For Research Use Only

Vandetanib

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Catalog Number: CM06873

产品信息

Catalog Number:
CM06873

CAS号:
443913-73-3

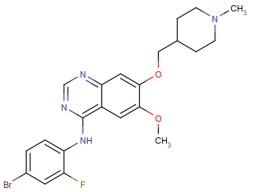
分子式:
$C_{22}H_{24}BrFN_4O_2$

主要靶点:
VEGFR|Autophagy|Apoptosis|EGFR

主要通路:
蛋白酪氨酸激酶|血管生成|凋亡|JAK/STAT信号通路|自噬

分子量:
475.35

溶解度:
DMSO:27.5 mg/mL (57.85 mM),Sonification is recommended.



靶点活性

EGFR:500 nM (cell free)|VEGFR3:110 nM (cell free)|VEGFR2:40 nM (cell free)

体外活性

Vandetanib (ZD6474) is a potent inhibitor of KDR/VEGFR 2 tyrosine kinase activity (IC50: 40 nM). This compound has some additional activity versus the tyrosine kinase activity of VEGFR3 (IC50: 110 nM) and EGFR/HER1 (IC50: 500 nM). The activity of ZD6474 versus KDR tyrosine kinase translates into potent inhibition of VEGF-stimulated endothelial cell (human umbilical vein endothelial cell) proliferation in vitro (IC50: 60 nM) [1]. ZD6474 causes a dose-dependent inhibition of EGFR phosphorylation in mouse NIH-EGFR fibroblasts and human MCF-10A ras breast cancer cells. ZD6474 treatment resulted in a dose-dependent inhibition of soft agar growth in seven human cell lines with functional EGFR but lacking VEGFR-2. A dose-dependent supra-additive effect in growth inhibition and in apoptosis in vitro was observed by the combined treatment with ZD6474 and paclitaxel or docetaxel [2]. Vandetanib and neratinib displayed an inhibitory effect on the basal ABCG2-ATPase. At relatively high concentrations (10–20 mM), vandetanib inhibited the stimulated ABCG2-ATPase [3].

体内活性

Administration of ZD6474 (2.5 mg/kg, i.v.) reversed a hypotensive change induced by VEGF (by 63%) but did not significantly affect that induced by basic fibroblast growth factor. Administration of 50 mg/kg/day ZD6474 (once-daily, p.o.) to athymic mice with intradermally implanted A549 tumor cells also inhibited tumor-induced neovascularization significantly (63% inhibition after 5 days). Histological analysis of Calu-6 tumors treated with 50 mg/kg/day ZD6474 for 24 days showed a significant reduction (>70%) in CD31 (endothelial cell) staining in nonnecrotic regions [1]. ZD6474 treatment of nude mice bearing palpable GEO colon cancer xenografts induced dose-dependent tumor growth inhibition. The antitumor activity of ZD6474 in GEO tumor xenografts was also found to be enhanced when combined with paclitaxel. Tumor regression was observed in all mice after treatment with ZD6474 plus paclitaxel, and it was accompanied by a significant potentiation in the inhibition of angiogenesis [2]. Vandetanib (15 mg/kg) had similar effects on the growth of H1650/PTEN and H1650 parental xenograft tumors [4].

动物实验

Methodology to enable blood pressure measurement in anesthetized rats was as described previously. Briefly, anesthesia was induced in male Alderley Park rats using α-chloralose by the i.v. route and then maintained with thiopentone via the i.p. route. Once surgical anesthesia was established, the carotid artery was cannulated to enable blood pressure recording using a pressure transducer and a Lectromed MT8P amplifier. The jugular vein was cannulated to allow growth factor administration. Body temperature was maintained with a thermostatically controlled heated blanket coupled to a rectal thermometer. Human VEGF165 (32 μg/kg) or bFGF (40 μg/kg) was administered as a bolus injection [0.1 ml/250 g body weight in 0.85% (w/v) sodium chloride], and a maximal blood pressure drop was recorded within 2 min (typically 26–30 mm Hg). These changes were sustainable for more than 20 min in control experiments. ZD6474 (2.5 mg/kg) or vehicle alone [25% (w/v) hydroxypropyl-β-cyclodextrin in Sorensons phosphate buffer (pH 5.5)] was administered i.v., and blood pressure was recorded 5 min later to determine the effect on growth factor-induced hypotension [1].

细胞实验

HUVEC proliferation in the presence and absence of growth factors was evaluated using [3H]thymidine incorporation. Briefly, HUVECs isolated from umbilical cords were plated (at passage 2–8) in 96-well plates (1000 cells/well) and dosed with ZD6474 ± VEGF or EGF (3 ng/ml) or bFGF (0.3 ng/ml). The cultures were incubated for 4 days (37°C; 7.5% CO2) and then pulsed with 1 μCi/well [3H]thymidine and reincubated for 4 h. Cells were harvested and assayed for the incorporation of tritium using a beta counter. IC50 data were interpolated as described above [1].

描述

Vandetanib is a potent inhibitor of VEGFR2 (IC50: 40 nM). It also inhibits VEGFR3 and EGFR.

储存

Powder: -20°C for 3 years | In solvent: -80°C for 2 years