

Product Data Sheet

Product Name: TAK-285
Cat. No.: GC11172

Chemical Properties

Cas. No. 871026-44-7

Chemical Name N-[2-[4-[3-chloro-4-[3-(trifluoromethyl)phenoxy]anilino]pyrrolo[3,2-d]pyrimidin-5-yl]ethyl]-3-hydroxy-3-methylbutanamide

SMILES CC(C)(C)C(=O)NCCN1C=CC2=C1C(=NC=N2)NC3=CC(=C(C=C3)OC4=CC=CC(=C4)C(F)(F)F)Cl)O

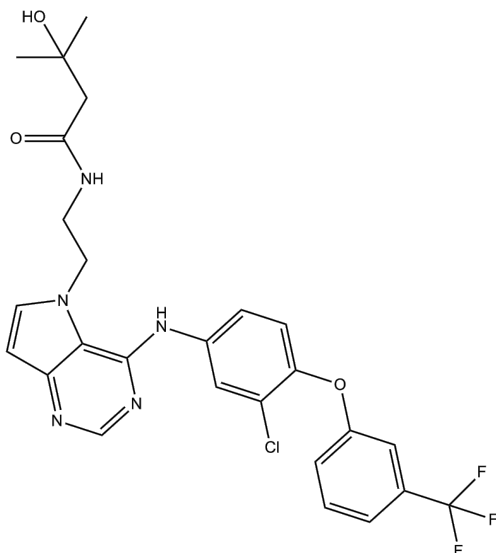
Formula $C_{26}H_{25}ClF_3N_5O_3$ M.Wt 547.96

Solubility $\geq 27.4\text{mg/mL}$ 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

Cell experiment [1]:

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Cell lines	The BT-474 human breast cancer cell line, MES-SA human uterine sarcoma cells and multidrug-resistant MES-SA/DX-5 cells
Preparation method	The solubility of this compound in DMSO is >27.4mg/mL. 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.
Reacting condition	0.00097-25 µmol/L, 3-7 days
Applications	In BT-474 cells, TAK-285 inhibited cell growth with IC50 value of 0.017 µmol/L, compared with the IC50 values of 1.1 and 20 µmol/L in A-431 and MRC-5 cells which did not overexpress HER2. TAK-285 inhibited HER2, Akt and MAPK phosphorylation with IC50 values of 0.0093 µmol/L, 0.015 µmol/L and <0.0063 µmol/L, respectively. In A-431 cells, TAK-285 inhibited EGFR phosphorylation with IC50 value of 0.053 µmol/L.
Animal experiment [1]:	
Animal models	Female BALB/c nu/nu mice implanted subcutaneously with BT-474 cells or 4-1ST tumors; female F344/N athymic (rnu/rnu) rats implanted with A-431 cells or 4-1ST tumors
Dosage form	100 mg/kg BID or 12.5 mg/kg BID, emulsified in 0.5% methyl cellulose, administered orally, 2 weeks

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Application

In murine xenograft models, TAK-285 (100 mg/kg BID) inhibited BT-474 breast tumors and 4-1ST gastric tumor growth with T/C values of 29% and 11%, respectively. In rat xenografts, TAK-285 (12.5 mg/kg BID) inhibited growth of tumors that overexpressed HER2 (4-1ST) or EGFR (A-431) with T/C values of 14% and 13%, respectively. The pharmacokinetic profile for TAK-285 showed much greater drug exposure in rats compared with mice.

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]. Nakayama, A., et al., Antitumor Activity of TAK-285, an Investigational, Non-Pgp Substrate HER2/EGFR Kinase Inhibitor, in Cultured Tumor Cells, Mouse and Rat Xenograft Tumors, and in an HER2-Positive Brain Metastasis Model. J Cancer, 2013. 4(7): p. 557-65.

Background

TAK-285 is a potent inhibitor of HER2 and EGFR with IC₅₀ value of 17 nM and 23 nM, respectively [1].

EGFR (epidermal growth factor receptor) and HER2 are members of ErbB family of receptors and play an important role in stimulating its intrinsic intracellular protein-tyrosine kinase activity. It has been shown that the over-expressions of HER-2 and EGFR are correlated with a variety of cancers and thus be regarded as promising target in clinic [2].

TAK-285 is a selective HER2 and EGFR inhibitor and has a different selectivity with the reported HER inhibitor AST-6. When tested with a panel of breast cancer cell lines, cells over-expressed HER2 (BT-474, NCI-N87, SK-BR-3, Calu-3, and MDA-MB-453) or EGFR (A-431) were more sensitive to TAK-285 treatment while normal expressed cell line (MRC-5) was less sensitive [1]. [3].

In rat model with 4-1ST (over-express HER2) or A-431 (over-express EGFR) subcutaneous

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xenograft, administration of TAK-285 caused significant reduction of tumor growth with T/C values of 14% and 13%, respectively, at a dose of 12.5 mg/kg, compared with control group [1]. In a panel of human breast cancer cell lines expressing EGFR, HER2, HER3, and HER4, administration of TAK-285 significantly inhibited cell proliferation in a dose-dependent manner with IC₅₀ values range from 0.011 to 17 μ M [3].

It is also reported that TAK-285 inhibited Akt and MAPK phosphorylation with IC₅₀ value of 0.015 μ M and <0.0063 μ M, respectively [1].

References:

- [1]. Nakayama, A., et al., Antitumor Activity of TAK-285, an Investigational, Non-Pgp Substrate HER2/EGFR Kinase Inhibitor, in Cultured Tumor Cells, Mouse and Rat Xenograft Tumors, and in an HER2-Positive Brain Metastasis Model. J Cancer, 2013. 4(7): p. 557-65.
- [2]. Lyakhov, I., et al., HER2- and EGFR-specific affiprobos: novel recombinant optical probes for cell imaging. Chembiochem, 2010. 11(3): p. 345-50.
- [3]. Takagi, S., et al., HER2 and HER3 cooperatively regulate cancer cell growth and determine sensitivity to the novel investigational EGFR/HER2 kinase inhibitor TAK-285. Oncoscience, 2014. 1(3): p. 196-204.

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