

Product Data Sheet

Product Name: Vandetanib (ZD6474)

Cat. No.: GC15022

Chemical Properties

Cas. No. 443913-73-3

Chemical Name N-(4-bromo-2-fluorophenyl)-6-methoxy-7-[(1-methylpiperidin-4-yl)methoxy]quinazolin-4-amine

SMILES CN1CCC(CC1)COC2=C(C=C3C(=C2)N=CN=C3NC4=C(C=C(C=C4)Br)F)OC

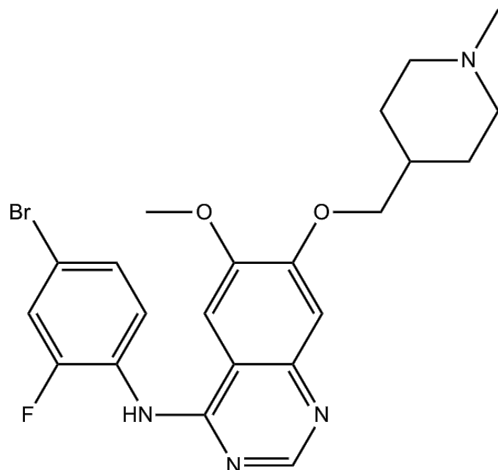
Formula $C_{22}H_{24}BrFN_4O_2$ M.Wt 475.35

Solubility $\geq 11.9\text{mg/mL}$ in DMSO with gentle 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 TT and MZ-CRC-1 cells

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

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Product Data Sheet

Preparation method The solubility of this compound in DMSO is <10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Reaction Conditions 250 nM, 5 days for TT cells 6 days for MZ-CRC-1 cells

Applications After 5 days of treatment, TT (harboring RET/C634W) cells treated with vehicle numbered 1300×10^3 and those treated with 250 nM ZD6474 numbered 800×10^3 . MZ-CRC-1 (harboring RET/M918T) cells treated (for 6 days) with vehicle or 250 nM ZD6474 numbered 1144×10^3 and 712×10^3 respectively. In TT cells, ZD6474 exerted modest cytotoxicity at doses in the range of its IC₅₀ for the RET kinase. A trypan blue exclusion viability assay confirmed that the compound exerted, instead, cytotoxicity at 1 week of treatment at doses of 1–5 µM.

Animal experiment: [2]

Animal models Female BALB/c-nu/nu athymic mice injected with TKKK-Luc and OZ-Luc cells

Dosage form Oral administration; 50, 25, or 12.5mg/kg; daily

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Applications

Mice were randomly divided into four treatment groups, namely vandetanib 50, 25, or 12.5mg/kg per b.w. per day, or vehicle control. Treatment started from the next day and continued for at least 4 weeks. The growth of the TKKK-Luc xenograft was significantly suppressed by vandetanib treatment at a lower dose, 12.5–25 mg/kg, whereas reduction of the OZ-Luc xenograft tumor was observed at a vandetanib dose of 50 mg/kg. At the end of the study, tumor volume was significantly lower in the vandetanib 50 mg/kg group of the OZ-Luc xenograft and in the 12.5–50 mg/kg group of the TKKK-Luc xenograft than in the vehicle-treated control group.

Other notes

Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

- [1] Vitagliano D, De Falco V, Tamburrino A, et al. The tyrosine kinase inhibitor ZD6474 blocks proliferation of RET mutant medullary thyroid carcinoma cells. *Endocrine-related cancer*, 2011, 18(1): 1-11.
- [2] Yoshikawa D, Ojima H, Kokubu A, et al. Vandetanib (ZD6474), an inhibitor of VEGFR and EGFR signalling, as a novel molecular-targeted therapy against cholangiocarcinoma. *British journal of cancer*, 2009, 100(8): 1257-1266.

Background

ZD6474 is a dual inhibitor of VEGFR-2 and EGFR with IC50 values of 40 nM and 500 nM, respectively [1].

ZD6474 showed potent inhibition activities against recombinant VEGFR-2 and EGFR in the in vitro assays. The inhibition of VEGFR-2 was 2.7-fold more potent than that of VEGFR-3 (Flt-4) kinase and 40-fold more potent than that of VEGFR-1. In human umbilical vein endothelial cells, treatment of

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ZD6474 resulted in significant inhibition of cell proliferation stimulated by VEGF and EGF with IC₅₀ values of 60 and 170 nM, respectively. Through inhibiting the kinase activity of EGFR, ZD6474 can inhibit cell growth of various cancer cell lines, including lung, ovarian, breast and colon cancers. Besides that, ZD6474 administration inhibited tumor growth in a dose-dependent manner in many tumor xenograft models.

References:

[1] Ryan A J, Wedge S R. ZD6474—a novel inhibitor of VEGFR and EGFR tyrosine kinase activity[J]. British journal of cancer, 2005, 92: S6-S13.

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