Agenda MDS ELN WP8, Mannheim 31-01-2012

General issues	
•Future of ELN MDS WP8 / EHA MDS WP	P. Fenaux
•Report activities WP8 for ELN Newsletter	All
•Cooperation with Pharma	All
EU-MDS Registry	
•Future meetings	All
•Iron substudy	M.MacKenzie
•EPO - studies	A. Smith (E. Hellström-Lindbergh)
•Diabetis Mellitus	A. Symeonidis
•Cytopenias	R. Itzykson / P. Fenaux
•Quality of Life	R. Stauder
•Proteomics	D. Bowen
•Cytology review	M. MacKenzie
Translational research / biobanking:	
relationship with EUMDS-Registry activities	J. Jansen (E. Hellström-Lindbergh)
GO MDS - application 7th FP EU	T. de Witte
Platform for international studies, progress	U. Platzbecker
Flow cytometry on MDS, report Pavia meeting	A. v.d. Loosdrecht
Therapeutic guidelines	L. Malcovati, M. Cazzola

Evidence based Guidelines for Optimal treatment of patients with lower risk Myelodysplastic Syndrome (MDS)

GO-MDS

GO-MDS

De novo Low risk and intermediate-1 MDS patients

Current EUMDS registry 1200 subjects in 13 European countries, median follow up 18 months

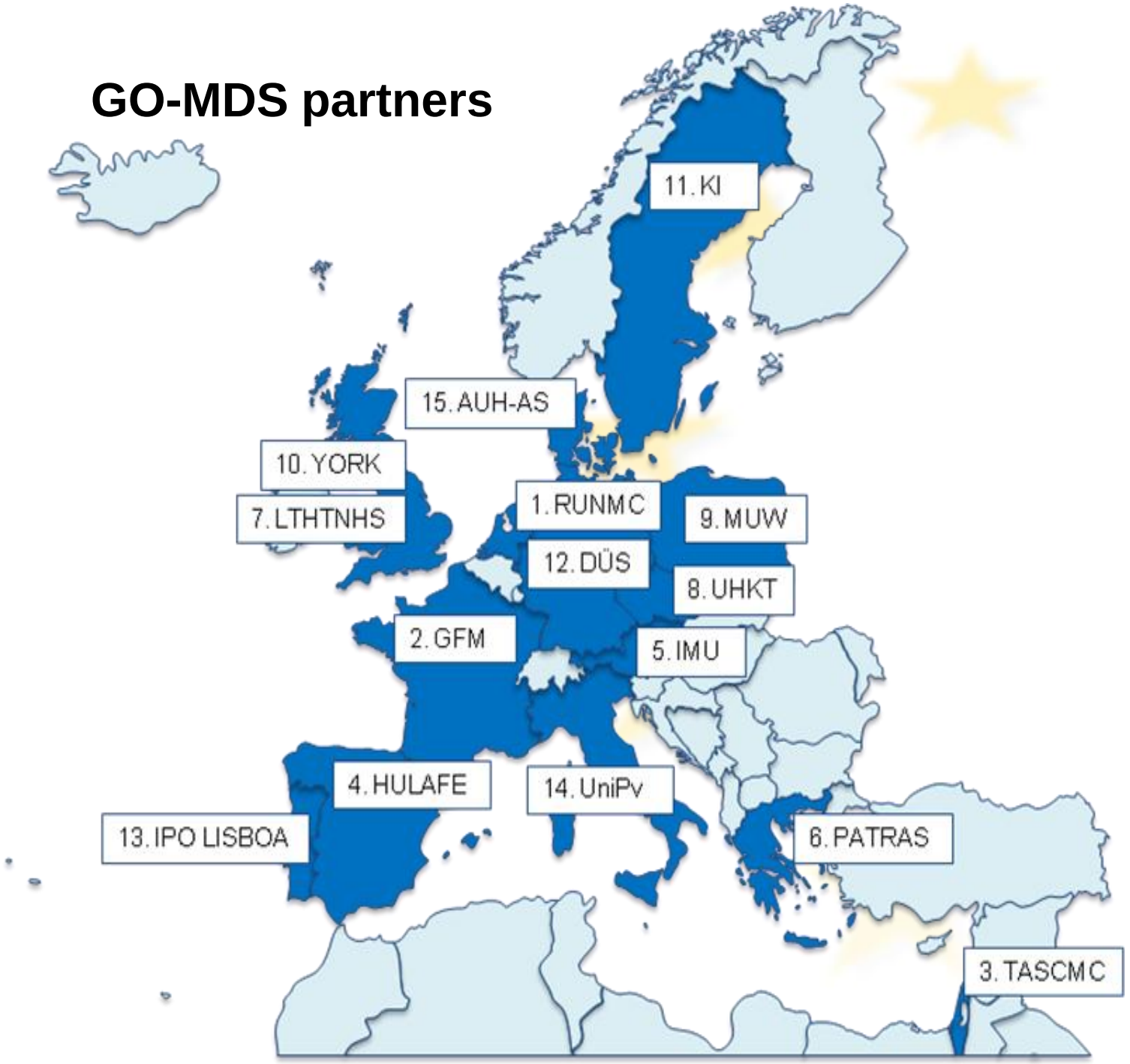
Increased mortality and impaired Quality of Life due to bone marrow failure

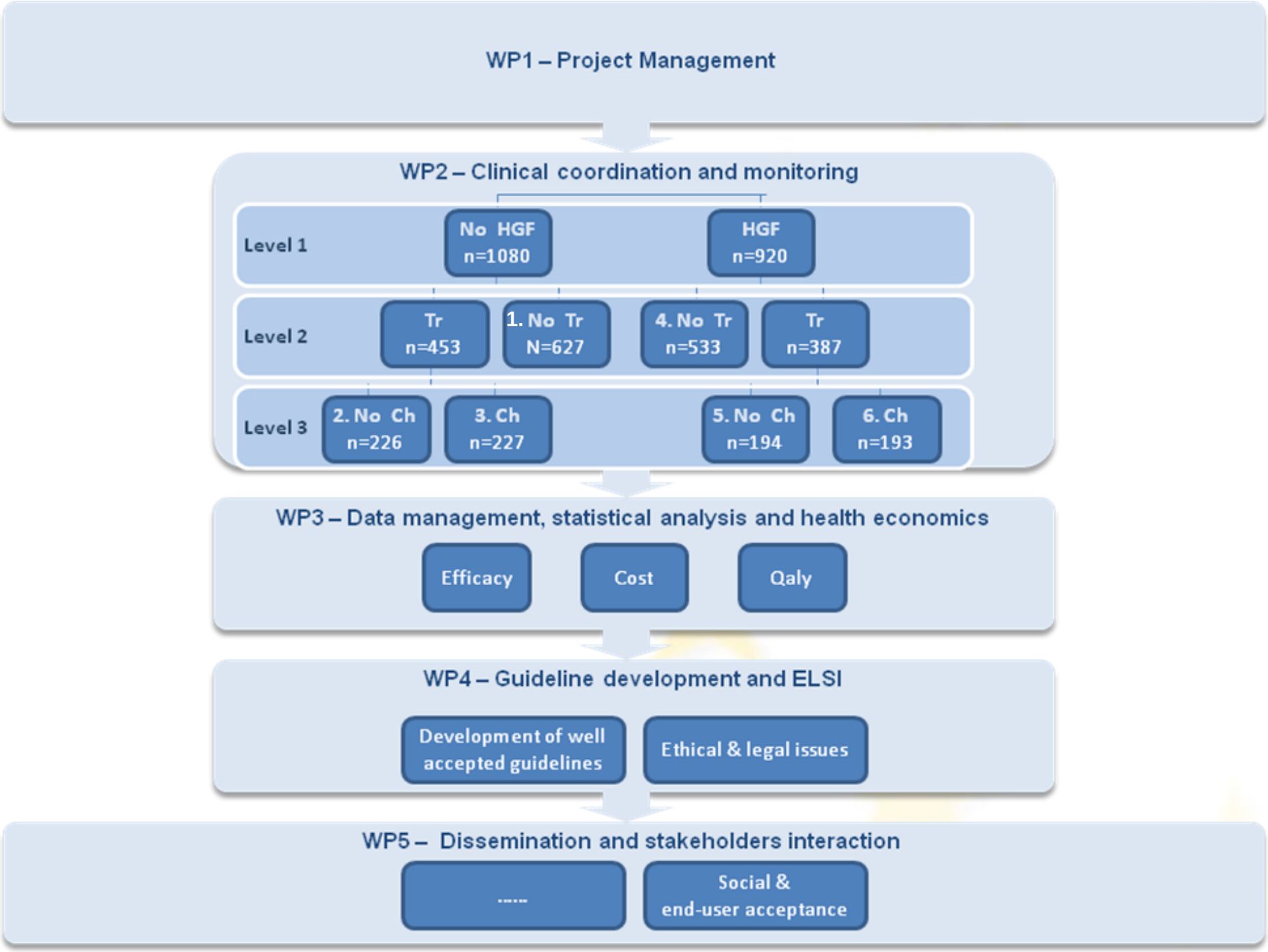
Major impact: severe anaemia for which 3 treatment options: HGFs, transfusions and iron chelation

Aim: development and implementation of guidelines for optimal treatment of lower risk MDS

Treatment	MDS patients treated (%)	Efficacy	Annual cost per patient (€)	ELSI
HGF	46%	Retrospective studies showed a survival advantage of HGF treatment: HR of 0.43 (P<0.005) and HR of 0.61; p=0.002 respectively (Park et al. 2008; Jadersten et al. 2008; Casadevall et al., 2004; Ross et al. 2003). Early treatment with HGFs prolongs time to transfusion need (Park et al. 2010).	19.263	Ethical analysis must balance prognosis, survival, and quality of life with cost of treatment (Goss et al. 2006).
Tr	42%	A regular need for blood transfusion is associated with a significantly lower probability of survival (HR of, 1.58; P = 0.005) (Cazzola et al. 2005).	8.158	Still missing
Ch	9% at 18 months will increase to 21% (50% of the transfusion dependent patients) at 5 year follow-up	A retrospective analyses by the GFM in 97 regularly transfused patients adequately treated with iron chelation showed an improved survival with a HR of 0.3 (p<0.003) compared to a control group not treated with iron chelation (Rose et al. 2010).	12.000 (s.c.) to 24.000 (oral)	Though oral medication may be preferred by the patient, clinicians supervision of injectable or infusible medication may provide better compliance (Kogan et al. 2009)

GO-MDS partners




WP1 – Project Management
WP2 – Clinical coordination and monitoring
Level 1
No HGF n=1080
HGF n=920
Level 2
Tr n=453
1. No Tr N=627
4. No Tr n=533
Tr n=387
Level 3
2. No Ch n=226
3. Ch n=227
5. No Ch n=194
6. Ch n=193
WP3 – Data management, statistical analysis and health economics
Efficacy
Cost
Qaly
WP4 – Guideline development and ELSI
Development of well accepted guidelines
Ethical & legal issues
WP5 – Dissemination and stakeholders interaction
.....
Social & end-user acceptance

Time schedule FP7 Call

Publication of call	*20 July 11*
Deadline for submission of stage one proposals	*04 October 11,*
Evaluation of stage one proposals	*2 December 11*
Letter to coordinators of successful stage one proposals invitation to submit a full stage two proposal	*08 December 11*
Coordinators informed of results of stage one proposals	*end-December 11*
Deadline for submission of stage two proposals	*08 February 2012 , 17:00:00 Brussels time*
Evaluation of stage two proposals *Finalised by beginning of*	*April 2012*
Coordinators informed of results of stage two proposals	*April 2012*
Invitation letter to successful coordinators to launch grant agreement negotiations with Commission services	*April 2012*
Letter to unsuccessful applicants	*April 2012*
Signature of first grant agreements	*September 2012*

Do we need an ELN based MDS studies coordinating office ?

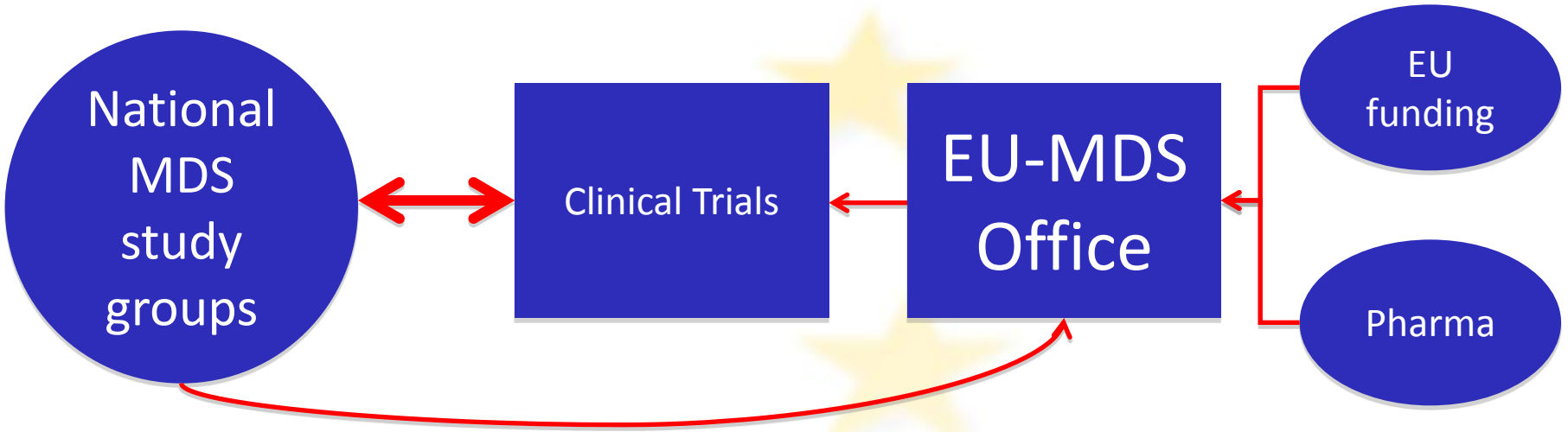
U. Platzbecker
Medizinische Klinik und Poliklinik I
Universitätsklinikum „Carl Gustav Carus“ Dresden

Advantages of an ELN MDS Studies Coordination Office

- Goal: to improve the quality of clinical MDS research

- Initiate discussion on:
  - Standardization and international cooperation
  - Exchange of relevant information regarding designed / planned / ongoing clinical trial
  - a “common arm” in randomized studies
- Enabling:
  - IITs within different MDS groups
  - fast patient recruitment
  - More meaningful clinically relevant conclusions
  - Common data analyses from trials

ELN MDS Studies Coordination Office



ELN MDS Studies Coordination Office

Phase 1 (2012):

1. Agreement from ELN MDS Group that they would like to set-up an MDS Studies Coordination Office

2. Set-up a common trial (GFM/GMDS-SG)
- sharing biostatistician, possibly CRAs, data collection and management with the goal
- to identify hurdles and practical problems (e.g. submission to IRB and national authorities, insurance, central randomization, monitoring etc.)

ELN MDS Studies Coordination Office

Phase 2 (2013): also depending on phase 1,

1. Final agreement to set-up an ELN MDS Studies Coordination Office
2. Decide the name and location (suggestion: "EMSCO" = **E**uropean **M**DS **S**tudies **C**oordinating **O**ffice)
3. Decide which studies e.g. Phase I/II/III/IV and countries to be involved
4. Set-up Committee to present idea to Pharma.
6. Use funding from studies to make ELN MDS Group financially independent.

Summary

1. The complexity of MDS requires better collaboration in clinical trials within the EU

2. ELN – ideal platform

3. Importance of clinical trial office

4. A stepwise set-up suggested

5. Robust infrastructure and funding is needed

Flow Cytometry in Myelodysplastic Syndromes

Arjan A. van de Loosdrecht, MD, PhD
Theresia M. Westers, PhD
On behalf of the ELN flowcytometry group in MDS

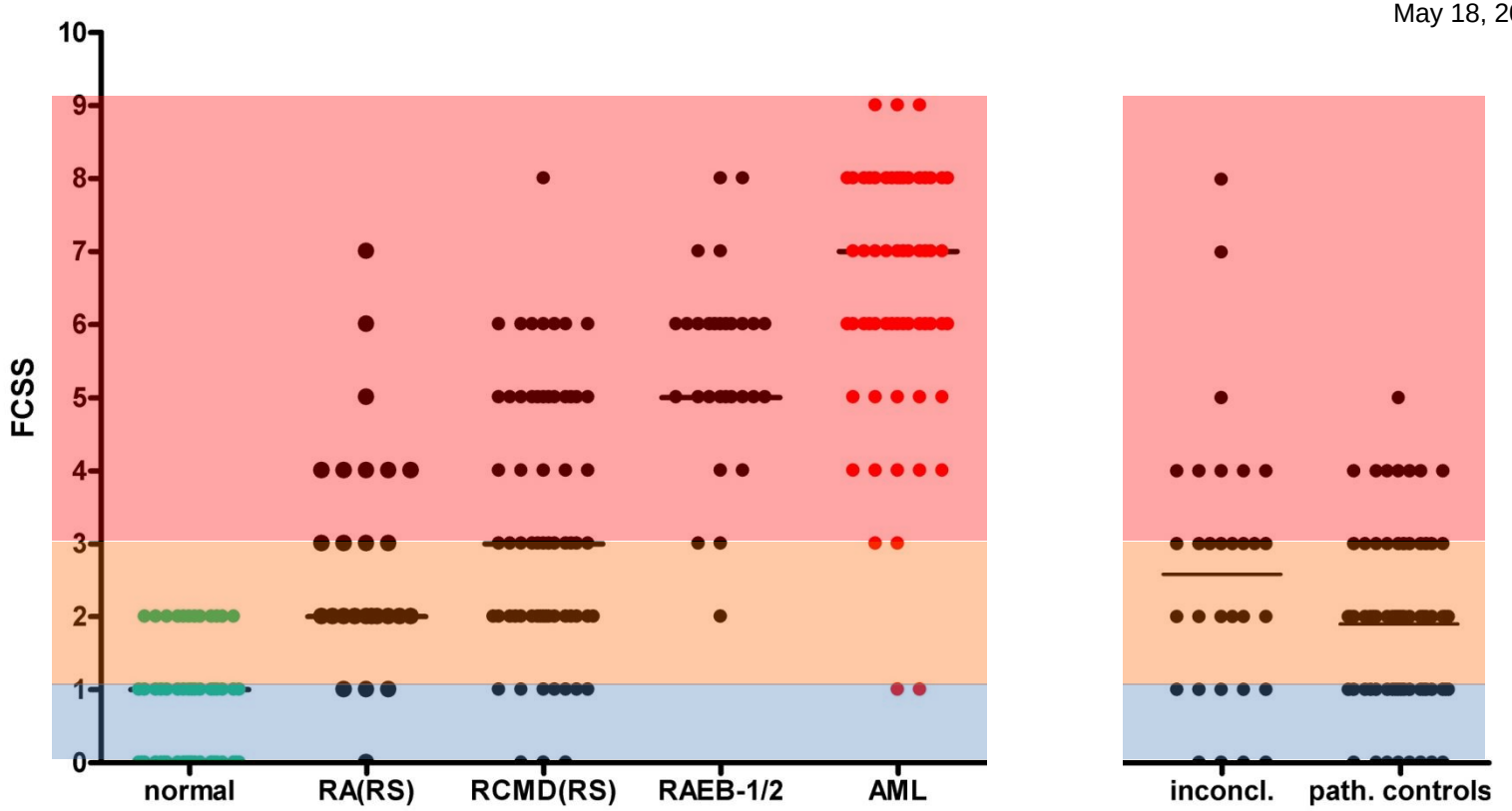
Department of Hematology
VU University Medical Center
VU-Institute of Cancer and Immunology (V-ICI)
Cancer Center Amsterdam (CCA)
Amsterdam, The Netherlands

Mannheim Jan 31 2012

ELN European LeukemiaNet

Flow cytometric scoring system and WHO2008

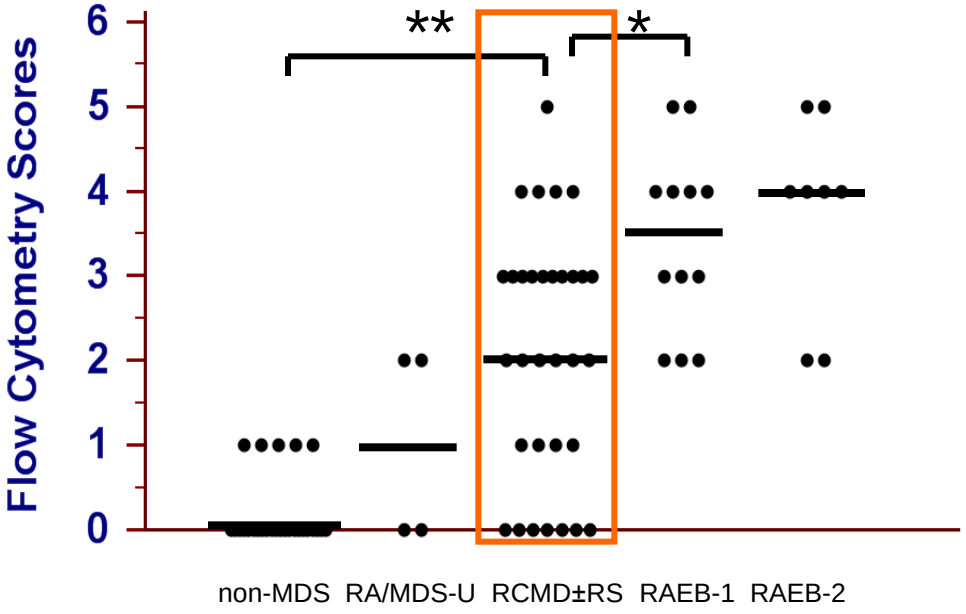
May 18, 2011

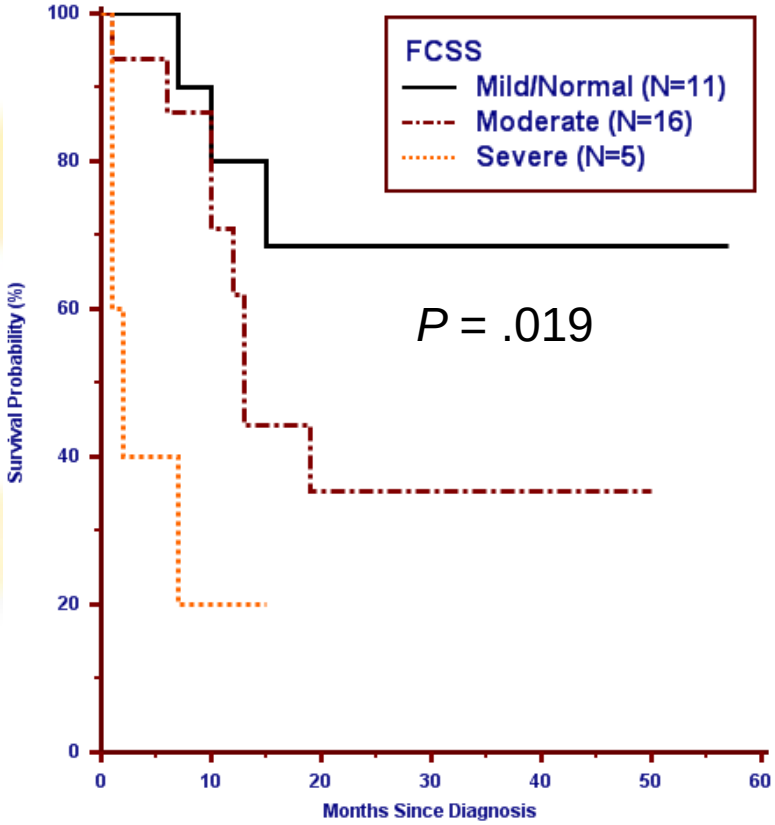


n=55 n=26 n=70 n=32 n=62

Van de Loosdrecht and Westers et al., Blood, 2008
Alhan et al., unpublished data (May 18; 2011)

FCSS in MDS-RCMD is associated with worse overall survival





Chu SC et al., Leuk Res 2011:35:868-73; Ogata K. Leuk Res 2011:35:848-9
Van de Loosdrecht AA et al., Leuk Res 2011:35:850-2

Current Activities of WP on MDS/FC

- Submission of clinical implementation document ELNet *[consensus]* [< March 1th]
- Focus on dysplastic erythropoiesis: a retrospective multicenter study [initiated]
- Prognostic models beyond FCSS: A retrospective multicenter study [initiated]
- **Collaboration with the Dutch prospective validation study in low risk MDS [HOVON89: lenalidomide +/- Epo/G-CSF]**
- 5th international flow/MDS ELN meeting q4-2012 (Amsterdam, NL)

Diagnosis and treatment of primary MDS in adults Recommendations from the European LeukemiaNet

- First complete draft ready: 29-01-2011
- First authors: Mario Cazzola and Luca Malcovati
- First review by core authors (6): February 2012
- Second review by all co-authors (20): April 2012
- Submission Blood June 2012

Diagnosis and treatment of primary MDS in adults Recommendations from the European LeukemiaNet

1. Introduction
2. Design and Methods
    - 2.1 Systematic review of the literature and synthesis of evidence
    - 2.2 Consensus phase
3. Diagnostics Procedures
    - 3.1 Morphology
    - 3.2 Bone marrow biopsy
    - 3.3 Flow cytometry immunophenotyping
    - 3.4 Cytogenetics
    - 3.5 Molecular genetics
4. Classification

5. Risk assessment

- 5.1 Disease-related factors
- *5.1.1 Prognostic relevance of somatic mutations*
- 5.2 Patient-related factors

6. Therapeutic options

- 6.1 Watchful-waiting strategy
- 6.2 Human Leukocyte Antigen (HLA)-typing
- 6.3 Allogeneic stem cell transplantation
- 6.4 Remission induction chemotherapy
- 6.5 Low dose chemotherapy
- 6.6 Hypomethylating agents
- 6.7 Hematopoietic growth factors
- 6.8 Immunomodulatory drugs
- 6.9 Immunosuppressive therapy
- 6.10 Red cell transfusion and iron chelation therapy

7. Discussion

Therapeutic algorithm for adult patients with primary MDS and intermediate-2 or high IPSS score