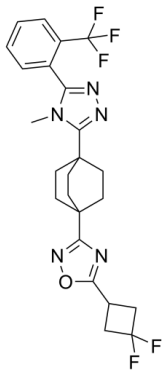
Data Sheet

Product Name:	MK-4101
Cat. No.:	CS-5749
CAS No.:	935273-79-3
Molecular Formula:	$C_{24}H_{24}F_5N_5O$
Molecular Weight:	493.47
Target:	Apoptosis; Hedgehog; Smo
Pathway:	Apoptosis; Stem Cell/Wnt
Solubility:	DMSO : ≥ 50 mg/mL



BIOLOGICAL ACTIVITY:

MK-4101 is a **Smoothened (SMO)** antagonist (**IC_{50}** of 1.1 μM for 293 cells) and also a potent inhibitor of the **hedgehog pathway** (**IC_{50}** of 1.5 μM for mouse cells; **IC_{50}** of 1 μM for KYSE180 oesophageal cancer cells). MK-4101 has robust antitumor activity that inhibits tumor cell proliferation and induces extensive **apoptosis**[1]. IC50 & Target: IC50: 1.1 μM (293 cells); 1.5 μM (mouse cells); 1 μM (KYSE180 oesophageal cancer cells)[1] ***In Vitro:*** MK-4101 inhibits Hh signaling both in a reporter gene assay in an engineered mouse cell line with an **IC_{50}** of 1.5 μM, and in human KYSE180 oesophageal cancer cells with an **IC_{50}** of 1 μM. MK-4101 displaces a fluorescently-labeled cyclopamine derivative from 293 cells expressing recombinant human SMO with an **IC_{50}** of 1.1 μM, implying that the compound binds to SMO. MK4101 also inhibits the proliferation of medulloblastoma cells derived from neonatallyirradiated $Ptch1^{-/+}$ mice in vitro with an **IC_{50}** of 0.3 μM[1].

MK-4101 (10 μM; 60 hours, 72 hours; medulloblastoma or BCC cells) treatment shows 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 [1].

MK-4101 (10 μM; medulloblastoma or BCC cells) treatment significantly reduces cyclin D1 protein and accumulation of cyclin B1 protein[1]. ***In Vivo:*** MK-4101 (40-80 mg/kg; oral administration; for 3.5 weeks; CD1 nude female mice) treatment shows tumor growth inhibition (40 and 80 mg/kg) and tumor regression at the highest dose (80 mg/kg). MK-4101 treatment shows a dose-dependent down-regulation of Gli1 mRNA. The maximum effect for tumor inhibition and hedgehog pathway downregulation is achieved at 80 mg/kg[1].

References:

[1]. Filocamo G et al. 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.

CAIndexNames:

1,2,4-Oxadiazole, 5-(3,3-difluorocyclobutyl)-3-[4-[4-methyl-5-[2-(trifluoromethyl)phenyl]-4H-1,2,4-triazol-3-yl]bicyclo[2.2.2]oct-1-yl]-

SMILES:

FC(C1=CC=CC=C1C2=NN=C(C34CCC(C5=NOC(C6CC(F)(F)C6)=N5)(CC4)CC3)N2C)(F)F

Caution: Product has not been fully validated for medical applications. For research use only.

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