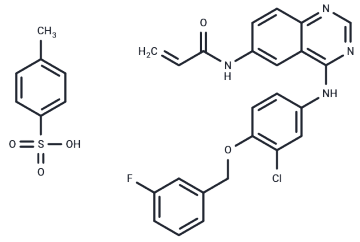
Data Sheet (Cat.No.T6331)

TargetMol
YOUR TARGET MOLECULES

Allitinib tosylate

Chemical Properties



CAS No. : 1050500-29-2

Formula: C31H26ClFN4O5S

Molecular Weight: 621.08

Appearance: no data available

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

Biological Description

Description	Allitinib tosylate (AST-1306) is a novel irreversible inhibitor of EGFR and ErbB2 with IC50 of 0.5 nM and 3 nM, respectively.
Targets(IC50)	EGFR,FLT
In vitro	AST-1306 also ErB2 and EGFR T790M/L858R double mutant. AST-1306 is approximately 500-fold more potent than lapatinib and more than 3000-fold selective for ErbB family kinases over other kinase families including PDGFR, KDR and c-Met. AST-1306 might covalently bind to specific amino acid residues of EGFR and ErbB2. AST-1306 acts in a concentration dependent manner to significantly inhibit the growth of HIH3T3-EGFR T790M/L858R cells. AST-1306 effectively suppresses EGFR phosphorylation in HIH3T3-EGFR T790M/L858R cells. Moreover, AST-1306 blocks the growth of NCI-H1975 cells that harbor the EGFR T790M/L858R mutation in a concentration-dependent manner. AST-1306 blocks phosphorylation of EGFR and downstream pathways as well. In addition, AST-1306 dose-dependently and markedly inhibits EGF-induced EGFR phosphorylation in A549 cells. AST-1306 inhibits the phosphorylation of EGFR and ErbB2, and downstream signaling in human cancer cells including A549 cells, Calu-3 cells and SK-OV-3 cells. [1]
In vivo	Twice daily oral administration of AST-1306 gives rise to a dramatic prevention of tumor growth in SK-OV-3 and Calu-3 xenograft models. In SK-OV-3 models, tumors nearly disappears after treatment with AST-1306 for 7 days. In contrast, AST-1306 only slightly inhibits the growth of tumor in HO-8910 and A549 xenograft models. Therefore, the antitumor efficacy of AST-1306 is greater in ErbB2-overexpressing tumor models than in models expressing low levels of ErbB2. AST-1306 is well tolerated. Lapatinib displays antitumor activity in these ErbB2-overexpressing tumor models, but AST-1306 is more efficacious than lapatinib in the SK-OV-3 xenograft tumor model when given at the same dose and schedule. In addition, oral administration of AST-1306 twice daily for 3 weeks dramatically suppresses the growth of tumor in the FVB-2/Nneu models. After treatment for 11 days, tumors almost completely disappears. The body weights of the mice reduces by less than 20% during treatment. [1]
Kinase Assay	Tyrosine kinase assays: The tyrosine kinase activities are determined in 96-well ELISA plates precoated with 20 μg/mL Poly (Glu,Tyr)4:1. First, 80 μL of 5 μM ATP solution diluted in kinase reaction buffer (50 mM HEPES pH 7.4, 20 mM MgCl2, 0.1 mM MnCl2, 0.2 mM Na3VO4, 1 mM DTT) is added to each well. Various concentrations of AST-1306 diluted in 10 μL of 1% DMSO (v/v) are then added to each reaction well, with 1% DMSO

	(v/v) used as the negative control. Subsequently, the kinase reaction is initiated by the addition of purified tyrosine kinase proteins diluted in 10 μL of kinase reaction buffer solution. Experiments at each concentration are performed in duplicate. After incubation for 60 min at 37 °C, the plate is washed three times with phosphate buffered saline (PBS) containing 0.1% Tween 20 (T-PBS). Next, 100 μL anti-phosphotyrosine antibody (PY99, 1:500 dilution) diluted in T-PBS containing 5 mg/mL BSA is added. After 30 min incubation at 37 °C, the plate is washed three times as before. Horseradish peroxidase-conjugated goat anti-mouse IgG (100 μL) diluted 1:2000 in T-PBS containing 5 mg/mL BSA is added. The plate is reincubated at 37 °C for 30 min, and then washed with PBS. Finally, 100 μL of a solution containing 0.03 % Water2 and 2 mg/mL o-phenylenediamine in 0.1 M citrate buffer, pH 5.5, is added and samples are incubated at room temperature until color emerged. The reaction is terminated by the addition of 50 μL of 2 M H2SO4, and the plate is read using a multi-well spectrophotometer at 490 nm. The inhibition rate (%) is calculated using the following equation: [1-(A490 treated /A490 control)] ×100%. IC50 values are determined from the results of at least three independent tests and calculated by Logit method.
Cell Research	Cell (including Calu-3, A-549 cell line et al.) proliferation is evaluated using the SRB (Sulforhodamine B) assay. Briefly, cells are seeded into 96-well plates and grown for 24 hours. The cells are then treated with increasing concentrations of AST-1306 and grown for a further 72 hours. The medium remains unchanged until the completion of the experiment. The cells are then fixed with 10% precooled trichloroacetic acid (TCA) for 1 hour at 4 °C and stained for 15 min at room temperature with 100 μL of 4 mg/mL SRB solution in 1% acetic acid. The SRB is then removed, and the cells are quickly rinsed five times with 1% acetic acid. After cells are air-dried, protein-bound dye is dissolved in 150 μL of 10 mM Tris base for 5 min and measured at 515 nm using a multiwell spectrophotometer. The inhibition rate on cell proliferation is calculated as (1 - A515 treated/A515 control) × 100%. The IC50 value is obtained by the Logit method and is determined from the results of at least 3 independent tests.(Only for Reference)

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: < 1 mg/mL (insoluble or slightly soluble), DMSO: 114 mg/mL (183.6 mM), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.6101 mL	8.0505 mL	16.101 mL
5 mM	0.322 mL	1.6101 mL	3.2202 mL
10 mM	0.161 mL	0.805 mL	1.6101 mL
50 mM	0.0322 mL	0.161 mL	0.322 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

Xie H, et al. PLoS One. 2011, 6(7), e21487.

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