Tuspetinib

Cat. No.: HY-145015

CAS No.: 2294874-49-8

Molecular Formula: $C_{29}H_{33}ClN_6$

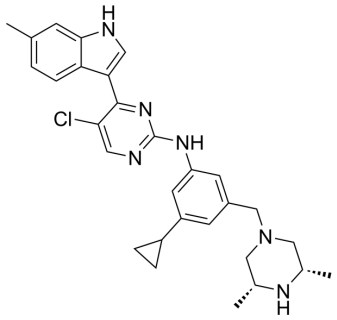
Molecular Weight: 501.07

Target: FLT3; Apoptosis

Pathway: Protein Tyrosine Kinase/RTK; Apoptosis

Storage: 4°C, protect from light

* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (249.47 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9957 mL	9.9786 mL	19.9573 mL
	5 mM	0.3991 mL	1.9957 mL	3.9915 mL
	10 mM	0.1996 mL	0.9979 mL	1.9957 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.15 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tuspetinib (HM43239) is an orally active and selective FLT3 inhibitor with IC_{50}s of 1.1 nM, 1.8 nM and 1.0 nM for FLT3 WT, FLT3 internal tandem duplication (ITD) and FLT3 D835Y kinases, respectively. Tuspetinib inhibits the kinase activity of FLT3 as a reversible type I inhibitor and modulates p-STAT5, p-ERK, SYK, JAK1/2, and TAK1. Tuspetinib inhibits the proliferation and induces the apoptosis of leukemic cells[1][2][3].

IC_{50} & Target

FLT3 WT	FLT3 ITD	FLT3 D835Y
1.1 nM (IC_{50})	1.8 nM (IC_{50})	1.0 nM (IC_{50})

In Vitro

Tuspetinib potently inhibits the growth of acute myeloid leukemia cell lines harboring FLT3 ITD mutation, such as MV4-11 (IC_{50}: 1.3 nM), MOLM-13 (IC_{50}: 5.1 nM), and MOLM-14 (IC_{50}: 2.9 nM). Tuspetinib also inhibits KG1a cells (CD34+/CD38- cells) proliferation[1].

Tuspetinib induces the caspase 3/7-dependent apoptosis of leukemic stem cell (LSC) marker-expressing KG1a cells (CD34+/CD38- cells)[1].

Tuspetinib potently inhibits phosphorylation of SYK, STAT3, and STAT5 in KG1a cells[3].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Tuspetinib shows the excellent dose proportional antitumor activity in mouse models xenografted with both MV4-11 and MOLM-13 cell lines without any significant toxicity[1]. Tuspetinib prolongs survival in FLT3 ITD/TKD double mutated xenograft mouse models[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Miyoung Lee, et.al. Abstract 804: Antitumor activity of the potent and novel FLT3 inhibitor HM43239 in acute myeloid leukemia. Cancer Res July 1 2018 (78) (13 Supplement) 804.

[2]. Naval G. Daver, et.al. HM43239, a Novel Potent Small Molecule FLT3 Inhibitor, in Acute Myeloid Leukemia (AML) with FMS-like Tyrosine Kinase 3 (FLT3) Mutations: Phase 1 /2 Study. Blood 2019; 134 (Supplement_1): 1331.

[3]. JiSook Kim, et.al. Abstract 1293: HM43239, a novel FLT3 inhibitor in overcoming resistance for acute myeloid leukemia. Cancer Res July 1 2019 (79) (13 Supplement) 1293.

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