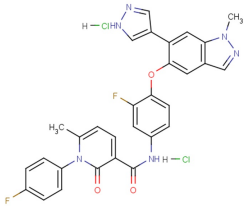
Data Sheet (Cat.No.T15808)

TargetMol
A DRUG SCREENING EXPERT

Merestinib dihydrochloride

Chemical Properties



CAS No.:	1206801-37-7
Formula:	C30H24Cl2F2N6O3
Molecular Weight:	625.45
Appearance:	N/A
Storage:	0-4℃ for short term (days to weeks), or -20℃ for long term (months).

Biological Description

Description	Merestinib dihydrochloride is an effective and orally bioavailable c-Met inhibitor (Ki=2 nM). It has anti-tumor activities and also has potent activity against MST1R (IC50=11 nM), FLT3 (IC50=7 nM), AXL (IC50=2 nM), MERTK (IC50=10 nM), TEK (IC50=63 nM), ROS1, DDR1/2 (IC50=0.1/7 nM) and MKNK1/2 (IC50=7 nM).
Targets(IC_{50})	c-Met: (ki)2 nM MST1R: 11 nM FLT3: 7 nM AXL: 2 nM MERTK: 10 nM TEK: 63 nM DDR1/2: 0.1/7 nM MKNK1/2: 7 nM
In vitro	Merestinib demonstrates the effects on MET pathway-dependent cell scattering and cell proliferation. The mean IC50 value (n=6 determinations) of Merestinib for inhibition of MET auto-phosphorylation in HGF-stimulated H460 cells is 35.2±6.9 nM and the IC50 for MET auto-phosphorylation in S114 cells is 59.2 nM. Merestinib also inhibits MST1R (IC50=11 nM), AXL (IC50=2 nM), MERTK (IC50=10 nM), TYRO3 (IC50=28 nM), ROS1, PDGFRA (IC50=41 nM), FLT3 (IC50=7 nM), TEK (IC50=63 nM), DDR1/2 (IC50=0.1/7 nM) and MKNK1/2 (IC50=7 nM)[1]. Merestinib (2, 5, and 10 μM) decreases the number of viable TFK-1 and SZ-1 cells in a dose and time-dependent manner, and significant inhibits wound healing for TFK-1 and SZ-1 cell lines. Transfection with the MET variants confers growth-factor independence and treatment with Merestinib inhibits the growth of these MET variant clones with an IC50 ranging from 3-fold more potent (V1092I) to approximately 6-fold less potent (L1195V) compare with the growth inhibition of cells with the MET wild-type sequence[1]. Merestinib inhibits cell invasion in TFK-1 and SZ-1 cells in a concentration-dependent manner[2].
In vivo	Merestinib is a type-II ATP competitive, slow-off inhibitor of MET tyrosine kinase with a pharmacodynamic residence time (Koff) of 0.00132 min-1 and t1/2 of 525 min. Merestinib (20 mg/kg) decreases TFK-1 tumor growth significantly relative to vehicle control. Merestinib treatment inhibits MET phosphorylation with a composite TED50 (50 % target inhibition dose) of 1.2 mg/kg and a composite TED90 (90 % target inhibition dose) of 7.4 mg/kg[1]. Merestinib inhibits the growth of intra- and extrahepatic CCC xenograft tumors[2]. Merestinib demonstrates anti-tumor effects in MET amplified (MKN45), MET autocrine (U-87MG, and KP4), and MET over-expressed (H441) xenograft models; and in vivo vessel normalization effects.

Solubility Information

Solubility	DMSO: 100 mg/mL (159.88 mM) (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.599 mL	7.994 mL	15.988 mL
5 mM	0.32 mL	1.599 mL	3.198 mL
10 mM	0.16 mL	0.799 mL	1.599 mL
50 mM	0.032 mL	0.16 mL	0.32 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. The storage conditions and period of the stock solution: - 80 ℃ for 6 months; - 20 ℃ for 1 month. Please use it as soon as possible.

Reference

1. Yan SB, et al. LY2801653 is an orally bioavailable multi-kinase inhibitor with potent activity against MET, MST1R, and other oncoproteins, and displays anti-tumor activities in mouse xenograft models. Invest New Drugs. 2013 Aug;31(4):833-44.
2. Barat S, et al. Targeting c-MET by LY2801653 for treatment of cholangiocarcinoma. Mol Carcinog. 2016 Jan 12.

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