

Product Data Sheet

Product Name: Vandetanib trifluoroacetate

Cat. No.: GC37886

Chemical Properties

Cas. No. 338992-53-3

SMILES FC1=CC(Br)=CC=C1NC2=NC=NC3=CC(OCC4CCN(CC4)C)=C(C=C23)OC.O=C(O)C(F)(F)F

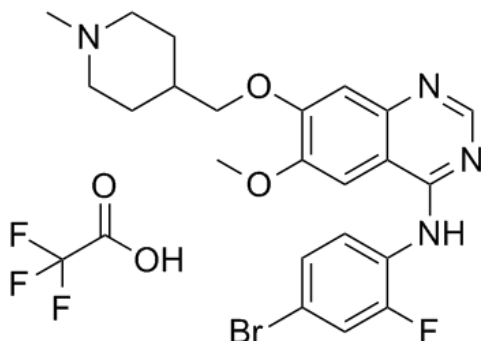
Formula $C_{24}H_{25}BrF_4N_4O_4$ M.Wt 589.38

Solubility Soluble in DMSO 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

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

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Cell experiment: Growth inhibition is measured by a modified MTT assay. Briefly, the cells are plated on 96-well plates at a density of 2000 cells per well and exposed to each gefitinib or vandetanib for 72 h. Each assay is performed in triplicate. The 50% inhibitory concentration (IC₅₀) of each drug is determined as the mean±standard deviation (SD).

Animal experiment: One million H1650 cells or H1650/PTEN cells (H1650 cells with a transfected PTEN gene) are injected subcutaneously into the backs of each mouse. On 10th day after injection, mice are randomly assigned to three groups, which receive either vehicle, vandetanib (15 mg/kg/day), or gefitinib (15 mg/kg/day). Vehicle, vandetanib, and gefitinib are administered once per day p.o., five times per week. Tumor volume (width×width×length/2) and body weight are determined periodically. Tumor volumes are expressed as mean±SD. Differences in tumor volume are evaluated using Student's t-test.

References:

- [1]. Wedge SR, et al. ZD6474 inhibits vascular endothelial growth factor signaling, angiogenesis, and tumor growth following oral administration. *Cancer Res.* 2002 Aug 15;62(16):4645-55.
- [2]. Hegedus C, et al. Interaction of the EGFR inhibitors gefitinib, vandetanib, pelitinib and neratinib with the ABCG2 multidrug transporter: implications for the emergence and reversal of cancer drug resistance. *Biochem Pharmacol.* 2012 Aug 1;84(3):260-7.
- [3]. Takeda H, et al. Vandetanib is effective in EGFR-mutant lung cancer cells with PTEN deficiency. *Exp Cell Res.* 2013 Feb 15;319(4):417-23.
- [4]. Inoue K, et al. Vandetanib, an inhibitor of VEGF receptor-2 and EGF receptor, suppresses tumor development and improves prognosis of liver cancer in mice. *Clin Cancer Res.* 2012 Jul 15;18(14):3924-33.

Background

Vandetanib trifluoroacetate is a potent inhibitor of VEGFR2 with IC₅₀ of 40 nM. VEGFR2|40 nM (IC₅₀)

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Vandetanib inhibits VEGFR3 and EGFR with IC₅₀ of 110 nM and 500 nM, respectively. Vandetanib is not sensitive to PDGFR β , Flt1, Tie-2 and FGFR1 with IC₅₀ of 1.1-3.6 μ M, while almost has no activity against MEK, CDK2, c-Kit, erbB2, FAK, PDK1, Akt and IGF-1R with IC₅₀ above 10 μ M. Vandetanib inhibits VEGF-, EGF- and bFGF-stimulated HUVEC proliferation with IC₅₀ of 60 nM, 170 nM and 800 nM, with no effect on basal endothelial cell growth. Vandetanib inhibits tumor cell growth with IC₅₀ of 2.7 μ M (A549) to 13.5 μ M (Calu-6)[1]. Olanacatib is a weak inhibitor of antigen presentation, measured in a mouse B cell line (IC₅₀=1.5 $\pm$ 0.4 μ M), compared to the Cat S inhibitor LHVS (IC₅₀=0.001 μ M) in the same assay. Olanacatib also shows weak inhibition of the processing of the MHC II invariant chain protein Iip10 in mouse splenocytes compared to LHVS (minimum inhibitory concentration 1-10 μ M versus 0.01 μ M, respectively)[2]. Vandetanib suppresses phosphorylation of VEGFR-2 in HUVECs and EGFR in hepatoma cells and inhibits cell proliferation[4].

Vandetanib (15 mg/kg, p.o.) has a superior anti-tumor effect than gefitinib in the H1650 xenograft model, and suppresses tumor growth with IC₅₀ of 3.5 $\pm$ 1.2 μ M[3]. In tumor-bearing mice, vandetanib (50 or 75 mg/kg) suppresses phosphorylation of VEGFR-2 and EGFR in tumor tissues, significantly reduces tumor vessel density, enhances tumor cell apoptosis, suppresses tumor growth, improves survival, reduces number of intrahepatic metastases, and upregulates VEGF, TGF- α , and EGF in tumor tissues[4].

[1]. Wedge SR, et al. ZD6474 inhibits vascular endothelial growth factor signaling, angiogenesis, and tumor growth following oral administration. *Cancer Res.* 2002 Aug 15;62(16):4645-55. [2]. Hegedus C, et al. Interaction of the EGFR inhibitors gefitinib, vandetanib, pelitinib and neratinib with the ABCG2 multidrug transporter: implications for the emergence and reversal of cancer drug resistance. *Biochem Pharmacol.* 2012 Aug 1;84(3):260-7. [3]. Takeda H, et al. Vandetanib is effective in EGFR-mutant lung cancer cells with PTEN deficiency. *Exp Cell Res.* 2013 Feb 15;319(4):417-23. [4]. Inoue K, et al. Vandetanib, an inhibitor of VEGF receptor-2 and EGF receptor, suppresses tumor development and improves prognosis of liver cancer in mice. *Clin Cancer Res.* 2012 Jul 15;18(14):3924-33.

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