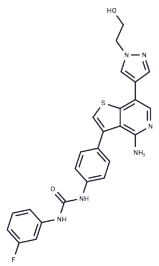
Data Sheet (Cat.No.TQ0059)

TargetMol

Ilorasertib

Chemical Properties



CAS No. : 1227939-82-3

Formula: C25H21FN6O2S

Molecular Weight: 488.54

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Ilorasertib (ABT-348) (ABT-348) is an ATP-competitive multitargeted kinase inhibitor, which inhibits Aurora A/Aurora B/Aurora C (IC50s: 120 nM/7 nM/1 nM). It also suppresses RET tyrosine kinase, PDGFRβ, and Flt1 (IC50s: 7 nM, 3 nM, and 32 nM).
Targets(IC50)	FLT,c-RET,Aurora Kinase,PDGFR,VEGFR
In vitro	In addition to targeting Aurora kinases, Ilorasertib is a potent inhibitor of the VEGFR and PDGFR kinase families and, to a lesser extent, the Src family of cytoplasmic tyrosine kinases. Ilorasertib induces a concentration-dependent increase in the extent and number of two NSCLC cell lines exhibiting polyploidy (EC50: 5, 10 nM). Ilorasertib shows antiproliferative activity against BCR-ABL expressing CML cells and cells expressing the Gleevec-resistant BCR-ABL T315I mutation (IC50: 47, 260 nM) [2].
In vivo	Ilorasertib inhibits the VEGF response with a potency (ED50: 0.2 mg/kg, i.v.) in a uterine edema model. Ilorasertib (25 mg/kg, s.c.) leads to an inhibition of histone H3 phosphorylation in circulating tumor cells obtained from an engrafted leukemia model. Ilorasertib (20 mg/kg, p.o.) inhibits the growth of established tumors and causes regression of advanced tumors in human xenograft models [2]. Ilorasertib demonstrates significant antitumor efficacy in both solid and hematological xenograft models after intravenous, mini-pump or parenteral once-weekly dosing [3].
Cell Research	Noncycling primary HUVEC are used to assess the effect of Ilorasertib on nonproliferating cells. Cells (35,000/well) are seeded in growth medium in a 96-well tissue culture plate, and after 2 days, the medium is changed and the cells are treated with Ilorasertib. After an additional 3 days, cell viability is measured with Cell TiterGlo reagent [2].
Animal Research	For flank xenograft models, cells are suspended in PBS, mixed with Matrigel (phenol red-free) in a ratio of 1:4 (v/v), and inoculated into the flank of female SCID/beige mice (5 million cells per site). Inoculated mice are randomized into groups of 10, and treatment is initiated when mean tumor volume is approximately 0.4 cm^3 or 0.5 cm^3. Tumor growth in the flank is assessed by measuring tumor size with calipers and calculating volume using the formula (L × W2/2). Study groups are terminated before tumor volume reaches 3 cm^3. Inhibition of tumor growth is assessed at the time the vehicle-treated group is terminated by calculating the ratio of the mean volume of the test drug group to the mean volume of the untreated (control) group (T/C) and calculating the percentage of inhibition of control [(1 ? T/C) × 100]. The dosing formulation of test agents is prepared by stepwise addition, with mixing, of the

Animal Research	following reagents: EtOH, Tween 80, polyethylene glycol 400, and 2% hydroxypropyl methylcellulose (2:5:20:73, v/v). The dosing volume is 10 mL/kg [2].

Solubility Information

Solubility	DMSO: 75 mg/mL (153.52 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+90% Saline: < 7.5 mg/mL (15.35 mM),Lower concentrations may be soluble, but exact solubility limit is unknown. 10% DMSO+40% PEG300+5% Tween 80+45% Saline: 7.5 mg/mL (15.35 mM),Solution. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
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
50 mM	0.0409 mL	0.2047 mL	0.4094 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

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.

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.

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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