Tandutinib

Cat. No.: HY-10202

CAS No.: 387867-13-2

Molecular Formula: $C_{31}H_{42}N_6O_4$

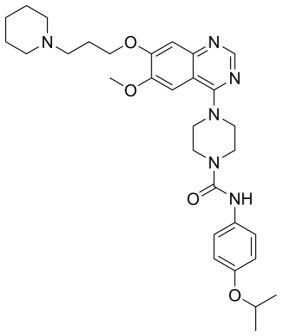
Molecular Weight: 562.7

Target: FLT3; c-Kit; PDGFR; Apoptosis

Pathway: Protein Tyrosine Kinase/RTK; Apoptosis

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 : 50 mg/mL (88.86 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7771 mL	8.8857 mL	17.7715 mL
	5 mM	0.3554 mL	1.7771 mL	3.5543 mL
	10 mM	0.1777 mL	0.8886 mL	1.7771 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: ≥ 2.5 mg/mL (4.44 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.44 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.44 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tandutinib (MLN518) 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 can be used for acute myelogenous leukemia (AML)[1][2]. Tandutinib has the ability to cross the blood-brain barrier[3].

IC_{50} & Target			
	PDGFR	FLT3	c-Kit
	0.2 μM (IC_{50})	0.22 μM (IC_{50})	0.17 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, 1(5), 421-432.

[2]. Griswold IJ, et al. Effects of MLN518, a dual FLT3 and KIT inhibitor, on normal and malignant hematopoiesis. Blood, 2004, 104(9), 2912-2918.

[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.

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