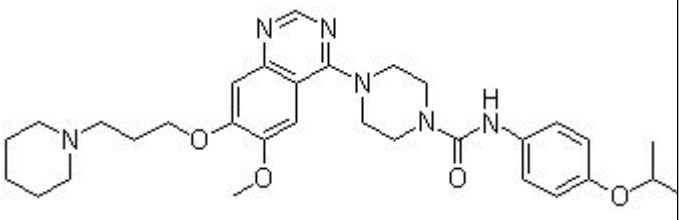
Product Introduction

Tandutinib (MLN518)

Tandutinib (MLN518, CT53518) is a potent **FLT3** antagonist with **IC50** of 0.22 μM, also inhibits PDGFR and c-Kit, 15 to 20-fold higher potency for FLT3 versus CSF-1R and >100-fold selectivity for the same target versus FGFR, EGFR and KDR. Phase 1/2.

Technical Data:

Molecular Weight (MW):	562.7	
Formula:	$C_{31}H_{42}N_6O_4$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 5 mg/mL	
	Water <1 mg/mL	
	Ethanol 6 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	387867-13-2	

Biological Activity

Tandutinib has little activity against EGFR, FGFR, KDR, InsR, Src, Abl, PKC, PKA and MAPKs. Tandutinib inhibits IL-3-independent cell growth and FLT3-ITD autophosphorylation with an IC50 of 10-100 nM. Tandutinib also inhibits the proliferation of human leukemia Ba/F3 cells containing FLT3-ITD mutations with IC50 values of 10-30 nM, and the FLT3-ITD-positive Molm-13 and Molm-14 cells with an IC50 of 10 nM. In FLT3-ITD-positive Molm-14 cells but not the FLT3-ITD-negative THP-1 cells, Tandutinib treatment

leads to significant apoptosis by 51% and 78% at 24 and 96 hours, respectively, due to specific FLT3 inhibition. [1] Tandutinib preferentially inhibits the growth of blast colonies from FLT3 ITD-positive compared with ITD-negative patients with AML, without affecting colony formation by normal human progenitor cells. [2]

Oral administration of Tandutinib at 60 mg/kg bid significantly increases the survival in mice bearing Ba/F3 cells expressing W51 FLT3-ITD mutant, and gives a significant reduction in mortality in a mouse bone marrow transplantation model. [1] Tandutinib treatment at 180 mg/kg twice daily has mild toxicity toward normal hematopoiesis, however, it is a dose at which Tandutinib is effective in treating FLT3 ITD-positive leukemia in mice. [2]

References

[1] Kelly LM, et al. Cancer Cell, 2002, 1(5), 421-432.

[2] Griswold IJ, et al. Blood, 2004, 104(9), 2912-2918.

[3] Schittenhelm MM, et al. Cell Cycle, 2009, 8(16), 2621-2630.

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