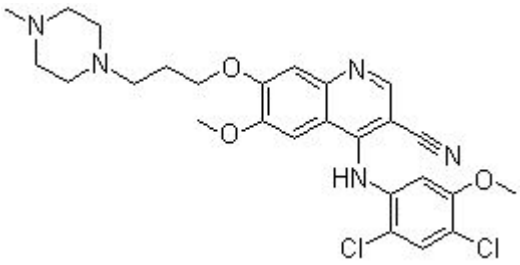
Product Introduction

Bosutinib (SKI-606)

Bosutinib (SKI-606) is a novel, dual **Src/Abl** inhibitor with **IC50** of 1.2 nM and 1 nM, respectively.

Technical Data:

Molecular Weight (MW):	530.45	
Formula:	$C_{26}H_{29}Cl_2N_5O_3$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 100 mg/mL	
	Water <1 mg/mL	
	Ethanol 2 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	380843-75-4	

Biological Activity

Bosutinib is selective for Src over non-Src family kinases with an IC50 of 1.2 nM, and potently inhibits Src-dependent cell proliferation with an IC50 of 100 nM. [1] Bosutinib significantly inhibits the proliferation of Bcr-Abl-positive leukemia cell lines KU812, K562, and MEG-01 but not Molt-4, HL-60, Ramos, and other leukemia cell lines, with IC50 of 5 nM, 20 nM and 20 nM, respectively, more potently than that of STI-571. Similar to STI-571, Bosutinib displays antiproliferative activity against the Abl-MLV-transformed fibroblasts with IC50 of 90 nM. Bosutinib ablates tyrosine phosphorylation of Bcr-Abl and STAT5 in CML cells and of v-Abl expressed in fibroblasts at the concentration of ~50 nM, 10-25 nM and 200 nM, respectively, leading

to the Bcr-Abl downstream signaling inhibition of Lyn/Hck phosphorylation. [2] Although unable to inhibit the proliferation and survival of breast cancer cells, Bosutinib significantly decreases the motility and invasion of breast cancer cells with IC50 of ~250 nM, involved with an increase in cell-to-cell adhesion and membrane localization of β-catenin. [3]

Bosutinib (60 mg/kg/day) is active against Src-transformed fibroblasts xenografts and HT29 xenografts in nude mice with T/C of 18% and 30%, respectively. [1] Oral administration of Bosutinib for 5 days significantly suppresses K562 tumor growth in mice in a dose-dependent manner, with the large tumors eradicated at dose of 100 mg/kg and tumor free at 150 mg/kg without overt toxicity. [2] As being inactive against Colo205 xenografts in nude mice at 50 mg/kg twice daily, Bosutinib dosing at 75 mg/kg twice daily is necessary against Colo205 xenografts, and increasing the dose of Bosutinib has no additional benefit, in contrast to the significant dose-dependent ability against HT29 xenografts. [4]

References

[1] Boschelli DH, et al. J Med Chem, 2001, 44(23), 3965-3977.

[2] Golas JM, et al. Cancer Res, 2003, 63(2), 375-381.

[3] Vultur A, et al. Mol Cancer Ther, 2008, 7(5), 1185-1194.

[4] Golas JM, et al. Cancer Res, 2005, 65(12), 5358-5364.

[5] Redaelli S, et al. Leukemia, 2010, 24(6), 1223-1227.

[6] Sakuma Y, et al. Oncol Rep, 2011, 25(3), 661-667.

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