Tandutinib hydrochloride

Cat. No.: HY-10202A

CAS No.: 2438900-70-8

Molecular Formula: $C_{31}H_{43}ClN_6O_4$

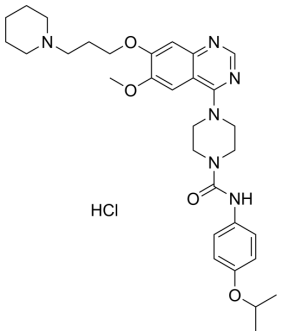
Molecular Weight: 599.16

Target: FLT3; c-Kit; PDGFR; Apoptosis

Pathway: Protein Tyrosine Kinase/RTK; Apoptosis

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

H_2O : 100 mg/mL (166.90 mM; Need ultrasonic)

DMSO : ≥ 100 mg/mL (166.90 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6690 mL	8.3450 mL	16.6900 mL
	5 mM	0.3338 mL	1.6690 mL	3.3380 mL
	10 mM	0.1669 mL	0.8345 mL	1.6690 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 100 mg/mL (166.90 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 (4.17 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.17 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tandutinib hydrochloride (MLN518 hydrochloride) is a potent and selective inhibitor of the FLT3 with an IC_{50} of 0.22 μM, and also inhibits c-Kit and PDGFR with IC_{50}s of 0.17 μM and 0.20 μM, respectively. Tandutinib hydrochloride can be used for acute myelogenous leukemia (AML)[1][2]. Tandutinib hydrochloride has the ability to cross the blood-brain barrier[3].

IC_{50} & Target			
	FLT3	c-Kit	PDGFR
	0.22 μM (IC_{50})	0.17 μM (IC_{50})	0.2 μM (IC_{50})

In Vitro

Tandutinib (0-3 μM; 30 minutes; Ba/F3 cells) treatment inhibits IL-3-independent cell growth and FLT3-ITD autophosphorylation with an IC_{50} of 10-100 nM in Ba/F3 cells expressing different FLT3-ITD mutants[1].
Tandutinib (1 μM; 24-96 hours; Molm-14 and THP-1 AML cells) treatment induces apoptosis in FLT3-ITD-positive AML cells[1].
In human FLT3-ITD-positive AML cell lines, Tandutinib inhibits FLT3-ITD phosphorylation (IC_{50} of ~30 nM). As with Erk2, a constitutively high level of Akt phosphorylation is readily detected and is efficiently blocked by pretreatment of the Molm-14 cells with 100-300 nM Tandutinib[1].
Tandutinib inhibits cell proliferation of the FLT3-ITD-positive Molm-13 and Molm-14 with an IC_{50} of 10 nM. And signaling through the MAP kinase and PI3 kinase pathways[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Apoptosis Analysis[1]

Cell Line:	Molm-14 and THP-1 AML cells
Concentration:	1 μM
Incubation Time:	24 hours, 48 hours, 72 hours, 96 hours
Result:	Induced apoptosis in FLT3-ITD-positive AML cells.

Western Blot Analysis[1]

Cell Line:	Ba/F3 cells
Concentration:	0 μM, 0.003 μM, 0.01 μM, 0.03 μM, 0.1 μM, 1 μM and 3 μM
Incubation Time:	30 minutes
Result:	In Ba/F3 cells expressing different FLT3-ITD mutants, inhibited IL-3-independent cell growth and FLT3-ITD autophosphorylation.

In Vivo

Tandutinib (60 mg/kg; oral gavage; daily; for 35 days; athymic nude mice) treatment causes a statistically significant increase in survival that was extended on average by 20 days[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Athymic nude mice injected with Ba/F3 cells[1]
Dosage:	60 mg/kg
Administration:	Oral gavage; daily; for 35 days
Result:	Caused a statistically significant increase in survival that was extended on average by 20 days.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Cancers (Basel). 2022, 14(23), 5854
- Drug Des Dev Ther. 2020 Oct 23;14:4439-4449.
- Drug Des Devel Ther. 2018 Apr 30;12:1009-1017.
- Biochem Biophys Res Commun. 2017 Aug 19;490(2):209-216.

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REFERENCES

[1]. Kelly LM, et al. CT53518, a novel selective FLT3 antagonist for the treatment of acute myelogenous leukemia (AML). Cancer Cell. 2002 Jun;1(5):421-32.

[2]. Griswold IJ, et al. Effects of MLN518, a dual FLT3 and KIT inhibitor, on normal and malignant hematopoiesis. Blood. 2004 Nov 1;104(9):2912-8.

[3]. Yang JJ, et al. P-glycoprotein and breast cancer resistance protein affect disposition of tandutinib, a tyrosine kinase inhibitor. Drug Metab Lett. 2010 Dec;4(4):201-12.

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

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