

Product Data Sheet

Product Name: Nilotinib (AMN-107)

Cat. No.: GC14129

Chemical Properties

Cas. No. 641571-10-0

Chemical Name 4-methyl-N-[3-(4-methylimidazol-1-yl)-5-(trifluoromethyl)phenyl]-3-[(4-pyridin-3-yl)pyrimidin-2-yl]amino]benzamide

SMILES CC1=C(C=C(C=C1)C(=O)NC2=CC(=CC(=C2)N3C=C(N=C3)C)C(F)(F)F)NC4=NC=CC(=N4)C5=CN=CC=C5

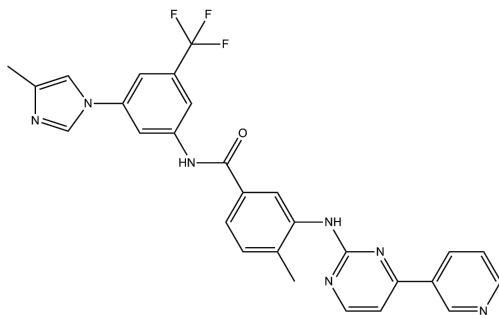
Formula $C_{28}H_{22}F_3N_7O$ M.Wt 529.53

Solubility $\geq 26.5\text{mg/mL}$ in DMSO, $\geq 5\text{mg/mL}$ in EtOH with ultrasonic and warming 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.

Structure



Protocol

Cell experiment [1]:

Cell lines $CD8^+$ T cells

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Preparation Method CD8⁺ T cells were labelled with CFSE at a final concentration of 1μM for 10min. at 37°C. Then, the cells were washed with ice-cold culture medium for three times and resuspended in culture medium. 4μM Nilotinib was added at different time points as indicated (0h, 24h and 48h). CD8⁺ T cells untreated with Nilotinib served as control. After 96 hrs of stimulation with PHA and IL-2, the proliferation of cells was measured by flow cytometry.

Reaction Conditions 4μM; 0, 24, 48h

Applications Nilotinib inhibits CD8⁺ T lymphocyte proliferation, even when added 48h after the start of culture, it can inhibit the proliferation of CD8⁺ T lymphocytes stimulated by PHA/IL-2.

Animal experiment [2]:

Animal models BALB/cSlc-nu/nu mice

Preparation Method Tumor tissue fragments (5mm³) were transplanted s.c. into the backs of BALB/cSlc-nu/nu mice that were randomized into 3 groups (n=6-8). Doses of 40mg/kg/day of Imatinib, Nilotinib or pure water (control) were administered by oral gavage daily for 28 days. Tumor size was measured every two to three days.

Dosage form 40mg/kg/day for 28 days; p.o.

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Applications Nilotinib inhibited tumor growth by 69.6%, 85.3% and 47.5% in GK1X, GK2X and GK3X xenograft lines, respectively.

References:

- [1]Chen J, Schmitt A, Chen B, et al. Nilotinib hampers the proliferation and function of CD8⁺ T lymphocytes through inhibition of T cell receptor signalling[J]. Journal of cellular and molecular medicine, 2008, 12(5b): 2107-2118.
- [2]Sako H, Fukuda K, Saikawa Y, et al. Antitumor effect of the tyrosine kinase inhibitor nilotinib on gastrointestinal stromal tumor (GIST) and imatinib-resistant GIST cells[J]. PloS one, 2014, 9(9): e107613.

Background

Nilotinib(AMN-107) is a selective oral tyrosine kinase inhibitor that inhibits the autophosphorylation of native Bcr-Abl (WT p210) and mutant Bcr-Abl (E281K, E292K, F317L, M351T, and F486S) with IC₅₀ values of 20, 42, 31, 38, 29, and 41nM, respectively^[1]. Nilotinib inhibits lymphocyte-specific protein tyrosine kinase (LCK) with an IC₅₀ of 550nM^[2]. Nilotinib is an aminopyrimidine-based high-affinity ATP-competitive inhibitor^[3].

In vitro, treatment of CD8⁺ T cells with Nilotinib (4μM) for 0-48h significantly inhibited PHA/IL-2-stimulated cell proliferation, downregulated the expression of CD8⁺ T cell activation markers CD69 and CD25, and reduced the phosphorylation of ERK 1/2 and LCK proteins^[4]. Nilotinib (5μM) treatment of CD34⁺ cells from chronic myeloid leukemia (CML) patients for 16h inhibited CrkL phosphorylation but did not induce apoptosis^[5].

In vivo, oral treatment of gastrointestinal stromal tumor (GIST) mice with Nilotinib (40mg/kg/day) for 4 weeks inhibited tumor growth by 69.6%, 85.3% and 47.5% in GK1X, GK2X and GK3X xenograft lines, respectively^[6]. Oral treatment of leukemia mice with Nilotinib (75mg/kg/day) for 30 days significantly prolonged the survival of the mice, and visible lymphoma masses disappeared within six days of treatment, and the number of leukemia cells in the peripheral blood was significantly

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reduced^[7].

References:

- [1] Weisberg E, Manley P, Mestan J, et al. AMN107 (nilotinib): a novel and selective inhibitor of BCR-ABL[J]. British journal of cancer, 2006, 94(12): 1765-1769.
- [2] Blake S J, Lyons A B, Hughes T P. Nilotinib inhibits the Src-family kinase LCK and T-cell function in vitro[J]. Journal of cellular and molecular medicine, 2009, 13(3): 599.
- [3] Swords R, Mahalingam D, Padmanabhan S, et al. Nilotinib: optimal therapy for patients with chronic myeloid leukemia and resistance or intolerance to imatinib[J]. Drug design, development and therapy, 2009: 89-101.
- [4] Chen J, Schmitt A, Chen B, et al. Nilotinib hampers the proliferation and function of CD8+ T lymphocytes through inhibition of T cell receptor signalling[J]. Journal of cellular and molecular medicine, 2008, 12(5b): 2107-2118.
- [5] Jørgensen H G, Allan E K, Jordanides N E, et al. Nilotinib exerts equipotent antiproliferative effects to imatinib and does not induce apoptosis in CD34+ CML cells[J]. Blood, 2007, 109(9): 4016-4019.
- [6] Sako H, Fukuda K, Saikawa Y, et al. Antitumor effect of the tyrosine kinase inhibitor nilotinib on gastrointestinal stromal tumor (GIST) and imatinib-resistant GIST cells[J]. PloS one, 2014, 9(9): e107613.
- [7] Kaur P, Feldhahn N, Zhang B, et al. Nilotinib treatment in mouse models of P190 Bcr/Abl lymphoblastic leukemia[J]. Molecular cancer, 2007, 6: 1-11.

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