PI3Kδ-IN-8

Cat. No.: HY-134472

CAS No.: 2101518-75-4

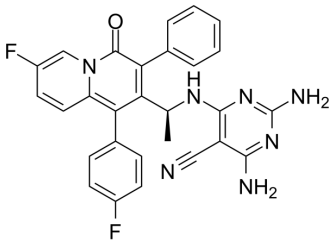
Molecular Formula: $C_{28}H_{21}F_2N_7O$

Molecular Weight: 509.51

Target: PI3K

Pathway: PI3K/Akt/mTOR

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

PI3Kδ-IN-8 is a potent, selective and orally active PI3Kδ inhibitor, with an IC_{50} of 3.3 nM. PI3Kδ-IN-8 shows selectivity for PI3K δ over PI3Kα, PI3Kβ, and PI3Kγ (IC_{50}=377.2, 241.6, 17.9 nM, respectively). PI3Kδ-IN-8 has anti-tumor activity[1].

IC_{50} & Target

PI3Kδ	PI3Kγ	PI3Kβ	PI3Kα
3.3 nM (IC_{50})	17.9 nM (IC_{50})	241.6 nM (IC_{50})	377.2 nM (IC_{50})

In Vitro

PI3Kδ-IN-8 (compound 34) (0.1 nM-10 μM; 96 h) shows excellent potency against representative DLBCL cell lines, of either GCB (SUDHL-6), or ABC subtype (OCI-Ly10 and TMD-8)[1].

PI3Kδ-IN-8 (1 h) inhibits the PI3K-induced AKT phosphorylation in anti-IgM stimulated Raji cells, with an IC_{50} of 9.5 nM[1].

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

Cell Viability Assay[1]

Cell Line:	SUDHL-6, OCI-Ly10, and TMD-8 cell lines
Concentration:	0.1, 1, 10, 100, 1000, 10000 nM
Incubation Time:	96 hours
Result:	Inhibited the viability of SUDHL-6, OCI-Ly10, and TMD-8 cells, with IC_{50}s of <0.1 nM, <1 nM, and <0.1 nM, respectively.

In Vivo

PI3Kδ-IN-8 (1-30 mg/kg; p.o. once daily for 24 d) significantly reduces the tumor volume and tumor weight in a dose-dependent manner in mice[1].

PI3Kδ-IN-8 (1 mg/kg; i.v.) displays a suitable half-life (1 h), C_{max} (2.3 μM) and low clearance (5.6 mL/min/kg) in mice[1].

PI3Kδ-IN-8 (10 mg/kg; p.o.) displays moderate oral bioavailability (39%), C_{max} (7.5 μM), and AUC_{last}(22 μM•h) in mice[1].

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

Animal Model:	Female NOD scid mice were injected OCI-Ly10 cells[1]
Dosage:	1, 3, 10, 30 mg/kg
Administration:	P.o. once daily for 24 days

Result:	Reduced the tumor volume, with an ED_{50} of 6.47 mg/kg. Tumor growth inhibition of 81.95% was seen with a highly significant reduction in both tumor volume and tumor weight.

Animal Model:	Male BALB/c mice[1]
Dosage:	1 mg/kg for i.v.; 10 mg/kg for p.o. (Pharmacokinetic Analysis)
Administration:	Intravenous administration and oral administration
Result:	I.v.: $t_{1/2}$=1 h, C_{max}=2.3 μM, CL=5.6 mL/min/kg. P.o.: F=39%, C_{max}=7.5 μM, AUC_{last}=22μM•h.

REFERENCES

[1]. Shukla MR, et, al. Discovery of a Potent and Selective PI3Kδ Inhibitor (S)-2,4-Diamino-6-((1-(7-fluoro-1-(4-fluorophenyl)-4-oxo-3-phenyl-4H-quinolizin-2-yl)ethyl)amino)pyrimidine-5-carbonitrile with Improved Pharmacokinetic Profile and Superior Efficacy in Hematological Cancer Models. J. Med. Chem. 2020 Dec 1.

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