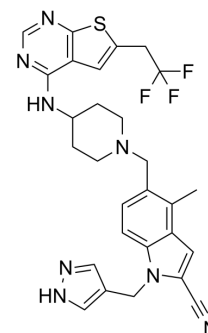


MI-503

Cat. No.:	HY-16925		
CAS No.:	1857417-13-0		
Molecular Formula:	C ₂₈ H ₂₇ F ₃ N ₈ S		
Molecular Weight:	564.63		
Target:	Epigenetic Reader Domain		
Pathway:	Epigenetics		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro	DMSO : 25 mg/mL (44.28 mM; Need ultrasonic)				
		Solvent Concentration	Mass		
			1 mg	5 mg	
	Preparing Stock Solutions	1 mM	1.7711 mL	8.8554 mL	
	5 mM	0.3542 mL	1.7711 mL		
	10 mM	0.1771 mL	0.8855 mL		
		10 mg	17.7107 mL	3.5421 mL	1.7711 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 (3.68 mM); Clear solution 2. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.08 mg/mL (3.68 mM); Clear solution				

BIOLOGICAL ACTIVITY

Description	MI-503 is a highly potent and orally bioavailable small molecule inhibitor of the menin-mLL interaction.
In Vitro	MI-503 occupies the F9 and P13 pockets on menin, forming a hydrogen bond with Tyr276, and also extends beyond the P13 pocket to form hydrogen bonds with Trp341 and Glu366. Treatment of murine bone marrow cells (BMC) transformed with the mLL-AF9 oncogene with MI-503 results in substantial growth inhibition, with GI ₅₀ of 0.22 μM. The cell growth inhibitory effect of MI-503 is time-dependent, with a pronounced effect achieved after 7-10 days of treatment ^[1] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	MI-503 achieves high level in peripheral blood following a single intravenous or oral dose, while also showing high oral bioavailability (75%). MI-503 induces strong inhibition of tumor growth with once daily intraperitoneal (i.p.) administration.

Treatment with MI-503 results in an over 80% reduction in MV4;11 tumor volume and complete tumor regression in two mice. Ten consecutive days of treatment with MI-503 results in a marked delay in progression of mLL leukemia in mice and significantly reduces leukemia tumor burden. Treatment with MI-503 and MI-463 leads to markedly reduced expression of Hoxa9 and Meis1, downstream targets of mLL fusion proteins substantially upregulated in mLL leukemias^[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-503 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-503 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 $\sim 100 \text{ mm}^3$. Vehicle (25% DMSO, 25% PEG400, 50% PBS) or compounds (MI-463 or MI-503) are administered 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

- Nat Commun. 2022 Feb 22;13(1):1006.
- J Exp Clin Cancer Res. 2021 Aug 26;40(1):270.
- Int J Oncol. 2020 Oct;57(4):1057-1071.
- Research Square Preprint. 2021 Aug.

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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.

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

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