Vandetanib

Cat. No.: HY-10260

CAS No.: 443913-73-3

Molecular Formula: $C_{22}H_{24}BrFN_4O_2$

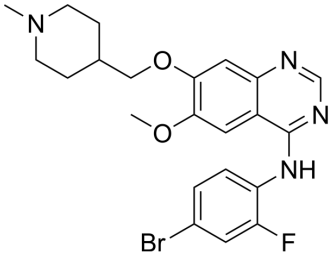
Molecular Weight: 475.35

Target: VEGFR; Autophagy; Apoptosis

Pathway: Protein Tyrosine Kinase/RTK; Autophagy; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 20.83 mg/mL (43.82 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1037 mL	10.5186 mL	21.0371 mL
	5 mM	0.4207 mL	2.1037 mL	4.2074 mL
	10 mM	0.2104 mL	1.0519 mL	2.1037 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 50% PEG300 >> 50% saline
   Solubility: 10 mg/mL (21.04 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.26 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.26 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Vandetanib (D6474) is a potent, orally active inhibitor of VEGFR2/KDR tyrosine kinase activity (IC_{50}=40 nM). Vandetanib also has activity versus the tyrosine kinase activity of VEGFR3/FLT4 (IC_{50}=110 nM) and EGFR/HER1 (IC_{50}=500 nM)[1].

IC_{50} & Target

VEGFR2	VEGFR3	EGFR/HER1
40 nM (IC_{50})	110 nM (IC_{50})	500 nM (IC_{50})

In Vitro

Vandetanib inhibits VEGFR3 and EGFR with IC_{50} of 110 nM and 500 nM, respectively. Vandetanib is not sensitive to PDGFRβ,

	Flt1, Tie-2 and FGFR1 with IC_{50} of 1.1-3.6 μM, while almost has no activity against MEK, CDK2, c-Kit, erbB2, FAK, PDK1, Akt and IGF-1R with IC_{50} above 10 μM. Vandetanib inhibits VEGF-, EGF- and bFGF-stimulated HUVEC proliferation with IC_{50} of 60 nM, 170 nM and 800 nM, with no effect on basal endothelial cell growth. Vandetanib inhibits tumor cell growth with IC_{50} of 2.7 μM (A549) to 13.5 μM (Calu-6)[1]. Odanacatib is a weak inhibitor of antigen presentation, measured in a mouse B cell line (IC_{50}=1.5±0.4 μM), compared to the Cat S inhibitor LHVS (IC_{50}=0.001 μM) in the same assay. Odanacatib 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 μM versus 0.01 μM, respectively)[2]. Vandetanib suppresses phosphorylation of VEGFR-2 in HUVECs and EGFR in hepatoma cells and inhibits cell proliferation[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Vandetanib (15 mg/kg, p.o.) has a superior anti-tumor effect than gefitinib in the H1650 xenograft model, and suppresses tumor growth with IC_{50} of 3.5±1.2 μM[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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [3]	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 (IC_{50}) of each drug is determined as the mean±standard deviation (SD). MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Nat Commun. 2020 Apr 20;11(1):1913.
- Cancer Lett. 2018 Jul 21;434:184-195.
- Acta Pharmacol Sin. 2021 Jan;42(1):108-114.
- Oncogene. 2018 Mar;37(11):1417-1429.

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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.

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