IHMT-PI3K-455

Cat. No.: HY-149493

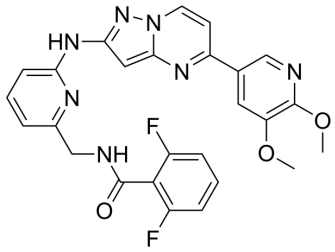
Molecular Formula: $C_{26}H_{21}F_2N_7O_3$

Molecular Weight: 517.49

Target: PI3K

Pathway: PI3K/Akt/mTOR

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



BIOLOGICAL ACTIVITY

Description

IHMT-PI3K-455 (Compound 15u) is a potent, selective, orally active PI3Kγ/δ dual inhibitor with IC_{50}s of 7.1 nM and 0.57 nM for PI3Kγ and PI3Kδ, respectively. IHMT-PI3K-455 suppresses the AKT phosphorylation. IHMT-PI3K-455 inhibits tumor growth by recruiting and activating more $CD8^+$ killing T cells.IHMT-PI3K-455 is used in cancer research[1].

IC_{50} & Target

PI3Kα	PI3Kβ	PI3Kγ	PI3Kδ
6.717 μM (IC_{50})	42.04 nM (IC_{50})	7.1 nM (IC_{50})	0.57 nM (IC_{50})

In Vitro

IHMT-PI3K-455 (1 μM, 2 h) suppresses the PI3Kγ/δ-mediated AKT phosphorylation in RAW264.7 cells and Raji cells[1].
IHMT-PI3K-455 (1 μM, 72 h) alters the macrophage polarization in M2 macrophages derived from THP-1 and BMDM cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Differentiation Assay[1]

Cell Line:	Macrophages
Concentration:	0.1, 1 μM
Incubation Time:	72 h
Result:	Increased the proinflammatory M1 macrophage phenotype in a dose-dependent manner, with a concomitant dose-dependent decrease of the anti-inflammatory M2 macrophage phenotype. Repolarized M2 phenotype toward M1 phenotype in THP-1 and BMDM macrophages.

Western Blot Analysis[1]

Cell Line:	RAW264.7 cells; Raji cells
Concentration:	0, 0.01, 0.03, 0.1, 0.3, 1 μM
Incubation Time:	2 h
Result:	Potently inhibited the PI3Kγ-mediated AKT473 phosphorylation in RAW264.7 cells (human C5a stimulation) with an IC_{50} value of 0.015 μM. Potently inhibited the PI3Kδ-mediated AKT473 phosphorylation in Raji cells (anti-IgM stimulation) with an IC_{50} value of 0.010 μM.

In Vivo

IHMT-PI3K-455 (40 mg/kg for p.o; once daily for 30 days) inhibits the tumor growth in a MC38 tumor xenograft model[1].
IHMT-PI3K-455 (40 mg/kg for p.o; once daily for 30 days) inhibits tumor growth by recruiting and activating more $CD8^+$ killing T cells[1].
Pharmacokinetic parameters of IHMT-PI3K-455 in Sprague-Dawley rats[1]

Dose (mg/kg)	Administration route	Cmax (ng/mL)	Tmax (h)	AUC0-∞ (h⊠ ng/mL)	T1/2 (h)	CL (L/h/kg)	Vz (L/kg)	F (%)
1	i.v.	1233	0.03	477	1.59	2.12	4.80	–
10	p.o.	157	3.42	838	2.71	14.76	56.02	17.6

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

Animal Model:	MC38 tumor model[1]
Dosage:	10 mg/kg, 40 mg/kg
Administration:	Oral gavage (p.o.); Once daily for 30 days
Result:	Significantly inhibited tumor size in a dose-dependent manner. Increased tumor-infiltrating $CD8^+$T cells.

REFERENCES

[1]. Liang X, et al. Discovery of Pyrazolo[1,5-a]pyrimidine derivative as a potent and selective PI3Kγ/δ dual inhibitor. Eur J Med Chem. 2023 Nov 15;260:115768.

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