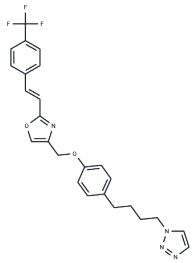
Data Sheet (Cat.No.T6124)

TargetMol

Mubritinib

Chemical Properties



CAS No. : 366017-09-6

Formula: C25H23F3N4O2

Molecular Weight: 468.47

Appearance: no data available

Storage: store at low temperature
Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Mubritinib (TAK-165) (TAK-165) is a potent inhibitor of HER2/ErbB2 with IC50 of 6 nM.
Targets(IC50)	EGFR,FGFR,JAK,PDGFR
In vitro	Mubritinib displays > 4000-fold selectivity over other tyrosine kinases, such as EGFR, FGFR, PDGFR, Jak1, Src and Blk. Mubritinib even at low concentration of 0.1 μM significantly blocks HER2 phosphorylation, leading to the downregulation of PI3K-Akt and MAPK pathway in cell line BT474 with high level of HER2. Mubritinib not only exhibits highly potent antiproliferative effect in ErbB2-overexpressing cancer cell line BT474 with an IC50 of 5 nM, but also displays marked antiproliferative effects in cell lines with HER2 expressed weakly with IC50 of 53 nM, 90 nM and 91 nM for LNCaP, LN-REC4 and T24, respectively. Mubritinib displays no inhibitory activities against PC-3 cells with HER2 expressed very faintly with IC50 of 4.62 μM, as well as EGFR-overexpressing HT1376 and ACHN cell lines with IC50 of >25 μM. [1]
In vivo	Mubritinib significantly inhibits LN-REC4 xenograft with treatment/control tumor volume ratio of 26.5%. Although ineffective to inhibit the growth of UMUC-3 and ACHN cells in vitro (IC50s of 1.812 and >25 μM, respectively), oral administration of Mubritinib (10 or 20 mg/kg per day) significantly inhibits the growth of UMUC-3 and ACHN xenografts with treatment/control tumor volume ratio of 22.9% and 26%, respectively, as compared with Herceptin (20 mg/kg) which is ineffective to UMUC-3 tumor growth. [1]
Kinase Assay	Inhibition of HER2/erbB2 tyrosine kinase activity: BT-474 cells are seeded on 24-well plates and cultured overnight. Mubritinib is then added at various concentrations. After incubation for 2 hours, the cells are harvested directly into sodium dodecyl sulfate (SDS) -sample buffer (200 μL). Aliquots containing equal amounts of total cell extract are run on 7.5% to 15% gradient SDS-polyacrylamide gel electrophoresis (PAGE). Following electrophoresis, proteins are transferred onto a polyvinylidene fluoride (PVDF) membrane, for western blot analysis using a relevant primary antibody. Detection of protein is accomplished by an enhanced chemiluminescent (ECL) detection method. The extent of tyrosine phosphorylation of HER2/erbB2 is measured by the LAS-1000 plus lumino-image analyser. The concentration of Mubritinib that inhibits HER2/erbB2 phosphorylation by 50% (IC50) is calculated from a dose-response curve generated by least-squares linear regression of the response using SAS software.

Cell Research	Cells are seeded into 6-well plates and cultured overnight. Mubritinib is then added at various concentrations, and the cells are treated continuously for 72 hours. After the incubation period, cells are counted for the measurement of antiproliferative activity. (Only for Reference)

Solubility Information

Solubility	DMSO: 35.1 mg/mL (74.92 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.1346 mL	10.673 mL	21.3461 mL
5 mM	0.4269 mL	2.1346 mL	4.2692 mL
10 mM	0.2135 mL	1.0673 mL	2.1346 mL
50 mM	0.0427 mL	0.2135 mL	0.4269 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Nagasawa J, et al. Int J Urol, 2006, 13(5), 587-592.
Hong J H, Yong C H, Heng H L, et al.Integrative multiomics enhancer activity profiling identifies therapeutic vulnerabilities in cholangiocarcinoma of different etiologies.Gut.2023