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产品名称：Altiratinib
产品别名： DCC-2701

生物活性：

Description

Altiratinib (DCC-2701) is a multi-targeted kinase inhibitor with IC50s of 2.7, 8, 9.2, 9.3, 0.85, 4.6, 0.83 nM for MET, TIE2, VEGFR2, FLT3, Trk1, Trk2, and Trk3 respectively.

IC_{50} & Target

VEGFR2	Trk1	Trk2	Trk3
9.2 nM (IC_{50})	0.85 nM (IC_{50})	4.6 nM (IC_{50})	0.93 nM (IC_{50})
MET	TIE2	FLT3	
2.7 nM (IC_{50})	8 nM (IC_{50})	9.3 nM (IC_{50})	

In Vitro

Altiratinib also inhibits MET isoforms MET^{D1228H}, MET^{D1228N}, MET^{Y1230C}, MET^{Y1230D}, MET^{Y1230H}, MET^{M1250T} with IC_{50}s of 3.6, 1.3, 1.2, 0.37, 1.5 and 6 nM, respectively. Altiratinib inhibits MET phosphorylation with IC_{50}values of 0.85 and 2.2 nM, respectively. In the U-87 glioblastoma cell line, MET and HGF are both expressed. Altiratinib blocks autocrine activation of MET phosphorylation in these cells (IC_{50}=6.2 nM). Altiratinib potently inhibits cellular proliferation in MET-amplified EBC-1 and MKN-45 cells, as well as TPM3-TRKA fusion KM-12 cells. Activation of MET is known to increase the motility and invasiveness of cancer cells: Altiratinib inhibits HGF-induced A549 cell migration, with an IC_{50} of 13 nM. Altiratinib also inhibits FLT3-ITD mutant MV-4-11 cell proliferation with an IC_{50} of 12 nM[1].

In Vivo

A single oral dose of 30 mg/kg Altiratinib leads to >95% inhibition of MET phosphorylation for the entire 24-hour period. A single 10 mg/kg oral dose of Altiratinib exhibits complete inhibition of MET phosphorylation through 12 hours and 73% inhibition at 24 hours postdose. Altiratinib dosed at 10 mg/kg twice a day leads to a significant 90% decrease in BLI signal. Altiratinib exhibits properties amenable to oral administration and exhibits substantial blood–brain barrier penetration, an attribute of significance for eventual treatment of brain cancers and brain metastases[1].

Solvent&Solubility

In Vitro:

DMSO : ≥ 33 mg/mL (64.65 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9590 mL	9.7951 mL	19.5902 mL
	5 mM	0.3918 mL	1.9590 mL	3.9180 mL
	10 mM	0.1959 mL	0.9795 mL	1.9590 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

References

[1]. Smith BD, et al. Altiratinib Inhibits Tumor Growth, Invasion, Angiogenesis, and Microenvironment-Mediated DrugResistance via Balanced Inhibition of MET, TIE2, and VEGFR2. Mol Cancer Ther. 2015 Sep;14(9):2023-34.

实验参考：

Cell Assay	Altiratinib is dispensed into assay plates. Cells are added to 96-well (EBC-1, M-NFS-60, and SK-MEL-28: 2,500 cells/well; MKN-45: 5,000 cells/well; MV-4-11: 10,000 cells/well) or 384-well plates (A375 and HCT-116: 625 cells/well; BT-474, KM-12, PC-3, and U-87-MG: 1,250 cells/well). Plates are incubated for 72 hours. Viable cells are quantified using resazurin using a plate reader with excitation at 540 nm and emission at 600 nm[1].
Animal Administration	Mice: Female nude mice are inoculated subcutaneously. On days 9 to 10, when tumor volumes reached 326 mg on average, mice are randomly assigned to groups and dosed once orally with 0.4% HMPC, (n=3); Altiratinib at 30 mg/kg (n=21); or Altiratinib at 10 mg/kg (n=21). At specified time points, whole blood and tumors are collected. Pharmacokinetic analysis is performed. Tumor samples are processed in the Western blot assay methods[1].
References	[1]. Smith BD, et al. Altiratinib Inhibits Tumor Growth, Invasion, Angiogenesis, and Microenvironment-Mediated DrugResistance via Balanced Inhibition of MET, TIE2, and VEGFR2. Mol Cancer Ther. 2015 Sep;14(9):2023-34.