largely focused on the assessment of diversity and the identification of protective and disease-associated species. More recently, metagenomic approaches to IBD microbiome investigation have facilitated predictive mapping of microbiome function. Treatment-induced changes to microbiome function may contribute to the strong therapeutic effect of EEN.

Our aims were to perform a functional assessment of microbial metabolic pathways in pediatric CD patients before and after induction of remission by EEN treatment.

Methods: Metagenomic sequences from stool samples obtained from 4 pediatric Crohn's disease patients who underwent EEN treatment were obtained using MiSeq whole-metagenome sequencing. Sequences were searched against 28 representative KEGG (Kyoto Kyoto Encyclopedia of Genes and Genomes) pathways to obtain functional assignment of sequences. Samples collected prior to EEN treatment were compared to samples collected after 8 to 12 weeks of EEN treatment. All participants achieved clinical remission (PCDAI <10) following EEN treatment.

Results: Functional profiling of CD patient microbiota before and after EEN treatment revealed significant changes in metabolic functions related to biodegradation and metabolism of xenobiotics (e.g. benzoate), $p<0.05$.

Conclusions: The microbiome of CD patients is functionally altered by EEN treatment, specifically increasing metabolic potential for xenobiotic biodegradation and metabolism relative to pre-treatment. Further investigations of how altered xenobiotics metabolism contributes to the CD pathology and the therapeutic modality of EEN is warranted.

P714
Intestinal microbial signature predicts postoperative Crohn's disease recurrence following ileocaecal resection with ileocolonic anastomosis

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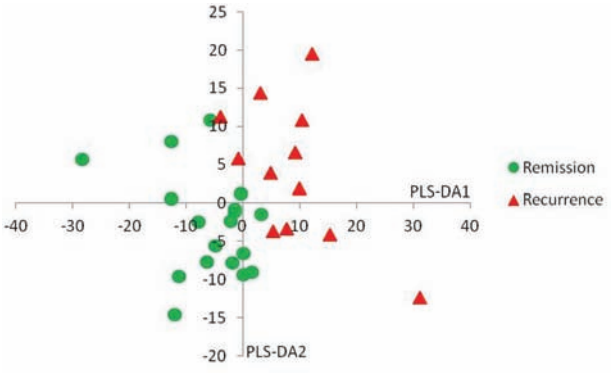
Background: Dysbiosis of the intestinal microbiota has been described in Crohn's disease (CD) and may play an important role in the early events triggering postoperative disease recurrence. We hypothesized that microbiota are altered in patients with early postoperative endoscopic recurrence (ER) and evaluated if the risk for postoperative ER can be predicted based on differences in the fecal microbial composition before surgery.

Methods: Fecal samples from 30 CD patients (median age 46 years, 16 male) undergoing ileocaecal resection with ileocolonic anastomosis were prospectively collected before surgery and at month 1, 3 and 6 after surgery. Postoperative ER - defined by a Rutgeerts score ≥i2 - was assessed at month 6. The predominant microbiota was studied using denaturing gradient gel electrophoresis (DGGE) and bands of interest were sequenced. Partial Least Squares Discriminant Analysis (PLS-DA) was used to cluster the microbial profiles using Unscrambler. Statistical analysis was performed using SPSS and R software.



"Figure 1: PLS-DA shows a clustering of patients with ER (N=12) versus patients in remission (N=18) at month 6, based on preoperative microbial profiles."

Results: Based on the preoperative microbial profiles, two clusters of patients were identified: those developing early ER (N=12) and patients without ER (N=18) (Figure 1).

Before surgery, a reduction of the Lachnospiraceae family (p=0.05) and Clostridium XVIII genus (p=0.032) was seen in the predominant microbiota of patients developing early postoperative ER whereas 3 members of Clostridium XIVa genus (p=0.073), Veillonellaceae family (p=0.028) and Bifidobacterium genus (p=0.01) were higher in patients with ER compared to patients without ER.

A score combining these five bacterial risk factors was calculated and showed an area under the curve of 0.87 (95% CI, 0.76–0.99). The occurrence of two or more risk factors had a sensitivity, specificity, positive predictive value, and negative predictive value of 100%, 56%, 60% and 100% respectively. At the time of postoperative endoscopy, we observed an overrepresentation of Lactobacillus genus (p=0.003) and Ruminococcus gauvreauii (p=0.01) in the patients with ER.

Conclusions: An overrepresentation of Clostridium XIVa spp., Veillonellaceae, Bifidobacteria and a lower abundance of Lachnospiraceae and Clostridium XVIII spp. in the predominant profile of preoperative fecal samples is associated with a higher risk to develop postoperative ER following ileocaecal resection. At the time of postoperative endoscopy, the predominant microbiota from patients with ER also differs from patients without recurrence, with as most prominent players lactobacilli and R. gauvreauii.

P715
Assessment of community structure and predictive functional profiling of the mucosa-associated microbiome implicates alterations in benzoate metabolism in 'de novo' IBD after pouch-surgery and in treatment-naïve pediatric IBD

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Background: Novel analytical frameworks to assess ecology and predictive function of the microbiome are now available. Post-surgical recurrence of IBD and treatment-naïve pediatric IBD are key populations to elucidate microbiome changes associated with the development of IBD. Our aims were to assess the community structure of the mucosa-associated microbiota of 'de novo' intestinal inflammation post-pouch surgery as well as treatment-naïve pediatric IBD and pediatric controls and to perform functional prediction of altered metabolic pathways.

Methods: Publicly-available 16S rRNA sequences from a cohort (n=71) of ileal pouch-anal anastomosis (IPAA) biopsies (Tyler AD et al. PLoS One 2013) were assessed for microbial features associated with post-surgical recurrence of disease/pouchitis vs non-inflammatory outcomes. For community structure analysis, we used a Bayesian analytical framework (BioMiCo - Shafiei et al. PLoS Comput Biolog 2014). Predictive functional profiling was performed using PICRUSt (Langille et al. Nat Biotechnol 2014). This approach was also applied to a pediatric IBD cohort: mucosal biopsies taken from 11 Crohn's disease and 10 ulcerative colitis patients at diagnosis were compared with 12 normal colon pediatric controls using 16S rRNA pyrosequencing (BISCUIT study by Hansen et al. Am J Gastro 2012).

Results: Community structure mapping revealed strong overlap between pediatric IBD and controls: >75% of all pediatric samples had a posterior probability > 85% of being labeled as IBD. In contrast, 28/37 (75%) non-inflamed samples from the adult IPAA cohort, had a posterior probability >85% to correctly differentiate non-inflammatory outcomes (no pouchitis in UC/Familial Adenomatous Polyposis) from inflammatory (pouchitis/complicated pouch). PICRUSt analysis of the IPAA cohort revealed significant alterations in several metabolic pathways (p<0.05): xenobiotics degradation and metabolism (including benzoate) were upregulated in inflamed pouches. PICRUSt analysis of the pediatric cohort recapitulated the observation that benzoate degradation was increased in the colonic mucosal microbiome of treatment-naïve pediatric IBD samples compared with pediatric non-inflamed controls (p=0.02).

Conclusions: Unlike the community structure divergences observed in post-pouch inflammatory outcomes, there was strong overlap between treatment-naïve pediatric-onset IBD colonic mucosal microbiome and pediatric controls. However, predictive functional profiling of the mucosal microbiome of both the post-pouch and pediatric IBD cohorts showed increased benzoate degradation relative to controls. Further investigations of the role of benzoate metabolism in IBD pathogenesis are warranted.

P716
Enterohepatic helicobacter species as a potentially causative factor of Inflammatory Bowel Disease: A meta-analysis

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Background: Enterohepatic Helicobacter species (EHS) colonized in the intestinal mucosa with some extent of Helicobacter pylori composed the Helicobacter species of gut microbiota, but their association with inflammatory bowel disease (IBD) were controversial with numerous studies. Therefore, we conducted a meta-analysis to examine this association.

Methods: Pubmed, Scopus, Cochrane Library, and Web of Science databases and meeting abstracts were searched for relevant studies

focused on Helicobacter species in the intestinal specimen from IBD by using PCR technique. Of 2955 records reviewed, 20 promising articles were reviewed in detail. Meta-analysis was performed with Stata12.0.

Results: A total of 14 articles were evaluated in this study, including 11 adult studies and 3 pediatric studies. Accordingly, the overall prevalence of Helicobacter species was relatively higher in patients with IBD than in controls, resulting in a pooled RR of 1.59 (95% CI: 1.12-2.27). Meanwhile, the RRs for adult and pediatric patients with IBD were 1.61 and 1.76 (95% CI: 1.03-2.52, 1.17-2.64), respectively. Compared with the controls, patients with IBD tended to show a much higher prevalence of EHS (RR: 2.10, 95% CI: 1.27-3.46) but not of H. pylori in the intestinal mucosa (RR: 1.25, 95% CI: 0.71-2.20). Additionally, the RRs of EHS in patients with CD (Crohn's disease) and in those with UC (ulcerative colitis) were 1.72 (95% CI: 1.20-2.47) and 3.27 (95% CI: 0.93-11.44), respectively.

Conclusions: In general, EHS were found to be associated with IBD compared with controls, especially in pediatric patients with higher prevalence in CD than UC. More studies are needed to identify the mechanisms of EHS in the microbiological etiology of IBD.

P717
C.difficile colonisation and infection rates are now low in IBD - a matched cohort study

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Background: Several studies in the last 10 years have reported higher rates of C.difficile colonisation (CDC) and C.difficile infection (CDI) in patients with IBD than in those without [1,2]. We have now reevaluated the incidence of CDC and CDI in diarrhoeal inpatients with IBD and a matched contemporaneous cohort of diarrhoeal patients without IBD.

Methods: All 2284 in-patient stool samples tested for C.difficile at Barts Health Trust in a 12-month period ending April 2013 were recorded in our microbiology database. A 2-step ELISA algorithm for C.difficile testing was used: the first was a test for CDC (presence of glutamate dehydrogenase, a C.difficile-specific enzyme); if present, a second step was performed to look for CDI (presence of toxin B). If more than 1 sample was sent during an admission, only the first was included in analysis. IBD patients from whom the samples were obtained were identified using electronic patient records. They were then matched with non-IBD controls, taken from the same cohort, for age and for the number of days they had been admitted when the sample was sent.

Results: 170/2284 (7%) samples were from patients with IBD. The IBD and non-IBD groups were well-matched: age - 34.0 (3.8-87.6) and 34.2 (3.4-88) years [median (range)] (R2 0.99), and days admitted until sample sent - 2.2 (0-31) and 2.5 (0-31) (R2 0.93). Nine/170 (5%) IBD patients had CDC vs 28/170 (16%) controls (p=0.0017). One/9 (11%) CDC-positive IBD patients had CDI, compared with 6/28 (21%) of the CDC-positive controls (p=ns). Current antibiotic exposure was lower in the IBD group (28%) than in the controls (57%) (p=0.0006). There were no significant differences between the IBD and control groups in 3-month mortality (1%, 5%), in 3-month re-admission rates (25%, 25%) or antibiotic exposure in the previous 3 months (11%, 20%).

Conclusions: CDC is less common in diarrhoeal inpatients with IBD than in matched controls without IBD. The higher incidence of CDC in the control patients may be due to increased antibiotic exposure in this group. C.difficile infection is now rare in IBD, being found in <1% of our IBD patients presenting with diarrhoea.

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P718
Diagnostic yield of colonoscopic images and biopsy Results by tuberculosis culture (solid and liquid) in patients with intestinal ulceration

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Background: Intestinal tuberculosis (TB) disease can be difficult to diagnose because its symptoms and laboratory results are nonspecific. Moreover, endoscopic lesions resemble those of other diseases such as Crohns disease (CD). The aim of this study was to evaluate the diagnostic yield of colonoscopic images and biopsy results by TB culture.

Methods: The medical records of 82 consecutive patient swith intestinal ulceration (colonic, ileal or both) were analyzed. None had active pulmonary tuberculosis. It was reported that the endoscopic findings most characteristic of intestinal TB that are (1) circular ulcers, (2) small diverticula (3-5 mm), and (3) sessile firm polyps were searched. We defined the patients with all 3 criteria as intestinal TB with 100% certanity according to the published literature, with 2 criteria as probable; and with just one criterion as no TB. More importantly, intestinal tissue PCR, liquid and solid TB cultures were performed in each patient.

Results: Of the 82 patients with intestinal ulceration, the endoscopic findings most characteristic for intestinal TB were found in 3 (3.65 %); 13 patients had probable intestinal TB; and the rest (66 patients) had no TB according to the endoscopic imaging findings.

Mycobacterium tuberculosis was isolated from the culture of biopsy specimens in 2 patients (2.43 %). One patient with solid TB culture positive had all 3 endoscopic futures of intestinal TB (circular ulcers, small diverticula (3-5 mm), and sessile firm polyps). Contrary, one patient without any endoscopic futures for TB had PCR (+) and liquid TB culture (+). PCR (+) were noted in 3 patients (3.65%). Two of them showed no endoscopic futures for intestinal TB, but PCR (+) and negative TB culture.

Mycobacterium culture established the diagnosis of intestinal TB, CORRECTY in 2 (2.43 %) patients.

Of the 82 patients, 4 had previous pulmonary tuberculosis history. One of them showed positive PCR and TB culture. One had only PCR (+). The rest 2 patients had negative PCR and TB culture.

Conclusions: Before getting the result of Mycobacterium culture, the WRONGLY diagnosis could be made by either endoscopic examination or the presence of PCR positivity. Differentiating between intestinal TB and CD is very important since steroid treatment can be life saving in CD and lethal in intestinal TB.

P719
Metronidazol verus rifaximin in the treatment of Clostridium difficile infection in inflammatory bowel disease children: a randomized study.

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Background: The aim of the study was to compare the effectiveness of metronidazole and rifaximin in the treatment of Clostridium difficile infection (CDI) in pediatric patients with inflammatory bowel disease (IBD).

Methods: We conducted a prospective, double-blinded, randomized trial with children age 12-18 years. Crohn's disease (CD) and ulcerative colitis (UC) were diagnosed according to Porto criteria. CDI diagnosis was based on a positive stool VIDAS® Clostridium difficile toxin A/B ELFA (bioMerieux, France) test. Patients were randomly assigned to receive metronidazole or rifaximin for 14 days; doses of drugs are presented in table below. Stool samples were collected before and 4 weeks after the end of treatment.

Results: In the present study, 26 patients were enrolled (mean age 14.3 years), including 9 with CD and 17 with UC. 14 received metronidazole and 12 received rifaximin. There were no statistically significant differences between study groups in age, gender and disease type. 4 weeks after the end of treatment Clostridium difficile toxins were found in 5/14 (36%) patients in metronidazole group and in 4/12 (33.3%) patients in rifaximin group (n=NS).

Conclusions: Metronidazole and rifaximin was equally effective in the treatment of CDI in pediatric patients with IBD.

Table

Body weight	Metronidazole, tabl. a 250 mg	Rifaximin tabl. a 200mg
30–40 kg	3 x 1 tabl.	3 x 1 tabl.
40–50 kg	1-2-1 tabl.	1-2-1 tabl.
50–60 kg	2-1-2 tabl.	2-1-2 tabl.
>60 kg	3 x 2 tabl.	3 x 2 tabl.

P720
Anti-TNF-a induction regimen modulates gut microbiota molecular composition while inducing clinical response in Crohn's Disease patients: Toward a personalised medicine

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Background: IBD is characterized by an imbalance between immune response and microbiota composition. Anti-TNF-a is one of strongest therapeutically options with high immune modulation potential. No information exists on how and whether anti-TNF-a modulates gut microbiota composition.

Aim of our study was to evaluate gut microbiota composition in Crohn's disease patients before and after 6 weeks of anti-TNF-a therapy (mean age 41, 3 male).

Methods: Fecal samples were collected in 6 consecutive CD patients, (3 Infliximab, 3 adalimumab) and stored at -80°C. No antibiotic were admitted 4 weeks before starting anti-TNF-a therapy or during the active treatment. Microbiota composition was assessment by 16S rRNA analysis (Roche 454 GS Junior), following DNA isolation from stool samples. Data obtained were analyzed by suite Qiime.

Clinical response was defined as a decrease of 2 points at Harvey Bradshaw Index (HBI) compared to baseline, while clinical remission was consider for HBI <4.

Results: Bacteria amplicons were detected in all samples. Six weeks after anti-TNF-a therapy, Bacteroidetes decreased in 2 patients (one of the 2 in clinical remission) and remained stable in 4 patients. Roseburia spp increased in one patient (not in clinical remission), Ruminococcus spp decreased in 2 patients (in one not responder to treatment). F. Prausnitzii increased in 3 patients (one in clinical remission). Finally, Enterobacteriaceae increased in 3 patients (one not responder to therapy). Chao index increased in 5 patients of six after 6 week. Patients non-responder to anti-TNF by 12 weeks did not show increase in Bacteroidetes at 6 weeks.

Conclusions: Anti TNF-a treatment is associated to active modulation of intestinal microbiota while inducing clinical response. Reduction of enterobacteriacee and ruminococcus were associated to clinical response to antiTNF-a, together with increase in bacteroidetes and F. Prausnitzii. Further studies are required considering a major number of patients.

P721
C.difficile infection rate in patients with IBD is falling in line with that of the general population

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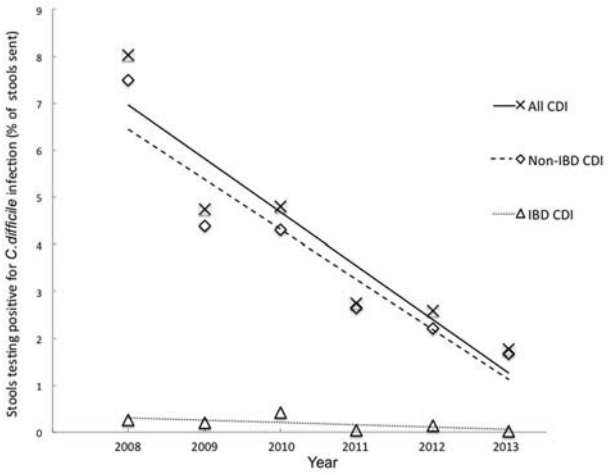
Background: Several studies have reported that the incidence of C.difficile infection (CDI) in patients with inflammatory bowel disease (IBD) continues to rise [1,2]. In the UK, the incidence of CDI in the general population has been falling since 2007. Our clinical suspicion that CDI was becoming less common in patients with IBD led us to investigate CDI rates in IBD patients between 2008 and 2013 to see if CDI in IBD is also in decline.

Methods: Results of stool microbiology from all diarrhoeal samples submitted for C. difficile detection (as an ELISA for toxin B) over a 6-year period ending 2013 were assessed using the microbiology database at Barts Health NHS Trust, London. Electronic patient records for CDI-positive patients were analysed for a diagnosis of IBD at the time of infection.

Results: 1079/25092 (4.3%) of all samples sent were positive for CDI, of which 49 (4.5%) were from patients with IBD. The median age (range) of the IBD CDI patients was 31.6 (1-88) years, and of the non-IBD patients 67.9 (1-98) years ($p<0.0001$). Of the IBD patients, 34 patients had ulcerative colitis, and 15 Crohn's disease (10 colonic, 3 ileocolonic, 2 ileal). The CDI rates in the entire group studied and in the non-IBD patients (as % of stools each year sent for investigation of CDI) decreased annually over the study period from about 7% in 2008 to 1.5% in 2013 (figure). The CDI rates in IBD patients were low throughout this period (<0.4% of stools sent).



"C.difficile infection rates 2008–2013"

Conclusions: Overall CDI rates at our hospital are falling. A very low and constant proportion of patients with IBD test positive for CDI. Although it remains important to test for CDI in diarrhoeal patients with IBD, the incidence of this infection in IBD has now stabilised and has remained low since 2008.

P722
Intestinal microbiota in paediatric ulcerative colitis differs from healthy controls

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Background: In the aetiology of ulcerative colitis (UC), intestinal microbiota is considered to play a crucial role, especially in adults. Knowledge on its role in children is limited. Here we studied intestinal microbiota in a cohort of children with newly diagnosed UC upon achieving remission.
Methods: Faecal samples were collected from patients suspected for UC, prior to bowel cleansing (t0) and at week 1, 3, 6 and 18 after initiation of therapy when diagnosis was confirmed. All patients were recruited from 2 tertiary centres in Amsterdam, The Netherlands. As control group, healthy children collected samples at similar time points. Disease activity was assessed by Global Physician Assessment (GPA) score, faecal calprotectin and CRP. Faecal samples were analysed by IS-pro, a clinically applicable PCR-based microbiome profiling technique.
Results: Faecal samples of 41 newly diagnosed UC patients (median 13 years; IQR 5.6) and 60 healthy controls (median 8 years; IQR 3.3) were compared. All patients were treated according to standard care guidelines, comprising aminosalycilates for induction of remission, dependent on disease severity, combined with corticosteroids, and also as maintenance (mono)therapy. All patients were in clinical remission at t6. Preliminary results showed microbiota profiles of UC and controls were distinguishable. At t0, diversity and total abundance of the phylum Firmicutes were significantly higher in UC compared to controls (p0.003 and p0.001 respectively). Total abundance of Firmicutes in CU increased even further at t6 (p0.039). For the phylum Bacteroidetes total abundance was lower in UC compared to controls at t0 (p0.003). Furthermore one of the core microbiota in controls, Alistipes putredinis, was absent in almost all CU patients. Microbiota profiles in CU did not shift towards those of controls upon achieving remission.
Conclusions: Microbiota-analysis demonstrated significant differences in composition between paediatric UC and controls. One of the core microbiota in controls, Alistipes putredinis, had a lower abundance or was totally absent in almost all UC patients. Upon achieving remission, overall microbiota composition of UC patients did not change towards that of healthy control.

P723
Differential DNA flexibility for symbiotic species involved in gastrointestinal symbiotic interactions

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Background: Changes in the abundance of firmicutes and bacteroidetes have been linked to dysbiosis in human disorders, to recognize how the symbiotic organism change and model this interaction is crucial. According to the recent Black Queen hypothesis, the genomic structure with a symbiotic lifestyle can be implied in events of reduction and change in genomic architecture and composition, bringing into events of reduction and public goods, this could even impact since bacterial communities and symbiosis events. The human microbiome is one of the most important event of symbiosis, with implications in health, economic impact and evolution and it is known that the Firmicutes and Bacteroidetes order is one of the most important bacterial involved in regulations and interaction with the microbiota as well as the gastrointestinal host epithelia. It is proposed that in some cases, the Firmicutes orders could even have a shared and a common signal in interactions and regulations within the human gut, however due to the black queen hypothesis it might be possible that the reduction and the genomic architecture could even be modified at symbiotic sequenced strains and types.The aim of the study was to recognized particular motifs of tandem repeats and high flexibility sequences in the chromosome of some species involved in symbiosis lifestyle for the human gut.
Methods: Using the UGENE software and R modules we compared the incidence of these sequences in complete genome sequences from the NCBI databases for Firmicutes and Bacteroidetes species involved in symbiotic lifestyle.
Results: After we compare 21 species from Bacteroidetes (10) and Firmicutes species (11), we recognize several regions of tandem repeats presented in differential proportion. We can recognize that the Firmicutes show a differential high signal of regions of DNA with higher flexibility bringing the possibility of a differential feature plasticity and recombination and possibly lateral gene transfer, bringing different general a particular configuration.
Conclusions: Firmicutes species resemble a high input into the microbiota of the human gut. however their signal and features involved in

regulation can not be generalized. With this approach we can suggest that some genera of Firmicutes and their interaction and particular plasticity of Bacteroides can even being implied in regulation systems and differential response in the gut microenvironment.

P724
Gut microbiota molecular spectrum in healthy controls, diverticular disease, IBS and IBD patients: Time for microbial marker of gastrointestinal disorders?

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Background: Increasing evidences have emerged on the analysis of bacterial species making up the gastrointestinal microbiota. However few data exist on differences in gut microbiota composition in GI diseases, such as IBD, IBS and diverticular disease compared to healthy controls.

Aim of our study was to evaluate the differences in gut microbiota composition between IBD, IBS and diverticular disease (DD) patients.

Methods: 10 Crohn's Disease (CD), 5 Ulcerative Colitis (UC), 4 DD, 3 IBS patients, and 8 controls (CD) were enrolled and fecal samples collected from each. Microbiota composition was assessed by a metagenomic gene-targeted approach (16S rRNA) using the Roche 454 GS Junior, following DNA isolation from stool samples stored at -80 °C. Data were analyzed in Qiime. Individual species richness was estimated using Chao1 alpha-diversity index. We also explored the differential relative abundance of several taxa of interest, selected according to literature.

Results: Bacteria amplicons were detected in all samples. Prevalent classes of bacteria were: Bacteroidia (min 13,06% - max 91,55%), Firmicutes (min 7,48% - max 86,10%) and Proteobacteria (min 0,48% - max 46,48%). Fusobacteria were found only in CD and DD patients (min 0,67%- max 50,71%). IBD microbiota composition differed significantly compared to all other. In particular, UC patients showed a reduced concentration in Bacteroidetes and an increased presence of Firmicutes vs. CT, DD and IBS. On the other side, Bacteroidetes and Firmicutes composition varied among CD patients, being increased or reduced when compared to the other groups. Proteobacteria were increased in all diseased group compared to CT, being more represented in CD and IBS-D. Moreover, Actinobacteria were increased in IBD and DD vs. IBS and CT. The most represented species in IBD and DD vs. other groups was Collinsella Aerofaciens. Rikenellaceae were suppressed in IBD patients, as well as Fecalibacterium Prausnitzii. Akkermansia Muciniphila was present only in IBS patients. Enterobacteriaceae were increased only in CD patients vs. other groups. Finally, while chao1 score was similar between CT, IBS and DD, it was deeply reduced in IBD patients.

Conclusions: These preliminary data show that starting from microbiota, gastro-intestinal disease represent a spectrum of continues diseases where IBD display one extreme in gut microbiota composition while controls display the other. Furthermore, GI diseases share some microbial patterns, sharing perhaps common pathophysiological pathways. New analyses are needed to confirm this hypothesis and evaluate therapeutical implications.

P725
The Effects of Change in the Intestinal Microbiota Through Antibiotics Administration on the Manifestion of DSS Colitis

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Background: The role of intestinal microbiota in maintaining mucosal homeostasis cannot be more emphasized. IL-17A have been shown to have both pathogenic and protective roles in animal models of colitis. We investigated the effects of intestinal microbiota change through antibiotics administration on dextran sodium sulfate (DSS) colitis in IL-17A-/- mice.

Methods: C57BL/6 wild-type (WT) and IL-17A-/- mice were assigned to different three groups: control group without treatment, antibiotics (vancomycin, ampicillin, neomycin and metronidazole) plus subsequent 1.7% DSS treated group, and DSS treated group. Clinical activities including weight loss and histologic findings of colonic segments were examined. Proinflammatory cytokine levels were measured by ELISA in the supernatants of colonic tissue explants. To characterize the change of intestinal microbiota, high throughput Illumina MiSeq sequencing for sequential feces was performed.

Results: Antibiotics treatment induced a transient weight loss in both WT and IL-17A-/- mice. WT mice developed more severe DSS colitis than IL-17A-/- mice. After antibiotics treatment, both mice displayed significantly enlarged ceca similar to germ-free mice. Antibiotics treatment attenuated DSS-induced increase of histologic inflammation and proinflammatory cytokine levels, especially in WT mice. There was a distinct difference in intestinal microbial composition between WT and IL-17A-/- mice. In both mice, after antibiotics treatment, the proportion of Firmicutes decreased while Proteobacteria increased in the phylum level, and Lachnospiraceae and Lactobacillaceae decreased while Enterobacteriaceae increased in the family level.

Conclusions: IL-17A ablation decreases severity of colitis in DSS murine model. The change of intestinal microbiota through antibiotics administration affects the susceptibility of DSS colitis.

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Nurses presentations

Nurses presentations

Nurses oral presentations

NO001
Application of a Japanese version of the morisky medication adherence scale and related factors to low medication adherence in patient with Ulcerative Colitis

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Background: Non-adherence to medication taking behaviour among patients with ulcerative colitis (UC) has been reported 30-45% and can be a serious risk factor for disease relapse. The Morisky Medication Adherence Scale (MMAS-8) is a relevant approach for evaluating medication adherence in a clinical setting. We were interested to evaluate the clinical relevance of a Japanese MMAS-8 version, and the related factors when applied to low adherence among UC outpatients.
Methods: A multicenter, cross-sectional study was undertaken in outpatients with UC who had taken aminosalicylates. The patients completed a self-administered questionnaire, and the medical information was obtained from the medical records. To concurrent validity of the MMAS-8, kappa coefficient between the low adherence in the MMAS-8 (less than 6 points) and low adherence calculated from self-reported missed dose, defined as taking less than an 80% of the prescribed dose was computed. Scale discrimination validity was tested by known group comparisons to assess whether the scale score could discriminate subgroups of patients differing in clinical status, like with or without concomitant UC induction therapy. Internal consistency of the multi-item scale was assessed by the Cronbach's alpha coefficient. Then, logistic regression model was applied to assess the relationships between low-adherence in MMAS-8 and other factors including disease factors, medication characteristics, abdominal symptoms, and socio-demographics characteristics.
Results: Of 429 UC patients, MMAS-8 identified 245 (57.4%) as low adherents to aminosalicylates. The patients without concomitant UC induction therapy showed significantly higher MMAS-8 scores vs the patients with induction therapy. Cronbach's alpha was 0.74, meaning the internal consistency was confirmed to a certain extent. The kappa coefficient for low-adherence in MMAS-8 and self-reported missed dose was 0.4, suggesting concurrent test was moderate. Multiple logistic regression analyses showed that patients with low adherence had difficulties in taking aminosalicylates (OR = 1.12, 95% CI = 1.10-1.17), rectum in disease region (OR = 1.73, 95% CI = 1.10-3.09), less than 5 years UC duration (OR = 2.20, 95% CI = 1.32-3.66) and younger age (OR = 0.95, 95% CI = 0.93-0.97).
Conclusions: The Japanese version of the MMAS-8 was found to be clinically relevant measure and can be used to evaluate medication adherence of UC patients. We also found additional significant factors defining low-adherence. Our findings suggest that patients who have difficulties in taking aminosalicylates should be provided with tailored support. Moreover, development of an effective medication taking behavior program appears to be a serious challenge for the health care providers.

NO002
Assessing the satisfaction levels of older patients with different types of follow-up care for inflammatory bowel disease

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Background: Inflammatory Bowel Disease (IBD) affects approximately 240,000 individuals in the UK (Mowett et al 2011). Although it predominantly affects young people, recent evidence suggests a second peak of onset in the over 60's (Charpentier et al 2013). In addition, an aging population means increasing numbers of older people are living with IBD. Long term follow-up (FU) in secondary care is undertaken to monitor IBD and its treatment. New approaches to FU promote self-management and the use of telephone and web access (Kennedy 2004, Kreir 2011). Such approaches reduce unnecessary FU in clinic, whilst enabling ease of access when required. Whilst data suggests such FU methods are well recieved (Pearson 2006, Cima 2007),it is possible that IBD patients diagnosed at an older age, or with a lot of FU experience, may feel less familiar with such approaches and therefore less supported. Aims of Study: 1. To explore levels of engagement of IBD patients aged 60 or over with current FU approaches. 2. To determine their satisfaction levels with services provided. 3. To identify unmet needs specific to older patients.
Methods: 179 male and female patients aged > 60 with confirmed IBD who had attended FU services for at least one year were identified from the hospital's IBD database. A postal Likert-type satisfaction tool was used, with prepaid reply envelopes, and reminder letters sent once to non-responders. Quantitative and qualitative data was collected to elicit views on current FU services. Quantitative data was analysed using SPSS. Qualitative data was grouped into themes where possible.
Results: 52 patients responded (29%). Mean age was 67 (range 60-79) and median length of diagnosis 30 (4-60) years. Overall, satisfaction levels with FU arrangements were mixed. 49% respondents disagreed with the idea of telephone appointments replacing face-to-face appointments.

"Screen capture of BarcelonaWC web."

73% knew how to get in touch between appointments; of these, 49% had concerns about messages being picked up. Mean satisfaction scores were lower for email vs telephone contact (1.75 vs 3.11). 92% patients were confident about their IBD medications; 60% were confident to alter a dose, but only 22% were happy to start new medications by telephone.
Conclusions: Telephone FU replacing traditional appointments was not well received in this group, differing from other data in younger age groups suggesting such a service would be well recieved ((Bager et al 2013). Concerns were also raised about telephone and email access between appointments with lower satisfaction scores than previously reported in the literature(Pearson 2006, Cima 2007). More work is needed to determine if these findings are specific to this patient group, or a general view of the services provided at this hospital.

NO003
Development of a Web-based application to improve quality of life in IBD patients.

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Background: One of the major concerns of most people living with IBD is the unpredictable and urgent nature of defecation. The fear of urgent diarrhea and not getting to the toilet in time results in a significant curtailing of activities and can lead to a loss of self-worthiness and isolation. Loss of bowel control can have a devastating effect on psychological wellbeing and quality of life of IBD patients.
There is an acute scarcity of public toilets in most spanish cities. In Barcelona there is no city run public toilet system, however there are a thousand public bathrooms (in public facilities and municipal spaces) unknown to the majority of citizens. To facilitate their location would help IBD people to get on with everyday life outside the home.
This research aims to develop a web-based resource designed to give information on public toilets in the city of Barcelona, and to investigate if BarcelonaWC web use can improve the wellbeing and the quality of life in IBD patients.
Methods: The method used was "user-centred design". BarcelonaWC prototype was design in collaboration with a Crohn's disease patient who works as a computer engineer and undergoes regular follows-up at the IBD outpatient clinic.
To evaluate the prototype and its usability a before-after pilot study with no control group was conducted. A questionnaire pack comprising the IBDQ and an *ad hoc* satisfaction survey was used.
Descriptive statistics for qualitative variables and Paired samples t-tests for quantitative data.
This study was approved by Hospital del Mar Research Ethics Committee. A Creative Commons © license was obtained
Results: A total of 12 IBD patients were included in the pilot study. There were statistically significant differences between the before-after IBDQ scores [124 ± 39,06 vs 140,58 ± 40,59] and the feedback received from the patients group was very positive. Suggestions received will be used to improve website content.
Conclusions: Management of people with a chronic illness must go beyond the strictly medical. The incorporation of technology in health care has encouraged the creation of applications and web-based resources that provide solutions to real problems for people dealing with IBD, such as the location of public toilets in a city.
Preliminary study results showed the use of BarcelonaWC web is a step in the direction of improving quality of life of IBD patients. Final prototype will be available within 3 months time.
Acknowledgement: special thanks to Antartich, whose expertise and commitment have been vital to the project.

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Nurses presentations

Nurses poster presentations

N001
IBD clinical nurse specialist telephone advice lines: a clinical audit on the standard of information and outcomes.

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Background: Inflammatory Bowel Disease (IBD) clinical nurse specialists (CNS) provide direct telephone access via 'advice lines' to support patients during disease relapses (Phillips, 1995, Mowat et al., 2011). The intention is to analyse the nursing advice given in relation to the current IBD guidelines, and patients' clinical outcome.
Methods: A retrospective audit of 50 randomly selected telephone calls received to the telephone service at a large tertiary London hospital between 1st of March 2013 until 28th of February 2014 was undertaken. Records generated from the calls were retrieved and further analysis was restricted to patients who called to discuss a relapse of their IBD divided according to disease type. The documented advice was compared with the recommendations of the current IBD management guidelines (Dignass et al. 2010; Dignass et al. 2012b; Mowat et al. 2011). The documented patient outcomes following the calls were also analysed.
Results: Fifty four percent (n=27/50) of calls were from patients reporting a relapse; ulcerative colitis (UC; n=17) and Crohn's disease (CD; n=10). 96% (n=16/17) of UC and 60% (n=6/10) of CD patients were dealt with by advice, and the advice given was consistent with the guidelines in all cases. 100% of the UC and 100% of CD group had their call returned within the next working day (IBD Standards Group, 2013).
Six patients re-called the service after two weeks and the majority (n=5/6) were provided with further advice to manage their relapse. Two patients were provided with a clinic appointment within 5 working days (IBD Standards Group, 2013) and three patients were advised to attend the emergency department and an elective admission to hospital was arranged for a further patient (n=1).
Twelve patients required involvement by the patient's general practitioner for a medication prescription (n=9) or consultation (n=3).
Conclusions: This audit has demonstrated that the IBD CNS plays a pivotal role in the management of patients experiencing a relapse. They reply promptly, offer clinical advice compliant within the published IBD standards and optimise patient outcomes by directing patients towards an appropriate service: clinic appointment, hospital admission or medical therapy via the GP according to needs. Future studies should explore whether the use of disease severity indexes including HBI and SCCAI (Harvey et al. 1980; Walmsley et al. 1998) during the telephone nursing assessment may allow better assessments particularly to monitor progress for repeated calls. The tools may enhance communication with the GP whereby a score highlights the disease severity which may be delivered via brief email message with treatment recommendations.

N002
Healthcare professional advice to patients regarding topical therapies in Inflammatory Bowel Disease

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Background: A combination of both topical (suppositories or enemas) with oral mesalazines are first line treatments for mild to moderately active left sided colitis1,2 . There is evidence that topical therapy achieves higher rectal mucosal mesalazine concentrations than oral therapy3, Members of the UK Royal College of Nursing4 (RCN) IBD Nurse network in London and southeast region perceived there was variability in the advice given to patients prescribed topical treatments and aimed to investigate this.
Methods: An online audit was conducted between April-October 2014. A 20-item questionnaire was developed using Survey Monkey®. The questionnaire link was distributed by email to nurse members of the UK RCN IBD Network with a request to additionally forward it to non-IBD nurse colleagues.
Results: Healthcare professionals (HCPs) (86) who completed the questionnaire included nurses n=70, Gastroenterologist n=8, Specialist medical Registrar n=7, ward nurse n=1. Thirty eight responders were independent prescribers. The majority reported that patients generally accept topical treatments (69/86, 80%). The main barrier for using topical treatments was perceived as the patient's unwillingness to use (65/86,(76%), inconvenience to patients (50/86, 58%), inability to retain the treatment (51/86, 59%) and poor patient education on its use (42/86, 49%). Site of disease (81/86, 94%) and previous clinic efficacy (72/86, 84%) were the top influences to choose topical therapy. During patient education some professionals used examples of products to show the patient (25/86, 29%), used booklets (23/86, 27%) or visual aids (38/86, 44%). Patients were advised to lie down (44/86, 51%) or to use however they find comfortable (33/86, 38%) to administer topical preparations. Night time was the most usual time to advise patients to use the preparation (67/86, 78%). Lubricant use was advised by 34 (40%) professionals. Patients were advised to use topical treatment until symptoms improve (46/86, 53%). Only 46/86 (53%) of healthcare professionals felt that they had adequate information to give to patients.
Conclusions: HCPs perceive that patients accept topical treatment. However there are significant variations in advice and education provided. There appears to be a paucity of supporting educational aids. A further questionnaire study is planned exploring the patient's experience of using topical treatment.

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N003
Quality of life improves after intravenous iron treatment - but not if inflammation is present

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Background: Having inflammatory bowel disease (IBD) increases the risk of anaemia and/or iron deficiency. Intravenous administration of iron supplementation is often chosen when treatment in given.

Intravenous iron have proven good effect on correcting both anaemia and iron deficiency. However, the effect on the patients' health-related quality of life (HRQoL) has only slightly been investigated. Some patients expect a rapid effect on HRQoL parameters (such as less fatigue) after iron infusions. Can iron infusions fulfil this expectation? The aim of this study was to investigate outpatients HRQoL before and after intravenous iron infusions.

Methods: 60 outpatients treated at the Department of Hepatology and Gastroenterology, Aarhus University Hospital, filled in a 10 item questionnaire regarding HRQoL before intravenous iron infusion and 12 weeks after. Furthermore demographics and disease related data were collected, including blood samples.

A matched group from the background population (n = 60) was used as controls regarding the HRQoL questionnaires.

Results: The mean iron dose given was 1000 mg and the mean increase in haemoglobin levels were 2 g/dl at week 12. All HRQoL parameters improved significantly ($p < 0.05$) from baseline to week 12, except from physical activity, worries and depression.

At week 12 the level of physical activity and overall wellbeing were as in the background population.

16 (27%) patients with active inflammation (elevated CRP), both at baseline and week 12, did not have any significant improvement in HRQoL in the study period.

Conclusions: Intravenous iron infusion broadly improved HRQoL after 12 weeks in patients without active inflammation. This was not the case for patients with active inflammation. Inflammation seems to have a greater negative impact on HRQoL than the expected positive impact of intravenous iron infusions.

N004
Audit into the prevalence of injection site reaction following subcutaneous administration of adalimumab

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Background: During patient contact, the nurse specialist team had been made aware of a number of patients reporting injection site reaction following subcutaneous administration of adalimumab.

The patients had reported the incidents when reviewed in the outpatients department or via our telephone helpline. They represented all geographical areas served by the health board.

It was felt appropriate by the nurse specialist team to audit how prevalent these reactions where.

Methods: 50 patients receiving adalimumab therapy were randomly selected from the database held by the nurse specialist team. No one geographical site or consultant was prioritised. Patients who had stopped taking the medication where excluded. Patient anonymity was maintained by using their unique computer reference code.

A questionnaire was sent out by an independent secretary and the returned forms came back to the nurse specialist team. The returned forms were anonymous.

Results: Questionnaires where sent out to 50 patients of which 34 (68%) replied. The majority of patients had Crohn's Disease 31 (91%), 3 (9%) had IBD indeterminate and none had ulcerative colitis. Of the 34 who replied 10 (29%) reported an injection site reaction. The injection site used in all 10 patients was the abdomen and the reactive site or area had been used for subcutaneous injection previously in all patients. Of the 10 patients who had reacted, 8 (80%) self-administered and 2 (20%) had their injection administered by a relative. The most common reaction was a significant bruise which was noted by 8 of the patients, a subcutaneous rash and / or blister was next common and noted in 6 patients and injection site infection was only noted by 1 patient. All patients were aware of the correct procedure for pre injection cleaning and administration of the medication, including site rotation. Only one patient stated they felt that more input from the nurses would be beneficial.

Conclusions: Injection site reactions following subcutaneous administration of adalimumab was present in around a third (29%) of those surveyed. It is worth noting that not all patients felt that a bruise following a subcutaneous injection could be seen as a reaction. There was however greater concern regarding blistering at the injection site. The support given by the nurse specialist team was deemed appropriate and patients stated that they were aware of the sterile technique and safe administration of adalimumab. The exact reason for these reactions remains unclear. Repeated injections in the same area (although not exact site) appears to be a factor. Unfortunately a full review of site choice and use falls outside of the scope of this audit, however this could form a more in-depth future study.

N005
Emotional Stress and its Influence in the Clinical Evolution of Inflammatory Bowel Disease (IBD)

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Background: Inflammatory Bowel Disease (IBD) is an immunological condition, with two types being more representative and common: Ulcerative colitis (UC) and Crohn's disease (CD). IBD is important because: it is a worldwide chronic condition; it is becoming more common; it is complex to deal with; there is no cure; and responses to clinical treatment and surgery vary.The objective was to understand the influence of emotional stress and its significance in relation to the clinical evolution of patients with IBD.

Methods: Qualitative clinical treatment. This study examined fifty-three patients of both gender between the ages of 18 to 74 with IBD at the "Dr. Juvenal Ricardo Navarro Goes" Ambulatory Unit of the Diagnostic Center of Gastrointestinal Disease (GASTROCENTRO) of FCM-UNICAMP and a particular clinical in São Paulo/SP. A semi-structured interview was used to evaluate the following aspects: a) their knowledge of IBD; b) the feeling that IBD represents to them; c) the way in which they live with the symptoms of the disease; d) the feelings they felt the moment they were hospitalized. Data collection also included an examination of the patients' medical and life histories.

Results: The findings in the selected categories show that: a) 60% of the patients knew little about the disease; b) the feeling/significance of the disease for 75% of the patients was of much suffering, stress and solitude; c) 98% of them had felt infirm, both in the exacerbation of their condition and in its remission, in unique and singular ways, with consequences both psychological (anxiety, fear and depression) and social (isolation); d) 90% reported that they felt much anguish in relation to hospitalization due to its unpredictability.

Conclusions: The influence of emotional stress in the life of a human, whether young, middle-aged or old, in situations of conflict, was found to be relevant to the clinical evolution of this disease and its consequences, which can have various impacts on the organism depending on the individual's awareness of the disease and the psychological and biological resources that each individual can call upon to face it.

N006
Inflammatory Bowel Disease (IBD)Nurse Advice Line: A Single Centre Experience

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Background: The IBD standards 2013 stipulate that all IBD patients with concerns or questions regarding their disease should have access to a dedicated telephone service that is either answered or has an answer phone facility providing a response by the end of the next working day, those experiencing a possible relapse of their IBD should have access to specialist review within a maximum of five working days. The IBD advice line in Beaumont Hospital is accessed via an answerphone service which is available 24 hours a day and processed over 1,100 calls in 2013. Calls are prioritised and returned by the IBD Nurse from Monday to Thursday. Patients are educated regarding the IBD advice line at clinic visits.The aim of this audit was to identify the nature and outcome of calls to the IBD advice line.

Methods: 50 consecutive calls to the advice line were retrospectively reviewed by the IBD Nurse.

Results: Eighteen patients called with either a flare of IBD symptoms or an IBD related concern, 12 patients were referred for urgent Out Patients Appointments, and 2 were referred directly to endoscopy, with the remaining 4 needing only telephone advice.

The IBD Nurse is responsible for monitoring laboratory results of out patients on Thiopurines, Methotrexate and subcutaneous anti TNF medication.

10 calls related to blood test scheduling or were requests for laboratory results.

5 patients called requesting repeat prescriptions for IBD Medication

7 calls were related to administration issues such as change of address/telephone number or queries regarding scheduled appointments, letters of support etc

4 calls were related to medical queries that did not relate to IBD and these callers were referred to their General Practitioner (GP)

5 calls related to concerns such as emigration and transfer of medical care

1 person rang to say thanks for advice already received and to give an update on symptoms

Conclusions: The IBD advice line is pivotal in ensuring early access to specialist service for those experiencing a flare of their IBD. It also plays an essential role in supporting patients on treatments for their IBD. The number of calls regarding administration issues during the audit is noted and an information leaflet outlining the role of the IBD advice line service has been developed.

N007
Application of new technologies as educational tool for Inflammatory Bowel Disease patients

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Background: The internet offers a wealth of information for patients with chronic disease, facilitating education and self-control training; however this information can be inaccurate. The aim of this study was to evaluate the integration of an own educational IBD-dedicated website in clinical practice to promote education and patient support for IBD

Methods: Quality questionnaires were conducted in our IBD Unit, identifying a demand of 85% to have a reliable educational website, what prompted a project that included the multidisciplinary approach and the patient education. The website http://www.educainflamatoria.com/, has been developed since 2012 and it is structured into several sections including: Multidisciplinary training section, with an integrating view of the different clinical specialties related to the IBD. Self-care education section, with different questionnaires of self-control and positive management habits. Interactive section with medical specialists, where patients can ask questions about their disease. The site is continuously updated and it is supplemented with a twitter account: @educaEICI, with specific pieces of advice and news.

Results: An interactive presentation with patients and their families was performed in November 2013, in order to improve the website by providing suggestions. After the open access, our website has been registering a continuous increase in the number of users, achieving an average monthly of 2361 sessions and 15 questions, until October 2014. The website currently appears as link from different Spanish IBD associations (ACCU, GETECCU), and it is used by patients from other health care areas.

Conclusions: 1) New technologies can be integrated into the management of IBD Units increasing their quality of healthcare with their educational work. 2) Patients successfully interact with the website supported by their IBD Unit, registering a progressive increase in their use. 3) Our next goal will be to analyze the increase of knowledge and self-control between patients that employ the website.

N008
Assessing levels of fatigue and symptom reporting of fatigue in patients with Inflammatory Bowel disease

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Background: Inflammatory Bowel disease is a chronic condition which affects approximately 20,000 people in Ireland. It typically affects an age group of between 15-35 years of age and a person can be well for long periods or have repeated flare-ups. There is no cure and treatment can vary from person to person.

Fatigue is a problem associated with chronic conditions and may be underestimated in young people with inflammatory bowel disease. Fatigue can be physical, mental or both and can have a major impact on daily functioning.

Literature on fatigue related to inflammatory bowel disease was not available in the Rep. of Ireland

Methods: Patients reviewed by the Clinical Nurse Specialist expressed fatigue as a major symptom. Information on fatigue was not available for patients. A questionaire was devised and patients attending the out-patients department where randomly selected to complete the questionaire which included the Fatigue Severity Score. Fifty two patients completed the questionnaire over a 4 week period.

Results: Fatigue has been identified as a problem for patients with inflammatory bowel disease. Overall 93% of patients experinced fatigue with 58% experience severe symptoms of fatigue during relapse.

Sixty one per cent of patients reported fatigue as among their top three disabling symptoms rated from the Fatigue Severity Score.

38% of patients where asked by a health care professional about fatigue as a symptom and 62% were not asked.

Conclusions: Fatigue is a major problem for patients with Inflammatory Bowel Disease.Health care professionals need to acknowledge fatigue as a sypmtom.

The information leaflet produced in the Rep. of Ireland in 2013 by the author provides information on fatigue and how to cope.

N009
The knowledge gained by a novice Inflammatory Bowel Disease nurse in the first year of service in comparison to experienced IBD nurses knowledge.

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Background: The IBD nurse (IBDN) specialist role in Australia is relatively new; however there is an increasing demand for this type of service, as outcomes for Inflammatory Bowel Disease (IBD) patients have been proven to be superior where IBDNs are available. The IBD Unit at the Royal Adelaide Hospital has 2 experienced IBDNs (expIBDN), starting in 2008 and 2011 respectively. In January 2014 a new IBDN was appointed. A non-gastroenterology trained nurse was employed from a background of Burns nursing. The challenge was to up skill the novice IBDN (novIBDN) without formal IBDN education being readily or locally accessible.

Methods: Education was provided as follows:

° On the job education from the expIBDNs and IBD medical staff (sitting in on IBD clinic with the Unit Head, attending MDT meetings, listening in to "virtual" clinic)

° Attendance at several IBD conferences and evening lectures

° Self-directed learning

Questionnaires relating to IBD knowledge were completed by the novIBDN on her first day of employment and again 11 months later. The questionnaires used comprised: CCKnow and Leong which test general IBD knowledge and the CCPKnow which specifically assesses IBD-specific pregnancy-related knowledge. ExpIBDNs (from Royal Adelaide Hospital and Flinders Medical Centre - n=4) completed the same questionnaires (once only).

Results: All 4 expIBDNs scored 100% on the Leong questionnaire, as did the novIBDN both at initial and repeat testing. On the CCKnow questionnaire, experienced IBDNs scored between 10-12/12 (mean 11.5/12; 96%) and the novice scored 100% at both time points. On the CCPKnow, expIBDNs scored between 15-17/17 (mean 15.8; 93%), whilst the novIBDN scored 12/17 (71%) at baseline and 17/17 (100%) at follow-up.

The novIBDN also reported clear improvement in self-perceived IBD knowledge and specifically noted: confidence in being able to independently handle the blood monitoring schedule (for patients on thiopurines and biologics); greater confidence in biologic initiations, safety monitoring, prescribing restrictions and pre-screening; and a growing independence in handing helpline calls.

Conclusions: Current IBD knowledge questionnaires are insufficiently sensitive to assess differential IBD awareness in registered nurses in Australia, except for the CCPKnow, which specifically addresses pregnancy/fertility issues. This emphasises that pregnancy/fertility are areas of poor general medical/nursing knowledge outside of IBD units. On the job training in a specialty IBD unit delivers clear gains in knowledge and confidence in IBDNs over a year, however, formal educational assessments and training modules should be developed to ensure quality and consistency of practice standards.

N010
Flowchart-based monitoring of IBD patients on biological treatment

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Background: Biological agents have been shown to be an effective, but expensive treatment to induce and maintain clinical remission in patients with IBD, i.e. ulcerative colitis and Crohn's disease.

Biological treatment requires special attention to ensure correct indication, choice of drug and dosage as well as possible concomitant medication with immunomodulators. Accordingly, it is important to monitor patients regularly as regards therapeutic response and development of side effects.

There is increasing, international focus on optimizing the clinical course of IBD patients to ensure objective assessment of clinical activity and achievement of defined treatment goals, such as mucosal healing. This requires regular clinical controls with activity indices, blood tests, stool cultures, cross sectional imaging modalities (MR scanning), and endoscopy. Moreover, the biological treatment must be monitored with trough levels and antibody assessment. Concomitant treatment with thiopurin immunomodulators may also require an individualized approach based on metabolite measurements. Finally, it is also important that patients attending an IBD clinic are monitored closely in a

way that allows documentation of whether the standard of care complies with international standards, such as those produced by ECCO and other leading organisations.

To provide an overview on the clinical course during biological treatment that facilitates structured and uniform management of high quality

Methods: We have developed a set of flowcharts for structured care of patients on biological treatment. A flowchart is essentially a time line scheme with predefined clinical visits, assessments and examinations based on best practice management. There is a unique flowchart for each of the biological drugs, we use, and each patient will have their own scheme monitoring their clinical course. Each flowchart covers 0-1,5 year of treatment. At present, we have 210 patients on biological treatment in which the flowchart is being gradually implemented.

Results: The project started with a pilot phase and after review and feedback, the charts have subsequently been revised to fit the requirements in clinical practice. We now plan to evaluate the clinical value of this tool by registration of adherence to scheduled tests and examinations, including endoscopy, as well as by questionnaires to physicians, nurse staff and patients.

Conclusions: We have developed and implemented flowcharts that appear to facilitate more uniform management and systematic collection of relevant activity scores, blood tests and examinations during biological treatment in patients with IBD.

This increases quality of care in IBD nursing.

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