IPI-3063

Cat. No.: HY-111510

CAS No.: 1425043-73-7

Molecular Formula: $C_{25}H_{25}N_7O_2$

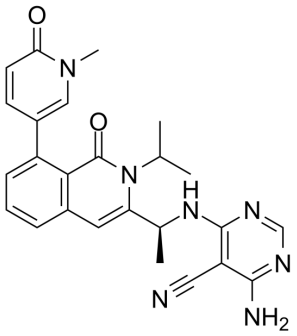
Molecular Weight: 455.51

Target: PI3K

Pathway: PI3K/Akt/mTOR

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 62.5 mg/mL (137.21 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	2.1953 mL	10.9767 mL	21.9534 mL
5 mM	0.4391 mL	2.1953 mL	4.3907 mL
10 mM	0.2195 mL	1.0977 mL	2.1953 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

IPI-3063 is a potent and selective PI3K p110δ inhibitor with an IC_{50} of 2.5 ± 1.2 nM.

IC_{50} & Target

p110δ	p110α	p110β	p110γ
2.5 nM (IC_{50})	1170 nM (IC_{50})	1508 nM (IC_{50})	2187 nM (IC_{50})

In Vitro

IPI-3063 inhibits p110α, p110β, and p110γ with IC_{50}s of 1171±533 nM, 1508±624 nM, and 2187±1529 nM, respectively. IPI-3063 potently reduces mouse B cell proliferation, survival, and plasmablast differentiation while increasing antibody class switching to IgG1. IPI-3063 is a p110δ selective compound with an IC_{50}=0.1 nM in p110δ-specific cell-based assays and cellular IC_{50} values for the other class I PI3K isoforms are at least 1,000-fold higher (IC_{50}=1901±1318 nM for p110α, IC_{50} =102.8±35.7 nM for p110β, IC_{50}=418.8±117.2 nM for p110γ). IPI-3063 is very potent in reducing p-AKT (significant effect at 1 nM). IPI-3063 also reduces p-ERK1/2 with a significant effect at 10 nM. IPI-3063 is very potent, achieving a significant decrease in B cell survival when present at 10 nM[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]

Human recombinant PI3K-α, PI3K-β, PI3K-δ, and PI3K-γ are used. Phosphatidylinositol 4,5 bis phosphate (diC8-PtdIns(4,5)P2) is used. PI3K-α, β, and δ are heterodimers consisting of full length p110α, p110β, or p110δ catalytic subunit and the p85α regulatory subunit. PI3K-γ is a monomer of the p110γ catalytic subunit. Samples of kinase (10 nM-α, β, and δ; 20 nM-γ) are incubated with IPI-3063 for 30 min at room temperature in reaction buffer (15 mM HEPES pH 7.4, 20 mM NaCl, 1 mM EGTA, 0.02% Tween 20, 10 mM $MgCl_2$, 0.2 mg/mL bovine-γ-globulins) followed by addition of ATP/diC8-PtdIns(4,5)P2 mixture to give final concentrations of 3 mM ATP and 500 μM diC8-PtdIns(4,5)P2. Reactions are incubated at room temperature for 2 h, with PI3K activity is assessed. Plates are read on plate reader in luminescence mode[1].

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Cell Assay [1]

Peripheral blood mononuclear cells (PBMCs) are first purified from blood by density gradient centrifugation. Human B cells are then purified from PBMCs by negative selection. B-cell purity is increased from 4% to >70% as measured by FACS analysis using anti-CD19 PE conjugated antibody. Purified B cells are seeded at a final concentration of 0.1×10^6 cells/mL and cultured with 2 μg/mL human CD40L+5 μg/mL anti-human IgM/IgG+100 μg/mL hIL-2+100 μg/mL hIL-21. All B cells are cultured in RPMI 1640 supplemented with 10% (vol/vol) heat-inactivated FCS, 5 mM Hepes, 2 mM L-glutamine, 100 U/mL Penicillin, 100 μg/mL Streptomycin, 50 μM 2-mercaptoethanol. Purified human B cells are pretreated with IPI-3063 (0.1, 1, 10, and 100 nM) for 30 min, then stimulated with human CD40L+anti-human IgM/IgG+human IL-2+human IL-21 for 120 h[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Chiu H, et al. The Selective Phosphoinoside-3-Kinase p110δ Inhibitor IPI-3063 Potently Suppresses B Cell Survival, Proliferation, and Differentiation. Front Immunol. 2017 Jun 30;8:747.

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