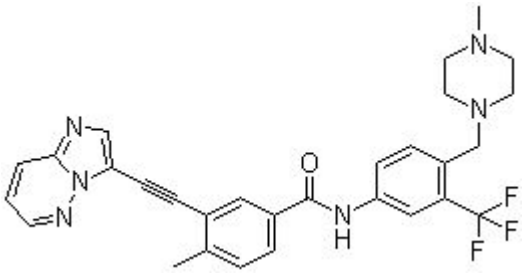
Product Introduction

Ponatinib (AP24534)

Ponatinib (AP24534) is a novel, potent multi-target inhibitor of **Abl**, PDGFRα, VEGFR2, FGFR1 and Src with **IC50** of 0.37 nM, 1.1 nM, 1.5 nM, 2.2 nM and 5.4 nM, respectively.

Technical Data:

Molecular Weight (MW):	532.56	
Formula:	C29H27F3N6O	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 30 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	943319-70-8	

Biological Activity

AP24534 potently inhibits native Abl, AblT315I, and other clinically important Abl kinase domain mutants with IC50 of 0.30 nM–2 nM. AP24534 doesn't inhibit Aurora kinase family members, nor does it inhibit insulin receptor or CDK2/cyclin E. AP24534 inhibits proliferation of Ba/F3 cells expressing Bcr-Abl with IC50 of 0.5 nM, as well as Ba/F3 cells expressing a range of Bcr-Abl mutants with IC50 of 0.5 nM–36 nM. The inhibition of proliferation by AP24534 is correlated with induction of apoptosis. [1-2] In leukemic cell lines containing activated forms of FLT3, KIT, FGFR1, and PDGFRα receptors, AP24534 potently inhibits

receptor phosphorylation and cellular proliferation with IC50 of 0.3 nM to 20 nM. In MV4-11 (FLT3-ITD(+/+)) but not RS4;11 (FLT3-ITD(–/–)) AML cells, AP24534 inhibits FLT3 signaling and induced apoptosis at less than 10 nM. AP24534 inhibits viability of primary leukemic blasts from a FLT3-ITD positive AML patient with IC50 of 4 nM but not those from patients with AML expressing native FLT3. [3]
In Ba/F3 cells engineered to express activated FGFR1-4, AP24534 potently inhibits FGFR-mediated signaling and viability with IC50 lower than 40 nM. In cell lines representing multiple tumor types (endometrial, bladder, gastric, breast, lung, and colon), and containing FGFRs dysregulated by a variety of mechanisms, AP24534 inhibits FGFR-mediated signaling with IC50 less than 40 nM and inhibits cell growth with IC50 of 7 nM–181 nM. [4]
In a mouse xenograft model of Ba/F3 cells expressing native Bcr-Abl, AP24534 (2.5 mg/kg and 5 mg/kg) prolongs mice median survival. In the xenograft model of Ba/F3 Bcr-AblT315I, AP24534 (10 mg/kg–50 mg/kg) significantly suppresses tumor growth. AP24534 (30 mg/kg) decreases the phosphorylated Bcr-Abl and phosphorylated CrkL levels in the tumors. [2]

References

[1] O'Hare T, et al. Cancer Cell, 2009, 16(5), 401-412.
[2] Huang WS, et al. J Med Chem, 2010, 53(12), 4701-4719.
[3] Gozgit JM, et al. Mol Cancer Ther, 2011, 10(6), 1028-1035.
[4] Gozgit JM, et al. Mol Cancer Ther, 2012, doi: 10.1158/1535-7163. [Epub ahead of print]
[5] O'Hare T, et al. Blood, 2004, 104(8), 2532-2539.

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