Ilorasertib

Cat. No.: HY-16018

CAS No.: 1227939-82-3

Molecular Formula: $C_{25}H_{21}FN_6O_2S$

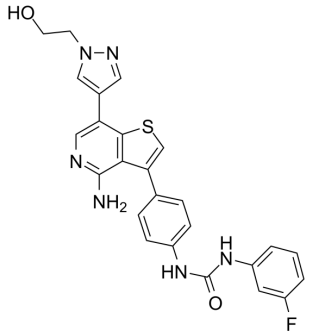
Molecular Weight: 488.54

Target: Aurora Kinase; VEGFR; PDGFR

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

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 41.67 mg/mL (85.29 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0469 mL	10.2346 mL	20.4692 mL
5 mM	0.4094 mL	2.0469 mL	4.0938 mL
10 mM	0.2047 mL	1.0235 mL	2.0469 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 (4.26 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (4.26 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Ilorasertib (ABT-348) 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 also is a potent VEGF, PDGF inhibitor. Ilorasertib 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 (0, 3, 10, 30 nM; 24 h) induces a concentration-dependent increase in the extent and number of H1299, H460 cells [2].

Ilorasertib (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 (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 (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 (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 (0.2 mg/kg; i.v.) shows anti-VEGF activity in mouse[2].

Ilorasertib (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]. Gao C, et al. Characterization of interactions and pharmacophore development for DFG-out inhibitors to RET tyrosine kinase. J Mol Model. 2015 Jul;21(7):167.

[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.

[3]. Curtin ML, et al. Thienopyridine ureas as dual inhibitors of the VEGF and Aurora kinase families. Bioorg Med Chem Lett. 2012 May 1;22(9):3208-12.

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