

Product Data Sheet

Product Name: Imatinib Mesylate (STI571)

Cat. No.: GC11759

Chemical Properties

Cas. No. 220127-57-1

Chemical Name methanesulfonic acid;4-[(4-methylpiperazin-1-yl)methyl]-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-yl)amino]phenyl]benzamide

SMILES CC1=C(C=C(C=C1)NC(=O)C2=CC=C(C=C2)CN3CCN(CC3)C)NC4=NC=CC(=N4)C5=CN=CC=C5.CS(=O)(=O)O

Formula $C_{29}H_{31}N_7O \cdot CH_4SO_3$ M.Wt 589.71

Solubility $\geq 29.5\text{mg/mL}$ in DMSO ; $> 50\text{mg/mL}$ in water Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

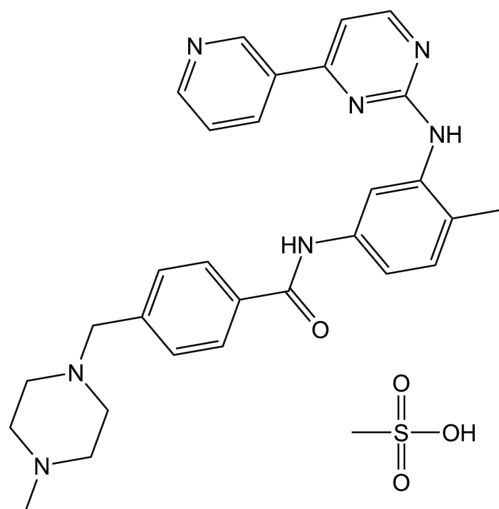
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Structure



Protocol

Cell experiment [1]:

Cell lines A549 cells

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Tested A549 cells were placed in 96-well flat-bottom plates (Sarstedt, Inc., Newton, NC, USA) at a density of 5×10^3 cells per well 24h before the addition of the test compounds. The cells were incubated for 96h with two different concentrations (10 and 100nM) of PRI-2191 and concurrently with various concentrations of Imatinib Mesylate (10, 100, 1000 and 10,000ng/mL) and other cytostatic drugs (DTX or ID: 0.1, 1, 10, 100ng/mL; CIS: 1, 10, 100, 1000ng/mL). The sulforhodamine B (SRB) assay was performed to evaluate the cytotoxic effect, as described previously. As a result, IC₅₀ (inhibitory concentration 50%), i.e., the dose of the tested compound that inhibited the proliferation of cancer cells by 50%, was calculated for each separate experiment in Cheburator 0.4, Dmitry Nevozhay software. Each compound concentration in a given experiment was tested in triplicate; each experiment was repeated 3–5 times. Ethanol, serving as the solvent of the tested agents, in a dilution corresponding to its highest concentration applied with the tested compounds, did not exert any inhibitory effect on cell proliferation ($p > 0.05$).

Preparation Method

Reaction Conditions 10, 100, 1000 and 10,000ng/mL; 96h

Applications The proliferation curves of each group of cells were compared. The results showed that the combined use of Imatinib Mesylate and PRI-2191 exhibited a cumulative inhibitory effect on cell proliferation, and there was a synergistic effect between the two.

Animal experiment [2]:

Animal models Lewis rats (IRI)

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Preparation Method	Male Lewis rats were heparinized and underwent left thoracotomy, and the left hilum was clamped for 90 minutes followed by reperfusion for 120 minutes. Imatinib Mesylate (50mg/kg) and a solvent were administered intraperitoneally 20 minutes before ischemia in the imatinib group and the vehicle group, respectively (n = 7 in each group). After reperfusion, lung function, lung wet to dry weight (W/D) ratio, and histologic findings were obtained. The expression of vascular endothelial cadherin (VEC), the phosphorylation level of CrkL (pCrkL) (an exclusive target of Abl kinases), and the cytokine level were evaluated using lung tissue lysate. The imatinib concentrations of plasma and lungs after reperfusion were measured in this hilar clamp model (n = 7).
Dosage form	50mg/kg once; i.p.
Applications	In the Imatinib Mesylate group, lung function was improved with a lower W/D ratio. Perivascular edema and neutrophil infiltration were ameliorated. The imatinib group demonstrated maintained expression of VEC, inhibition of pCrkL, and a significantly higher level of interleukin (IL)-10.

References:

- [1] Maj E, Filip-Psurska B, Switalska M, Kutner A, Wietrzyk J. Vitamin D Analogs Potentiate the Antitumor Effect of Imatinib Mesylate in a Human A549 Lung Tumor Model. *Int J Mol Sci.* 2015 Nov 13;16(11):27191-207.
- [2] Tanaka S, Chen-Yoshikawa TF, Kajiwarra M, Menju T, Ohata K, Takahashi M, Kondo T, Hijiya K, Motoyama H, Aoyama A, Masuda S, Date H. Protective Effects of Imatinib on Ischemia/Reperfusion Injury in Rat Lung. *Ann Thorac Surg.* 2016 Nov;102(5):1717-1724.

Background

Imatinib Mesylate (STI571) is an orally bioavailable multi-target inhibitor with IC₅₀ values for Bcr-Abl, c-Kit and PDGFR are 0.6μM, 0.1μM and 0.1μM respectively [1]. Tyrosine kinase Bcr-Abl is present throughout the entire disease process of almost all cases of chronic myeloid leukemia (CML) [2]. Imatinib Mesylate is used to treat chronic myeloid leukemia and gastrointestinal stromal tumors [3].

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In vitro, Imatinib Mesylate (10 μ M) incubated with T cells for 1h, reduced the phosphorylation of Lck, ERK 1/2 and Rb proteins, and decreased the levels of cyclin D3 and activated nuclear transcription factor κ B (NF- κ B) [4]. Different concentrations of Imatinib Mesylate (10, 100, 1000 and 10000ng/mL) were combined with PRI-2191 to treat human lung adenocarcinoma A549 cells for 96 hours. By comparing the proliferation curves of each group of cells, it was observed that the inhibition of cell proliferation exhibited a cumulative effect, and the two had a synergistic effect [5].

In vivo, Imatinib Mesylate (50mg/kg/day; i.p.) was administered 20 minutes before ischemia modeling in rats with ischemia/reperfusion injury (IRI), significantly increasing the level of interleukin (IL)-10, maintaining the expression of vascular endothelial cells (VEC) stable, and inhibiting pCrkL [6]. Imatinib Mesylate (75mg/kg/day; 19 days; i.p.) combined with the vitamin D3 analog PRI-2191 downregulated the expression of VEGF in the tumor tissues of mice, upregulated p53 and downregulated Bcl-2, and significantly inhibited tumor growth [5].

References:

- [1] Buchdunger E, Zimmermann J, Mett H, et al. Selective inhibition of the platelet-derived growth factor signal transduction pathway by a protein-tyrosine kinase inhibitor of the 2-phenylaminopyrimidine class [retracted in: Proc Natl Acad Sci U S A. 1998 Sep 29;95(20):12069.
- [2] Druker B J, Sawyers C L, Kantarjian H, et al. Activity of a specific inhibitor of the BCR-ABL tyrosine kinase in the blast crisis of chronic myeloid leukemia and acute lymphoblastic leukemia with the Philadelphia chromosome[J]. New England Journal of Medicine, 2001, 344(14): 1038-1042.
- [3] Tibullo D, Giallongo C, La Cava P, et al. Effects of imatinib mesylate in osteoblastogenesis[J]. Experimental hematology, 2009, 37(4): 461-468.
- [4] Dietz A B, Souan L, Knutson G J, et al. Imatinib mesylate inhibits T-cell proliferation in vitro and delayed-type hypersensitivity in vivo[J]. Blood, 2004, 104(4): 1094-1099.
- [5] Maj E, Filip-Psurska B, Świtalska M, Kutner A, Wietrzyk J. Vitamin D Analogs Potentiate the Antitumor Effect of Imatinib Mesylate in a Human A549 Lung Tumor Model. Int J Mol Sci. 2015 Nov 13;16(11):27191-207.
- [6] Tanaka S, Chen-Yoshikawa TF, Kajiwarra M, Menju T, Ohata K, Takahashi M, Kondo T, Hijiya K, Motoyama H, Aoyama A, Masuda S, Date H. Protective Effects of Imatinib on Ischemia/Reperfusion Injury in Rat Lung. Ann Thorac Surg. 2016 Nov;102(5):1717-1724.

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