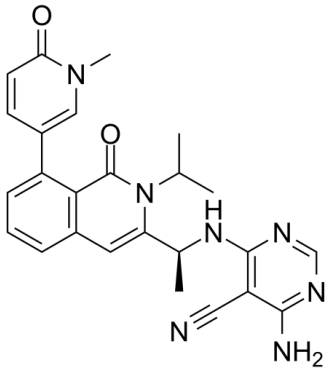
Data Sheet

Product Name:	IPI-3063
Cat. No.:	CS-0042285
CAS No.:	1425043-73-7
Molecular Formula:	C25H25N7O2
Molecular Weight:	455.51
Target:	PI3K
Pathway:	PI3K/Akt/mTOR
Solubility:	DMSO : ≥ 83.33 mg/mL (182.94 mM)



BIOLOGICAL ACTIVITY:

IPI-3063 is a potent and selective **PI3K p110δ** inhibitor with an **IC_{50}** of 2.5 ± 1.2 nM. IC50 & Target: IC50: 2.5±1.2 nM (p110δ), 1171±533 nM (p110α), 1508±624 nM (p110β), 2187±1529 nM (p110γ)[1] **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].

PROTOCOL (Extracted from published papers and Only for reference)

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 p85 α 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].

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].

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.

CAIndexNames:

5-Pyrimidinecarbonitrile, 4-amino-6-[[(1S)-1-[8-(1,6-dihydro-1-methyl-6-oxo-3-pyridinyl)-1,2-dihydro-2-(1-methylethyl)-1-oxo-3-isoquinolinyl]ethyl]amino]-

SMILES:

N#CC1=C(N[C@H](C2=CC3=C(C(N2C(C)C)=O)C(C(C=C4)=CN(C)C4=O)=CC=C3)C)N=CN=C1N

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