Ilorasertib hydrochloride

Cat. No.: HY-16018A

CAS No.: 1847485-91-9

Molecular Formula: $C_{25}H_{22}ClFN_6O_2S$

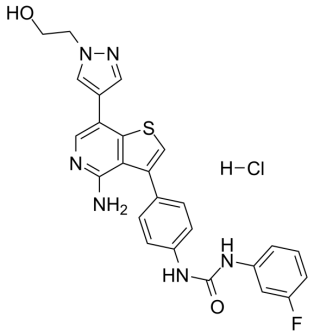
Molecular Weight: 525

Target: Aurora Kinase; PDGFR; VEGFR

Pathway: Cell Cycle/DNA Damage; Epigenetics; Protein Tyrosine Kinase/RTK

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 41.67 mg/mL (79.37 mM; Need ultrasonic)

Preparing Stock Solutions	Concentration / Solvent / Mass	1 mg	5 mg	10 mg
	1 mM	1.9048 mL	9.5238 mL	19.0476 mL
	5 mM	0.3810 mL	1.9048 mL	3.8095 mL
	10 mM	0.1905 mL	0.9524 mL	1.9048 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (3.96 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.96 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Ilorasertib (ABT-348) hydrochloride is a potent, orally active and ATP-competitive aurora inhibitor with IC_{50}s of116, 5, 1 nM for aurora A, aurora B, aurora C, respectively. Ilorasertib hydrochloride also is a potent VEGF, PDGF inhibitor. Ilorasertib hydrochloride has the potential for the research of acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS)[1][2].

IC_{50} & Target

Aurora C 1 nM (IC_{50})	Aurora B 7 nM (IC_{50})	Aurora B (Y156H) 12 nM (IC_{50})	Aurora A 120 nM (IC_{50})
PDGFRα 11 nM (IC_{50})	PDGFRβ 13 nM (IC_{50})	VEGFR1 1 nM (IC_{50})	VEGFR2 2 nM (IC_{50})
VEGFR3 43 nM (IC_{50})	FLT3 1 nM (IC_{50})	CSF-1R 3 nM (IC_{50})	c-KIT 20 nM (IC_{50})

In Vitro

Ilorasertib hydrochloride (0, 3, 10, 30 nM; 24 h) induces a concentration-dependent increase in the extent and number of H1299, H460 cells[2].
Ilorasertib hydrochloride (1-1000 nM) shows antiproliferative activity[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[2]

Cell Line:	H1299, H460 cells
Concentration:	0, 3, 10, 30 nM
Incubation Time:	24 h
Result:	Induced a concentration-dependent increase in the extent and number of cells exhibiting polyploidy with EC_{50}S of 5, 10 nM for H1299, H460 cells, respectively.

Cell Proliferation Assay[2]

Cell Line:	MV-4-11, SEM, K562, HCT-15, SW620, H1299, H460 cells
Concentration:	1-1000 nM
Incubation Time:	
Result:	Showed antiproliferative activity with IC_{50}s of 0.3, 1, 103, 6, 6, 2, 2 nM for MV-4-11, SEM, K562, HCT-15, SW620, H1299, H460 cells, respectively.

In Vivo

Ilorasertib hydrochloride (6.25, 12.5, 25 mg/kg; p.o.) shows anti-tumor activity in MV-4-11 tumor-bearing SCID mice with TGI of 80%, 86%, 94% at 6.25, 12.5, 25 mg/kg, respectively[1].
Ilorasertib hydrochloride (6.25, 12.5, 25 mg/kg; p.o.) shows anti-tumor activity in SKM-1 tumor-bearing SCID mice with TGI of 38%, 59%, 80% at 6.25, 12.5, 25 mg/kg, respectively[1].
Ilorasertib hydrochloride (0, 3.75, 7.5, 15 mg/kg; i.p.) inhibits the histone H3 phosphorylation at 4-8 h in blood-borne tumor cells[2].
Ilorasertib hydrochloride (0.2 mg/kg; i.v.) shows anti-VEGF activity in mouse[2].
Ilorasertib hydrochloride (20 mg/kg; p.o.;once weekly for 3 weeks) shows anti-tumor activity in mouse[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female SCID/beige mice[2]
Dosage:	25 mg/kg
Administration:	Subcutaneous minipump; 24 h
Result:	Inhibited the histone H3 phosphorylation and the tumor drug concentration associated with 50% inhibition of histone H3 phosphorylation.

Animal Model:	22-26 g, female NOD/SCID mice (xenograft model of multiple myeloma (KMS11))[2]
Dosage:	20 mg/kg
Administration:	P.o.; once weekly for 3 weeks
Result:	Inhibited the tumor growth in mouse.

REFERENCES

[1]. Yi-Chun Wang, et al. Abstract 858: Potent in vivo activity of the aurora kinase inhibitor ABT-348 in human acute myeloid leukemia and myelodysplastic syndrome xenograft models. Cancer Res (2012) 72 (8_Supplement): 858.

[2]. Glaser KB, et al. Preclinical characterization of ABT-348, a kinase inhibitor targeting the aurora, vascular endothelial growth factor receptor/platelet-derived growth factor receptor, and Src kinase families. J Pharmacol Exp Ther. 2012 Dec;343(3):617-27.

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