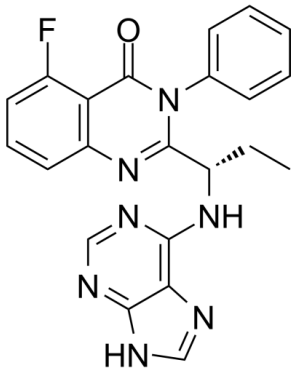
Data Sheet

Product Name:	Idelalisib
Cat. No.:	CS-0256
CAS No.:	870281-82-6
Molecular Formula:	C22H18FN7O
Molecular Weight:	415.42
Target:	Autophagy; PI3K
Pathway:	Autophagy; PI3K/Akt/mTOR
Solubility:	DMSO : ≥ 59.7 mg/mL (143.71 mM)



BIOLOGICAL ACTIVITY:

Idelalisib (CAL-101; GS-1101) is a highly selective and orally bioavailable **p110δ** inhibitor with an **IC_{50}** of 2.5 nM, showing 40- to 300-fold selectivity for p110δ over other PI3K class I enzymes. IC50 & Target: IC50: 2.5 nM (p110δ), 89 nM (p110γ), 565 nM (p110β), 820 nM (p110α)[1] **In Vitro:** Idelalisib (CAL-101; GS-1101) is a highly selective and potent p110δ inhibitor (EC_{50}=8 nM). Greater selectivity (400- to 4000-fold) is seen against related kinases C2β, hVPS34, DNA-PK, and mTOR, whereas no activity is observed against a panel of 402 diverse kinases at 10 μM. CAL-101 reduces PDGF-induced pAkt by only 25% at 10 μM. Idelalisib (CAL-101) inhibits LPA-induced pAkt with an EC_{50} of 1.9 μM. Idelalisib (CAL-101) blocks FcεRI p110δ-mediated CD63 expression with an EC_{50} of 8 nM, whereas formyl-methionyl-leucyl-phenylalanine activation of p110γ is inhibited with an EC_{50} of 3 μM. Thus, in cell-based assays, CAL-101 has 240- to 2500-fold selectivity for p110δ over the other class I PI3K isoforms[1]. CAL-101Idelalisib (CAL-101)-induced apoptosis of chronic lymphocytic leukemia (CLL) cells is significant compare with vehicle treatment alone (P<0.001). Idelalisib (CAL-101) induces selective cytotoxicity in CLL cells independent of IgVH mutational status or interphase cytogenetics[2]. **In Vivo:** A significant reduction is observed in the $CD11b^{+}Ly6G^{+}$ neutrophils from brain homogenates of both$p110\delta^{D910A/D910A}$ mice and Idelalisib (CAL-101) (40 mg/kg, i.v.) post-treated mice[3].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: Idelalisib (CAL-101) is dissolved in DMSO and stored, and then diluted with appropriate media before use[2].[2]MTT assays are performed to determine cytotoxicity. Briefly, 1×10^5 cells (CLL B cells or healthy volunteer T cells or NK cells) are incubated for 48 hours with different concentrations of Idelalisib (CAL-101) (0.1 μM, 1 μM, 5 μM, 10 μM), 25 μM LY294002, or vehicle control. MTT reagent is then added. DMSO is added, and absorbance is measured by spectrophotometry at 540 nm in a Labsystems plate reader. Cell viability is also measured at various time points with the use of annexin/PI flow cytometry. Data are analyzed with Expo-ADC32 software package. At least 10,000 cells are counted for each sample. Results are expressed as the percentage of total positive cells over untreated control. Experiments examining caspase-dependent apoptosis included the addition of 100 μM Z-VAD. Experiments examining survival signals include 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 is done by plating a 75-cm2 flask (80%-100% confluent) per 6-well plate 24 hours before the addition of CLL cells[2]. **Animal Administration:** Idelalisib (CAL-101) is prepared in DMSO and then diluted[3].[3]Mice[3]

For Idelalisib (CAL-101) treatment, wild-type C57BL/6 mice are administered either 40 mg/kg Idelalisib (CAL-101) or vehicle DMSO, by 25 μL 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 Idelalisib (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 an ~90-95% reduction in the blood flow to the MCAO infarct region, which does not differ between groups.

References:

[1]. 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, 117(2), 591-594.

[2]. 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, 116(12), 2078-2088.

[3]. Low PC, et al. PI3Kδ inhibition reduces TNF secretion and neuroinflammation in a mouse cerebral stroke model. Nat Commun. 2014 Mar 14;5:3450.

[4]. Cooney J, et al. Synergistic targeting of the regulatory and catalytic subunits of PI3Kδ in mature B cell malignancies. Clin Cancer Res. 2018 Mar 1;24(5):1103-1113.

CAIndexNames:

4(3H)-Quinazolinone, 5-fluoro-3-phenyl-2-[(1S)-1-(9H-purin-6-ylamino)propyl]-

SMILES:

O=C1N(C2=CC=CC=C2)C([C@@H](NC3=C4N=CNC4=NC=N3)CC)=NC5=C1C(F)=CC=C5

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