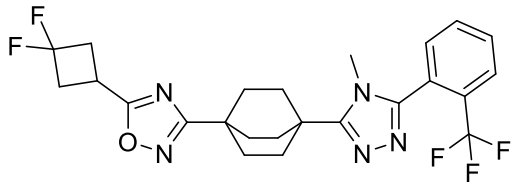
Product data sheet

MedKoo Cat#: 406833 Name: MK-4101 CAS#: 935273-79-3 Chemical Formula: $C_{24}H_{24}F_5N_5O$ Exact Mass: 493.1901 Molecular Weight: 493.482	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

MK-4101 is a potent and selective inhibitor of the Hedgehog Pathway. MK-401 Is Highly Active against Medulloblastoma and Basal Cell Carcinoma. MK-4101 showed anti-tumor activity through the inhibition of proliferation and induction of extensive apoptosis in tumor cells. MK-4101 was highly efficacious against primary medulloblastoma and BCC developing in the cerebellum and skin of Ptch1(+/-) mice. MK-4101 targets the Hh pathway in tumor cells, showing the maximum inhibitory effect on Gli1 MK-4101 also induced deregulation of cell cycle and block of DNA replication in tumors.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	59.0	119.56
Ethanol	64.0	129.69

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.03 mL	10.13 mL	20.26 mL
5 mM	0.41 mL	2.03 mL	4.05 mL
10 mM	0.20 mL	1.01 mL	2.03 mL
50 mM	0.04 mL	0.20 mL	0.41 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Filocamo G, Brunetti M, Colaceci F, Sasso R, Tanori M, Pasquali E, Alfonsi R, Mancuso M, Saran A, Lahm A, Di Marcotullio L, Steinkühler C, Pazzaglia S. MK-4101, a Potent Inhibitor of the Hedgehog Pathway, Is Highly Active against Medulloblastoma and Basal Cell Carcinoma. Mol Cancer Ther. 2016 Jun;15(6):1177-89. doi: 10.1158/1535-7163.MCT-15-0371. Epub 2016 Mar 9. PMID: 26960983.

In vivo study

1. Filocamo G, Brunetti M, Colaceci F, Sasso R, Tanori M, Pasquali E, Alfonsi R, Mancuso M, Saran A, Lahm A, Di Marcotullio L, Steinkühler C, Pazzaglia S. MK-4101, a Potent Inhibitor of the Hedgehog Pathway, Is Highly Active against Medulloblastoma and Basal Cell Carcinoma. Mol Cancer Ther. 2016 Jun;15(6):1177-89. doi: 10.1158/1535-7163.MCT-15-0371. Epub 2016 Mar 9. PMID: 26960983.

Product data sheet

7. Bioactivity

Biological target:

MK-4101 is a Smoothened (SMO) antagonist (IC50 of 1.1 μM for 293 cells) and also a potent inhibitor of the hedgehog pathway (IC50 of 1.5 μM for mouse cells; IC50 of 1 μM for KYSE180 oesophageal cancer cells).

In vitro activity

To further dissect the mechanism of tumor growth inhibition by MK-4101 and confirm microarray data, medulloblastoma and BCC single-cell suspensions were treated with a saturating dose MK-4101 (10 μmol/L) to maximize effects. Cell cycle was analyzed by FACS monitoring EdU incorporation. Medulloblastoma cells treated with MK-4101 for 60 hours showed cell-cycle arrest with a nearly complete disappearance of the S-phase subpopulation, a prominent increase of the G1 population and, to a minor extent, of the G2 population, indicative of a cell-cycle block in these two phases (Fig. 6A). Moreover, an increase in the sub-G1 population was observed, indicative of underlying cell death. BCC cells treated with MK-4101 for 72 hours showed similar, although less pronounced effect (Fig. 6B), probably due to the lower growth rate of BCC compared with medulloblastoma cells. The cell-cycle blocks in G1–S and G2–M phases were confirmed by a remarkable decrease in cyclin D1 protein and accumulation of cyclin B1 protein, detected by Western blot analysis after MK-4101 treatment both in medulloblastoma and BCC tumor cells (Fig. 6C and D). Altogether, these results confirmed that MK-4101 inhibits medulloblastoma and BCC tumor growth by arresting cell cycle and inducing apoptosis.

Reference: Mol Cancer Ther. 2016 Jun;15(6):1177-89. https://pubmed.ncbi.nlm.nih.gov/26960983/

In vivo activity

To further investigate the efficacy of MK-4101, primary medulloblastomas from neonatally irradiated Ptch1+/− mice, a highly penetrant model with 80% of mice developing full-blown medulloblastoma by 20 weeks of age were focused on. Quantification of tumor size in a subset of P1-irradiated Ptch1+/− mice (n = 5) of 8 weeks of age show an incidence of preneoplastic lesion of 80% (4/5) and an average size of 0.28 mm2 (range 0.053–0.75 mm2). It was therefore asked whether treatment with MK-4101 (80 mg/kg twice a day) at this stage could prevent medulloblastoma formation and improve mouse survival. By the end of the treatment (17 weeks of age), none (0/24) of the MK-4101–treated mice had developed medulloblastoma-related lethargy, compared with over 50% (13/23) of the vehicle-treated mice (Fig. 3A), demonstrating that MK-4101 treatment significantly improved survival (P = 0.0002). A significant brain weight decrease of 17% was detected in MK-4101–treated animals as compared with vehicle-treated mice (0.501 vs. 0.604 g; P = 0.0004, Fig. 3B), reflecting the absence of tumor masses in the brains of MK-4101–treated animals. Moreover, highly significant differences in medulloblastoma incidence (P < 0.0001), between vehicle- (13/23) and MK-4101–treated mice (0/24), were revealed by histologic examination (Fig. 3C–E). Only four of MK-4101–treated mice (17%) presented small ectopic foci of abortive tumor cells on the cerebellar surface (Fig. 3E). Collectively, these data showed that treatment with MK-4101 efficaciously eliminates both early and more progressed medulloblastoma stages.

Reference: Mol Cancer Ther. 2016 Jun;15(6):1177-89. https://pubmed.ncbi.nlm.nih.gov/26960983/