Menin-MLL inhibitor-22

Cat. No.: HY-151595

CAS No.: 2851841-61-5

Molecular Formula: $C_{29}H_{39}N_7O_3S$

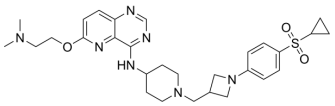
Molecular Weight: 565.73

Target: Epigenetic Reader Domain

Pathway: Epigenetics

Storage:

Powder	-20°C	3 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (220.95 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7676 mL	8.8381 mL	17.6763 mL
	5 mM	0.3535 mL	1.7676 mL	3.5353 mL
	10 mM	0.1768 mL	0.8838 mL	1.7676 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

Menin-MLL inhibitor-22 (compound C20) is an orally active inhibitor of the interaction between menin and mixed lineage leukemia (MLL) (IC_{50}=7 nM). Menin-MLL inhibitor-22 binds menin protein and inhibits cancer cell growth (MV4 cells, IC_{50}=0.3 μM). Menin is a putative tumor suppressor associated with multiple endocrine neoplasia type 1 (MEN-1 syndrome)[1].

In Vitro

Menin-MLL inhibitor-22 (1 μM; 60 min) possesses good stability and low clearance rate in liver microsomes[1].
Menin-MLL inhibitor-22 (1 and 10 μM; 24 h) inhibits MLL-r Leukemia cells MV4;11 growth and (0.1-10 μM; 24 h) decreases the expression of the HOXA9 and MEIS1 induced by menin-MLL interaction[1].
Menin-MLL inhibitor-22 (1, and 10 μM; 7 d) increases the amount of CD11b, a differentiation marker of myeloid cells, indicating a reverse the differentiation arrest of MLL-r leukemia cells[1].
Menin-MLL inhibitor-22 (1, and 10 μM; 24 h) induces cell apoptosis and G0/G1 cell cycle arrest[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

RT-PCR[1]

Cell Line:	MLL-r Leukemia cells MV4;11
Concentration:	0.1, 1, and 10 μM

Incubation Time:	24 hours
Result:	Reversed the over-expressing HOXA9 and MEIS1 induced by menin-MLL interaction, decreased the level of HOXA9 and MEIS1.

Apoptosis Analysis[1]

Cell Line:	MLL-r Leukemia cells MV4;11
Concentration:	1, and 10 μM
Incubation Time:	24 hours
Result:	Decreased in the population of cells in the S and G2/M phases, arrested cell cycle at G0/G1 phase.

In Vivo

Menin-MLL inhibitor-22 (6 mg/kg and 30 mg/kg; p.o.; every second day for 16 days) shows potent antitumor activity in the MV4;11 subcutaneous xenograft models of MLL-rearranged leukemia[1].

Pharmacokinetic Properties in SD Rats[1]

Route	Dose (mg/kg)	T_{max} (h)	$T_{1/2}$ (h)	MRT (h)	C_{max} (ng/mL)	AUC_{0-t} (ng·h/mL)	$AUC_{0-\infty}$ (ng·h/mL)	Cl_{total} (mL/h/kg)	V_{ss} (L/kg)	F (%)
i.v.	5	N/A	17.5	7.1	1187	1700	2495	2056	49.3	
p.o.	15	7.3	15.5	12.0	56.7	863.7	1476	10730	23	16.9

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

Animal Model:	Balb/C nude mice bearing MV4;11 cell xenografts[1]
Dosage:	6 mg/kg, 30 mg/kg
Administration:	Oral gavage; every second day for 16 days
Result:	Reduced the volume of tumor in mice.

REFERENCES

[1]. Lei H, et al. Discovery of Novel, Potent, and Selective Small-Molecule Menin-Mixed Lineage Leukemia Interaction Inhibitors through Attempting Introduction of Hydrophilic Groups. J Med Chem. 2022 Oct 13;65(19):13413-13435.

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