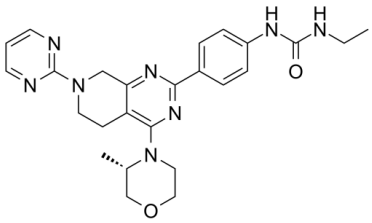
Data Sheet

Product Name:	mTOR inhibitor-3
Cat. No.:	CS-1383
CAS No.:	1207358-59-5
Molecular Formula:	C25H30N8O2
Molecular Weight:	474.56
Target:	mTOR
Pathway:	PI3K/Akt/mTOR
Solubility:	DMSO : 50 mg/mL (105.36 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

mTOR inhibitor-3 is a remarkably selective **mTOR** inhibitor with a K_i of 1.5 nM. mTOR inhibitor-3 suppresses **mTORC1** and **mTORC2** in cellular and in vivo pharmacokinetic (PK)/pharmacodynamic (PD) experiments. IC50 & Target: Ki: 1.5 nM (mTOR)[1] mTORC1, mTORC2[1] **In Vitro:** mTOR inhibitor-3 (Compound 12i) inhibits mTOR with a K_i of 1.5 nM, 500-fold selectivity over closely related PI3 kinases. mTOR inhibitor-3 inhibits NCI-PC3 and MCF7neo/Her2 cells proliferation with IC_{50}s of 150 nM and 57 nM, respectively[2]. **In Vivo:** mTOR inhibitor-3 (Compound 8h) has high free plasma clearance in both mice (1818 mL/min/kg) and rats (1538 mL/min/kg in rat) [1]. mTOR inhibitor-3 (Compounds 12i) is selected for this study due to its potency, selectivity, and favorable mouse PK profile. Plasma levels of mTOR inhibitor-3 6 h following oral administration in PC3 tumor-bearing mice along with the fold decreases of phosphorylated mTORC1 and -2 substrates relative to time-matched vehicle controls. mTOR inhibitor-3 has moderate terminal elimination half-life ($t_{1/2}$=1.7 h for mouse(1 mg/kg, iv)). mTOR inhibitor-3 achieves tumor stasis at the highest 200 mg/kg/day dose examined, which appears to also be approaching the limit of tolerability for this molecule[2].

PROTOCOL (Extracted from published papers and Only for reference)

Animal Administration: mTOR-IN-1 (Compounds 12i) is formulated as suspensions in 0.5% methylcellulose/0.2% Tween 80 (MCT) (Mice)[2].[2]Mice[2]

Human prostate cancer NCI-PC3 cells are implanted subcutaneously into the right hind flanks of female NCR nude mice (5×10^6 cells in 100 µL of Hank's balanced salt solution). Tumors are monitored until they reach a mean tumor volume of approximately 500 mm^3. Then similarly sized tumors are randomly assigned to groups (n=4). Compounds are formulated as suspensions in 0.5% methylcellulose/0.2% Tween 80 (MCT) and dosed orally at 25, 50, and 100 mg/kg (100 µL dose/25 g animal). Tumor and plasma samples are harvested at 1, 6, and 10 h postdose.

References:

[1]. Pei Z, et al. Discovery and Biological Profiling of Potent and Selective mTOR Inhibitor GDC-0349. ACS Med Chem Lett. 2012 Nov 29;4(1):103-7.

[2]. Koehler MF, et al. Potent, selective, and orally bioavailable inhibitors of the mammalian target of rapamycin kinase domain exhibiting single agent antiproliferative activity. J Med Chem. 2012 Dec 27;55(24):10958-71.

CAIndexNames:

Urea, N-ethyl-N'-[4-[5,6,7,8-tetrahydro-4-[(3S)-3-methyl-4-morpholinyl]-7-(2-pyrimidinyl)pyrido[3,4-d]pyrimidin-2-yl]phenyl]-

SMILES:

O=C(NC1=CC=C(C2=NC(N3[C@@H](C)COCC3)=C4C(CN(C5=NC=CC=N5)CC4)=N2)C=C1)NCC

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

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