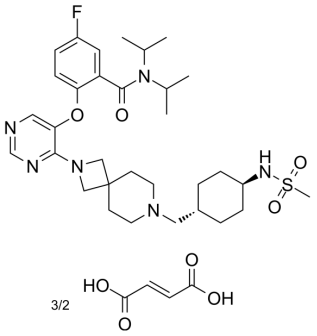
VTP50469 fumarate

Cat. No.:	HY-114162A
CAS No.:	2169919-29-1
Molecular Formula:	$C_{32}H_{47}FN_6O_4S.{}_3/_2C_4H_4O_4$
Molecular Weight:	804.93
Target:	Epigenetic Reader Domain; Apoptosis
Pathway:	Epigenetics; Apoptosis
Storage:	4°C, sealed storage, away from moisture and light * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (124.23 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.2423 mL	6.2117 mL	12.4234 mL
	5 mM	0.2485 mL	1.2423 mL	2.4847 mL
	10 mM	0.1242 mL	0.6212 mL	1.2423 mL

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

In Vivo

1. Add each solvent one by one: 0.5% Hypromellose
   Solubility: 13.33 mg/mL (16.56 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (3.11 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (3.11 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.11 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

VTP50469 fumarate is a potent, highly selective and orally active Menin-MLL interaction inhibitor with a K_i of 104 pM. VTP50469 fumarate has potently anti-leukemia activity[1][2].

IC_{50} & Target

Ki: 104 pM (Menin-MLL interaction)[1][2]

In Vitro

VTP50469 more potently and rapidly inhibits cell proliferation in a concentration-dependent manner in MLL-r cell lines

carrying (MOLM13 (IC_{50} of 13 nM), THP1 (IC_{50} of 37 nM), NOMO1 (IC_{50} of 30 nM), ML2 (IC_{50} of 16 nM), EOL1 (IC_{50} of 20 nM), and murine MLL-AF9 cells (IC_{50} of 15 nM)) and ALL (KOPN8 (IC_{50} of 15 nM), HB11;19 (IC_{50} of 36 nM), MV4;11 (IC_{50} of 17 nM), SEMK2 (IC50 of 27 nM), and RS4;11 (IC_{50} of 25 nM)) cell lines[1].
At early timepoints MLL-r B cell ALL (B-ALL) cell lines, but not MLL-r AML cell lines, underwent apoptosis in response to VTP50469 in a dose-dependent manner. MLL-r AML cell lines underwent dose-dependent differentiation starting at 4-6 days of exposure to VTP50469[1].
VTP50469 displaces Menin from protein complexes and inhibits chromatin occupancy of MLL at select genes. Loss of MLL binding led to changes in gene expression, differentiation, and apoptosis[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

VTP50469 (15-60 mg/kg; oral administration; twice a day; for 28 days; NSG mice) treatment is highly efficacious across all dosage levels and all treatment groups have a significant survival advantage. Mice dosed at 30 and 60 mg/kg VTP50469 extends survival advantage[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Unconditioned immunodeficient (NSG) mice with MV4;11 cells[1]
Dosage:	15 mg/kg, 30 mg/kg, and 60 mg/kg
Administration:	Oral administration; twice a day; for 28 days
Result:	Was highly efficacious across all dosage levels and all treatment groups had a significant survival advantage over the control group.

CUSTOMER VALIDATION

- Blood Cancer J. 2022 Jan 11;12(1):5.
- Int J Oncol. 2020 Oct;57(4):1057-1071.

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REFERENCES

[1]. Krivtsov AV, et al. A Menin-MLL Inhibitor Induces Specific Chromatin Changes and Eradicates Disease in Models of MLL-Rearranged Leukemia. Cancer Cell. 2019 Dec 9;36(6):660-673.e11.

[2]. Andrei V. Krivtsov, et al. Abstract 4958: VTP50469 is a novel, orally available menin-MLL1 inhibitor effective against MLL-rearranged and NPM1-mutant leukemia. Cancer Resceach. July 2018.Volume 78, Issue 13 Supplement.

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