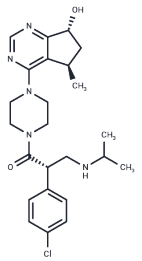
Data Sheet (Cat.No.T6252)

TargetMol

Ipatasertib

Chemical Properties



CAS No. : 1001264-89-6

Formula: C24H32ClN5O2

Molecular Weight: 458

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Ipatasertib (GDC-0068) is a selective, ATP-competitive pan-Akt inhibitor that inhibits Akt1 (IC50:5 nM), Akt2 (IC50:18 nM), and Akt3 (IC50:8 nM). Ipatasertib (GDC-0068) can lead to p53-independent PUMA activation by inhibiting Akt, thereby activating FoxO3a and NF-κB simultaneously, directly binding to the PUMA promoter, upregulating PUMA transcription and Bax-mediated intrinsic mitochondrial apoptosis.
Targets(IC50)	Akt
In vitro	**METHODS**: At 0, 3, 6, 12, and 24 hours after HCT116 cells were treated with Ipatasertib (GDC-0068) (1-20 μM), cell viability was detected in HCT116 by CCK-8 to study how ipatasertib affects tumor progression. **RESULTS** HCT116 cell viability decreased significantly with increasing dose or time, and Ipatasertib (GDC-0068) could inhibit cell proliferation in a dose- and time-dependent manner. [1] **METHODS**: HCT116 cells were treated with ipatasertib (GDC-0068) (10 μM), and the expression of p53 or PUMA in HCT116 WT and p53−/− was analyzed by Western blotting; ipatasertib (GDC-0068)-induced PUMA mRNA in WT, p53−/−HCT116 and DLD1 was analyzed by real-time qPCR and normalized to the housekeeping gene β-actin. **RESULTS** Ipatasertib (GDC-0068) treatment increased the expression level of PUMA with increasing doses; this upregulation was observed in WT (HCT116, RKO), p53 mutants (DLD1, HT29), and p53; Ipatasertib (GDC-0068) can lead to p53-independent transcriptional activation of PUMA and inhibit cell proliferation. [1]
In vivo	**METHODS**: Nude mice were subcutaneously injected with HCT116 WT or PUMA−/−, and model mice were treated with Ipatasertib (GDC-0068) (30 mg/kg, oral, 15 days). Representative tumors at the end of the experiment, tumor weights, and c tumor volumes at specified time points after treatment were calculated to investigate whether PUMA-mediated apoptosis is essential for the anti-tumor activity of ipatasertib. **RESULTS** Ipatasertib (GDC-0068) significantly inhibited the growth of WT tumors; immunohistochemical staining showed that the expression of P-Akt was reduced in both WT and PUMA; Ki67 was significantly reduced in WT tumors, but there was no significant change in PUMA; C-Caspase3 was significantly increased in WT tumors and slightly increased in PUMA; Ipatasertib (GDC-0068) has a PUMA-dependent anti-tumor effect in colon cancer. [1]
Kinase Assay	Kinase Assay: The fluorescence polarization assay for ATP competitive inhibition is done as follows: mPI3Kα dilution solution (90 nM) is prepared in fresh assay buffer (50 mM

	Hepes pH 7.4, 150 mM NaCl, 5 mM DTT, 0.05% CHAPS) and kept on ice. The enzyme reaction contains 0.5 nM mouse PI3Kα (p110α/p85α complex purified from insect cells), 30 μM PIP2, PF-04691502 (0, 1, 4, and 8 nM), 5 mM MgCl2, and 2-fold serial dilutions of ATP (0-800 μM). Final dimethyl sulfoxide is 2.5%. The reaction is initiated by the addition of ATP and terminated after 30 minutes with 10 mM EDTA. In a detection plate, 15 uL of detector/probe mixture containing 480 nM GST-Grp1PH domain and 12 nM TAMRA tagged fluorescent PIP3 in assay buffer is mixed with 15 uL of kinase reaction mixture. The plate is shaken for 3 minutes, and incubated for 35 to 40 minutes before reading on an LJL Analyst HT.
Cell Research	GDC-0068 is prepared in DMSO and stored, and then diluted with appropriate medium before use[2]. The 384-well plates are seeded with 2,000 cells per well in a volume of 54 μL per well followed by incubation at 37°C under 5% CO2 overnight (~16 hours). Compounds (e.g., GDC-0068) are diluted in DMSO to generate the desired stock concentrations then added in a volume of 6 μL per well. All treatments are tested in quadruplicates. After 4 days incubation, relative numbers of viable cells are estimated using CellTiter-Glo and total luminescence is measured on a Wallac Multilabel Reader. The concentration of drug resulting in IC50 is calculated from a 4-parameter curve analysis (XLfit) and is determined from a minimum of 3 experiments. For cell lines that failed to achieve an IC50, the highest concentration tested (10 μM) is listed[2].

Solubility Information

Solubility	DMSO: 85 mg/mL (185.59 mM),Sonication is recommended. Ethanol: 85 mg/mL (185.59 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.1834 mL	10.917 mL	21.8341 mL
5 mM	0.4367 mL	2.1834 mL	4.3668 mL
10 mM	0.2183 mL	1.0917 mL	2.1834 mL
50 mM	0.0437 mL	0.2183 mL	0.4367 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.

Reference

Sun L, et al. Ipatasertib, a novel Akt inhibitor, induces transcription factor FoxO3a and NF-κB directly regulates PUMA-dependent apoptosis. Cell Death Dis. 2018 Sep 5;9(9):911.
Huang Q, Ru Y, Luo Y, et al.Identification of a targeted ACSL4 inhibitor to treat ferroptosis-related diseases.Science Advances.2024, 10(13): eadk1200.
Blake JF, et al. Discovery and preclinical pharmacology of a selective ATP-competitive Akt inhibitor (GDC-0068) for the treatment of human tumors. J Med Chem. 2012 Sep 27;55(18):8110-27.
Buckingham L, et al. Ipatasertib, an oral AKT inhibitor, inhibits cell proliferation and migration, and induces apoptosis in serous endometrial cancer. Am J Cancer Res. 2022 Jun 15;12(6):2850-2862.
Heidi M. Savage, et al. Cancer Res, 2012, 72(8 Supplement), 966.
Roel Funke, et al. American Society of Clinical Oncology (ASCO) Annual Meeting, 1-5, 2012.

Tel:781-999-4286 E_mail:info@targetmol.com Address:36 Washington Street,Wellesley Hills,MA 02481