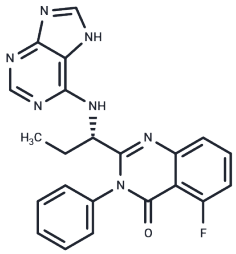
Data Sheet (Cat.No.T1894)

TargetMol

Idelalisib

Chemical Properties



CAS No. : 870281-82-6

Formula: C22H18FN7O

Molecular Weight: 415.42

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	Idelalisib (GS-1101) is a small molecule inhibitor of the PI3K catalytic subunit p110δ (IC50: 2.5 nM). The selectivity for p110δ is 40- to 300-fold than p110α/β/γ.
Targets(IC50)	Autophagy,PI3K
In vitro	Idelalisib is an oral p110δ inhibitor currently under clinical evaluation in patients with B-cell malignancies. Idelalisib was 40- to 300-fold more selective for p110δ relative to other PI3K class I enzymes (IC50 p110δ = 2.5nM; p110α, p110β, and p110γ IC50 were 820, 565, and 89nM, respectively). Greater selectivity (400- to 4000-fold) was seen against related kinases C2β, hVPS34, DNA-PK, and mTOR, whereas no activity was observed against a panel of 402 diverse kinases at 10μM [1]. Idelalisib promoted apoptosis in primary CLL cells ex vivo in a dose- and time-dependent fashion that was independent of common prognostic markers. Idelalisib-mediated cytotoxicity was caspase-dependent and was not diminished by coculture on stromal cells [2]. CAL-101 inhibits CLL cell chemotaxis toward CXCL12 and CXCL13 and migration beneath stromal cells (pseudoemperipolesis). Idelalisib also down-regulates secretion of chemokines in stromal cocultures and after BCR triggering. Idelalisib reduces survival signals derived from the BCR or from nurse-like cells, and inhibits BCR- and chemokine-receptor-induced AKT and MAP kinase (ERK) activation [3].
In vivo	A single intravenous dose of 40 mg/kg of Idelalisib, given 15 min before ischemia in wild-type mice (pre-treatment), significantly reduced infarction after 72 h. However, lower doses (20, 10 and 1 mg/kg) did not achieve significant protection. Importantly, even when given 3 h after the onset of reperfusion (post-treatment), a dose of 40 mg Idelalisib per kg body weight was still effective in reducing the infarct volume by an average of 44% compared with the vehicle-treated control group [4].
Kinase Assay	PI3K assay was performed on whole-cell lysates from CLL or normal B cells. A PI3K ELISA assay was performed according to the manufacturer's instructions. Briefly, whole-cell extracts were added to a mixture of PI(4,5)P2 substrate and reaction buffer containing adenosine triphosphate (ATP) and allowed to incubate at room temperature. The reaction was stopped by adding PI(3,4,5)P3 detector mixed with EDTA (ethylenediaminetetraacetic acid) and allowed to incubate at room temperature for 1 hour. After this time, the mixture was transferred from each well to a PI3K ELISA plate and allowed to incubate 1 hour. Plates were washed and then incubated with a secondary detector for 30 minutes. Plates were washed again, and 3,3',5,5'-

Kinase Assay	tetramethylbenzidine solution was added for 5 minutes at which time H2SO4 was added to stop all reactions. Plates were read at 450 nm on a Labsystems 96-well plate reader [2].
Cell Research	MTT assays were performed to determine cytotoxicity. Briefly, 1 × 10^5 cells (CLL B cells or healthy volunteer T cells or NK cells) were incubated for 48 hours with different concentrations of CAL-101, 25μM LY294002, or vehicle control. MTT reagent was then added, and plates were incubated for an additional 20 hours before washing with protamine sulfate in phosphate-buffered saline. Dimethyl sulfoxide was added, and absorbance was measured by spectrophotometry at 540 nm in a Labsystems plate reader. Cell viability was also measured at various time points with the use of annexin/PI flow cytometry. Data were analyzed with Expo-ADC32 software package. At least 10 000 cells were counted for each sample. Results were expressed as the percentage of total positive cells over untreated control. Experiments examining caspase-dependent apoptosis included the addition of 100μM Z-VAD. Experiments examining survival signals included the addition of 1 μg/mL CD40L, 800 U/mL IL-4, 50 ng/mL BAFF, 20 ng/mL TNF-α, or coculturing on fibronectin or stromal (HS-5 cell line) coated plates. Stromal coculture was done by plating a 75-cm2 flask (80%-100% confluent) per 6-well plate 24 hours before the addition of CLL cells [2].
Animal Research	For Idelalisib (CAL-101) treatment, wild-type C57BL/6 mice were administered either 40 mg kg 1 CAL-101 or vehicle DMSO, by 25 ml infusion into the femoral vein, 15 min before I/R (pre-treatment), or 3 and 6 h after initiation of reperfusion (post-treatment). Controls and animals treated with CAL-101 underwent cerebral blood flow (CBF) measurements using a laser Doppler perfusion monitor. The CBF measurements obtained immediately before and after MCAO and again at 3 h after reperfusion showed a B90–95% reduction in the blood flow to the MCAO infarct region, which did not differ between groups [4].

Solubility Information

Solubility	H2O: Insoluble, Ethanol: 22 mg/mL (52.96 mM),Sonication is recommended. DMSO: 250 mg/mL (601.8 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (4.81 mM),Sonication is recommended. *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	2.4072 mL	12.036 mL	24.072 mL
5 mM	0.4814 mL	2.4072 mL	4.8144 mL
10 mM	0.2407 mL	1.2036 mL	2.4072 mL
50 mM	0.0481 mL	0.2407 mL	0.4814 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

Lannutti BJ, et al. CAL-101, a p110delta selective phosphatidylinositol-3-kinase inhibitor for the treatment of B-cell malignancies, inhibits PI3K signaling and cellular viability. Blood. 2011 Jan 13;117(2):591-4.
Xiong W, Jia L, Cai Y, et al.Evaluation of the anti-inflammatory effects of PI3Kδ/γ inhibitors for treating acute lung injury.Immunobiology.2023: 152753.
Sugawara T, Nevedomskaya E, Heller S, et al.Dual targeting of the androgen receptor and PI3K/AKT/mTOR pathways in prostate cancer models improves antitumor efficacy and promotes cell apoptosis.Molecular Oncology.2024
Herman SE, et al. Phosphatidylinositol 3-kinase-δ inhibitor CAL-101 shows promising preclinical activity in chronic lymphocytic leukemia by antagonizing intrinsic and extrinsic cellular survival signals. Blood. 2010 Sep 23;116(12): 2078-88.
Hoellenriegel J, et al. The phosphoinositide 3'-kinase delta inhibitor, CAL-101, inhibits B-cell receptor signaling and chemokine networks in chronic lymphocytic leukemia. Blood. 2011 Sep 29;118(13):3603-12.
Low PC, et al. PI3Kδ inhibition reduces TNF secretion and neuroinflammation in a mouse cerebral stroke model. Nat Commun. 2014 Mar 14;5:3450.