MI-463

Cat. No.: HY-19809

CAS No.: 1628317-18-9

Molecular Formula: $C_{24}H_{23}F_3N_6S$

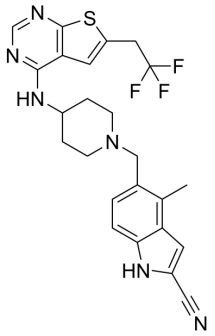
Molecular Weight: 484.54

Target: Epigenetic Reader Domain

Pathway: Epigenetics

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (257.98 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0638 mL	10.3191 mL	20.6381 mL
	5 mM	0.4128 mL	2.0638 mL	4.1276 mL
	10 mM	0.2064 mL	1.0319 mL	2.0638 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.29 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (4.29 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.29 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MI-463 is a highly potent and orally bioavailable small molecule inhibitor of the menin-mLL interaction.

In Vitro

MI-463 can reach the target protein in mammalian cells and effectively inhibit the menin-mLL-AF9 interaction at sub-micromolar concentrations. Treatment of murine bone marrow cells (BMC) transformed with the mLL-AF9 oncogene with MI-463 results in substantial growth inhibition, with GI_{50} of 0.23 μM[1].

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

In Vivo	MI-463 achieves high level in peripheral blood following a single intravenous or oral dose, while also showing high oral bioavailability (45%). Pharmacologic inhibition of the menin-mLL interaction substantially delays progression of mLL leukemia in murine models through on-target activity without causing toxicity. MI-463 induces strong inhibition of tumor growth with once daily intraperitoneal (i.p.) administration. The expression of mLL fusion protein target genes, HOXA9 and MEIS1, are significant reduced upon treatment with MI-463. 20 days treatment of MV4;11 xenograft recipient mice with MI-463 also results in a substantial delay in leukemia progression as manifested by a marked decrease in the bioluminescence level which is associated with a significant decrease in the population of leukemic cells in the peripheral blood, spleen and bone marrow samples[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Leukemia cells are treated with MI-463 or 0.25% DMSO and cultured at 37 °C for 7 days. Media is changed at day 4, viable cell numbers are restored to the original concentration and MI-463 are re-supplied. MTT cell proliferation assay kit is then employed, and plates are read for absorbance at 570 nm using a microplate reader[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: For efficacy studies in MV4;11 subcutaneous xenograft mice model, 5×10^6 cells are injected into the 4-6 week old female BALB/c nude mice. Treatment is started when the tumor size reached ~100 mm^3. Vehicle (25% DMSO, 25% PEG400, 50% PBS) or compounds (MI-463 or MI-503) are administrated once daily at designated doses using i.p. injections[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Acta Pharmacol Sin. 2021 Apr 13.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Borkin D, et al. Pharmacologic inhibition of the Menin-MLL interaction blocks progression of MLL leukemia in vivo. Cancer Cell. 2015 Apr 13;27(4):589-602.

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