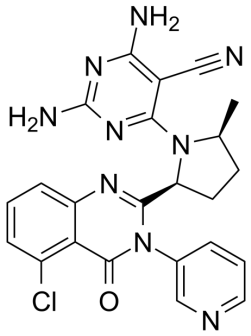
PI3Kδ/γ-IN-3

Cat. No.:	HY-150638
CAS No.:	2730151-31-0
Molecular Formula:	$C_{23}H_{20}ClN_9O$
Molecular Weight:	473.92
Target:	PI3K; Apoptosis
Pathway:	PI3K/Akt/mTOR; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

PI3Kδ/γ-IN-3 (Compound 58) is a potent and orally active PI3Kδ and PI3Kγ dual inhibitor with IC_{50}s of 1 nM and 16 nM, respectively. PI3Kδ/γ-IN-3 induces tumor cell apoptosis and can be used for B-cell malignancies research[1].

IC_{50} & Target

PI3Kδ	PI3Kγ
1 nM (IC_{50})	16 nM (IC_{50})

In Vitro

PI3Kδ/γ-IN-3 (Compound 58) (72 h) shows antiproliferative activity against B-cell lymphoma (DLBCL) cells[1].
PI3Kδ/γ-IN-3 (0.5 μM, 24 h) arrests cell cycle at G0/G1 phase in SUDHL-6 and DOHH2 cells[1].
PI3Kδ/γ-IN-3 (1.5 and 2 μM, 48 h) induces cell apoptosis in SUDHL-6 and DOHH2 cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	SUDHL-4, SUDHL-6 and DOHH2 cells
Concentration:	
Incubation Time:	72 h
Result:	Showed antiproliferative activity with IC_{50}s of 0.03 ± 0.03, 0.06 ± 0.01 and 0.20 ± 0.04 μM against SUDHL-4, SUDHL-6 and DOHH2 cells, respectively.

Cell Cycle Analysis[1]

Cell Line:	SUDHL-6 and DOHH2 cells
Concentration:	0.5 μM
Incubation Time:	Alone or in combination with Ibrutininb (HY-10997) (0.5 μM or 1 μM) for 24 h
Result:	Caused a loss of G2/M phase cells and an increase in the percentage of cells in the G0/G1 phase. Induced cell cycle arrest alone or in combination with Ibrutinib in both cells.

Apoptosis Analysis[1]

Cell Line:	SUDHL-6 and DOHH2 cells

Concentration:	1.5 μM and 2 μM
Incubation Time:	Alone or in combination with Ibrutininb (1.5 μM or 1 μM) for 48 h
Result:	Demonstrated the induction of apoptosis in both SUDHL-6 and DOHH2 cells, and the combination was stronger than treated alone.

In Vivo

PI3Kδ/γ-IN-3 (Compound 58) (5 and 10 mg/kg; p.o.; daily for 14d) suppresses the tumor volume in a dose-dependent manner without obvious toxicity in mice[1].

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Animal Model:	Female non obese diabetes/severe combined immunodeficient (NOD/SCID) mice, 6- to 8-week-old, SUDHL-6 xenograft model[1]
Dosage:	5 and 10 mg/kg alone or in combination with 10 mg/kg Ibrutinib
Administration:	Oral administration, daily for 14 days
Result:	Suppressed the tumor volume in a dose-dependent manner and demonstrated superior efficacy relative to Ibrutinib at 10 mg/kg QD administration. When in combination with Ibrutinib, showed greater tumor growth inhibitory effects.

Animal Model:	SD rats[1]
Dosage:	5 mg/kg
Administration:	Oral or intravenous administration (Pharmacokinetic Analysis)
Result:	PK Profiles of PI3Kδ/γ-IN-3 (Compound 58) in Male SD Rats[1]

Compound	dose (mg/kg)	administration route	C_{max} (ng/mL)	T_{max} (h)	AUC_{0-t} (h•μg/L)	$T_{1/2}$ (h)	CL (L/h/kg)	V_{ss} (L/kg)	F (%)
58	5	oral	3637.81	3.33	8612.57	9.46	0.79	--	126.5
	5	intravenous	860.09	0.08	6806.92	2.79	0.75	2.86	--

PK profiles: C_{max}, maximum plasma concentration; T_{max}, tim

REFERENCES

[1]. Liu K, et al. Discovery, Optimization, and Evaluation of Potent and Selective PI3Kδ-γ Dual Inhibitors for the Treatment of B-cell Malignancies. J Med Chem. 2022 Jul 13.

Caution: Product has not been fully validated for medical applications. For research use only.

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