Product Data Sheet

Product Name: Ilorasertib (ABT-348)
Cat. No.: GC34159

Chemical Properties

Cas. No.	1227939-82-3		
SMILES	O=C(NC1=CC=CC(F)=C1)NC2=CC=C(C3=CSC4=C3C(N)=NC=C4C5=CN(CCO)N=C5)C=C2		
Formula	$C_{25}H_{21}FN_6O_2S$	M.Wt	488.54
Solubility	DMSO : 83.33 mg/mL (170.57 mM);Water : < 0.1 mg/mL (insoluble)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	Ilorasertib (ABT-348)		

Protocol

Cell experiment: Carcinoma cells (2500 cells/well) are plated overnight in full-growth medium (containing 10% FBS). Compound is added to the cells in full-growth medium and incubated for 72 h at 37°C in a CO2 incubator. For leukemia cells, generally 50,000 cells/well are plated in full-growth medium, drug is added, and they are incubated for 72 h. The effects on proliferation are determined by the addition of alamarBlue (final solution 10%), incubation for 4 h, and analysis in a fluorescence plate reader (excitation 544; emission 590), or alternatively, medium is removed and replaced with 200 µL of Cell TiterGlo reagent and analyzed for luminescence. 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.

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Animal experiment:

sup>[2]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 cm3 or 0.5 cm3. 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 cm3. 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 following reagents: EtOH, Tween 80, polyethylene glycol 400, and 2% hydroxypropyl methylcellulose (2:5:20:73, v/v). Dosing volume is 10 mL/kg.

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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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Background

Ilorasertib is a multi-kinase inhibitor.[1] It inhibits Aurora C, VEGFR1, VEGFR2, FLT3, colony-stimulating factor 1 receptor (CSF1R), and Aurora B (IC_{50}s = 1, 1, 2, 1, 3, and 7 nM, respectively). It also inhibits PDGFRα, PDGFRβ, c-Kit, VEGFR3, and Aurora A (IC_{50}s = 11, 13, 20, 43, and 120 nM, respectively). Ilorasertib inhibits autophosphorylation of Aurora A, -B, and -C in HeLa cells with IC_{50} values of 189, 13, and 13 nM, respectively. It inhibits proliferation of a variety of cancer cells, including MV4-11 acute myeloid leukemia (AML), SUP-B15 acute lymphocytic leukemia (ALL), and H1299 non-small cell lung cancer (NSCLC) cells (IC_{50}s = 0.3, 4, and 2 nM, respectively). It decreases histone H3 phosphorylation in blood-borne tumor cells in an engrafted mouse model of leukemia when administered at a dose of 25 mg/kg and reduces tumor growth in fibrosarcoma, pancreatic carcinoma, ALL, and multiple myeloma mouse xenograft models.

1.Glaser, K.B., Li, J., Marcotte, P.A., 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 familiesJ. Pharmacol. Exp. Ther.343(3)617-627(2012)

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