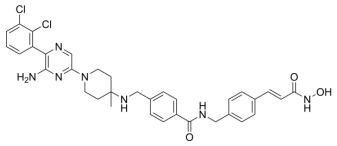
SHP2/HDAC-IN-1

Cat. No.:	HY-151464
CAS No.:	2831230-38-5
Molecular Formula:	$C_{34}H_{35}Cl_2N_7O_3$
Molecular Weight:	660.59
Target:	Phosphatase; HDAC; SHP2
Pathway:	Metabolic Enzyme/Protease; Cell Cycle/DNA Damage; Epigenetics; Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

SHP2/HDAC-IN-1 is a dual allosteric SHP2/HDAC inhibitor with IC_{50} values of 20.4 nM (SHP2) and 25.3 nM (HDAC1) respectively. SHP2/HDAC-IN-1 triggers efficient antitumor immunity by activating T cells, enhancing the antigen presentation function and promoting cytokine secretion. SHP2/HDAC-IN-1 can be used in the research of cancer immunoresearch[1].

IC_{50} & Target

HDAC1	HDAC2	HDAC3	HDAC6
25 nM (IC_{50})	79 nM (IC_{50})	233 nM (IC_{50})	27 nM (IC_{50})

SHP2
20.4 nM (IC_{50})

In Vitro

SHP2/HDAC-IN-1 (compound 8t, 0-10 μM approximately, 72 h) inhibits the proliferation of BxPC-3, SW1990, AsPC-1and MV4-11 cells[1].
SHP2/HDAC-IN-1 (0.25-1 μM, 24 h) increases the acetylation of α-tubulin and histone H3 in MV4-11 cells[1].
SHP2/HDAC-IN-1 (0.25 μM, 24 h) inhibits cell cycle progression in the G1 phase of MV4-11 cells[1].
SHP2/HDAC-IN-1 (0.25 and 0.5 μM, 24 h) decreases the mitochondrial membrane potential and activats caspase-3[1].
SHP2/HDAC-IN-1 (2 h) shows good stability in in mouse liver microsome[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	Pancreatic carcinoma (BxPC-3, SW1990, and AsPC-1), acute monocytic leukemia (MV4-11)
Concentration:	0-10 μM approximately
Incubation Time:	72 h
Result:	Inhibited cell proliferation with IC_{50}s range of 0.07 μM-3.92 μM.

Western Blot Analysis[1]

Cell Line:	MV4-11 cells
Concentration:	0.25, 0.5, 1 μM

Incubation Time:	24 h
Result:	Increased the acetylation of α-tubulin and histone H3. Inhibited the phosphorylation level of ERK.

In Vivo

SHP2/HDAC-IN-1 (compound 8t, 40 mg/kg, p.o.) inhibits tumor growth in MV4-11 and 4T1 tumor-bearing xenograft mice[1].
SHP2/HDAC-IN-1 (20 mg/kg p.o., 1 mg/kg i.v.) exhibits good maximum plasma concentrations in rats[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	MV4-11 tumor-bearing xenograft mice[1]
Dosage:	40 mg/kg
Administration:	Oral adminstration (p.o.), every day for 20 consecutive days.
Result:	Delayed tumor progression with a tumor growth inhibition rate (TGI %) value of 64.0%, with no obvious signs of toxicity.

Animal Model:	4T1 murine breast cancer model[1]
Dosage:	40 mg/kg
Administration:	Oral adminstration (p.o.), every day for 12 consecutive days.
Result:	Significantly decreased tumor burden with a TGI value of 72%. Increased the proportions of CD4+ T cells and CD8+ T cells in the spleen. Enhanced the proportion of mDCs in lymph nodes.

Animal Model:	Male Sprague-Dawley (SD) rats (Pharmacokinetic assay)[1]
Dosage:	20 mg/kg p.o., 1 mg/kg i.v.
Administration:	Oral adminstration (p.o.) or intravenous injection (i.v.)
Result:	Pharmacokinetic profile of SHP2/HDAC-IN-1 (compound 8t).

dose (mg/kg)	$T_{1/2}$ (h)	C_{max} (ng/mL)	Cl (mL/h/kg)	F (%)
20 (p.o.)	5.32	1835		21.42
1 (i.v.)	6.15	3517	326	

REFERENCES

[1]. Meng Liu, et al. Discovery of Novel Src Homology-2 Domain-Containing Phosphatase 2 and Histone Deacetylase Dual Inhibitors with Potent Antitumor Efficacy and Enhanced Antitumor Immunity. J Med Chem. 2022 Sep 22;65(18):12200-12218.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA