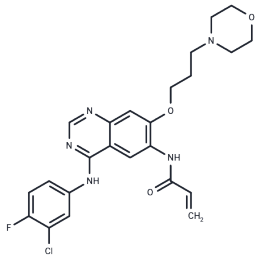
Data Sheet (Cat.No.T6136)

TargetMol

Canertinib

Chemical Properties



CAS No. : 267243-28-7

Formula: C24H25ClFN5O3

Molecular Weight: 485.94

Appearance: no data available

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

Biological Description

Description	Canertinib (CI-1033) is a pan-erbB tyrosine kinase inhibitor which work against esophageal squamous cell carcinoma in vitro and in vivo. Canertinib treatment significantly affects tumour metabolism, proliferation and hypoxia as determined by PET.
Targets(IC50)	EGFR
In vitro	CI-1033 shows excellent potency for irreversible inhibition of erbB2 autophosphorylation in MDA-MB 453 cells. CI-1033 also shows high permeability in Caco-2 cells and inhibits secretory transport of vinblastine, which indicates that CI-1033 is a likely inhibitor of the P-gp. [1] CI-1033 alone, significantly suppresses constitutively activated Akt and MAP kinase. In combination with gemcitabine, CI-1033 inhibits Akt and prevents increased levels of MAPK phosphorylation. CI-1033 stimulates p27 expression and p38 phosphorylation in MDA-MB-453 cells. [2] CI-1033 is highly specific to the erbB receptor family and not sensitive to PGFR, FGFR or IR even at 50 μM. CI-1033 shows high levels of inhibition in A431 cells expressing EGFR with IC50 of 7.4 nM. CI-1033 suppresses heregulin-stimulated tyrosine phosphorylation of erbB2, erbB3 and erbB4 with IC50 of 5, 14 and 10 nM, respectively. CI-1033 also inhibits expression of pp62c-fos in response to heregulin. [3] CI-1033 is predicted to modify Cys773 covalently within the ATP binding site of the HER2 kinase and enhances destruction of both mature and immature ErbB-2 molecules. [4] CI-1033 induces a significant decrease in measurable phosphorylation of tyrosine residues 845 and 1068 of EGFR, which are responsible for Src and Ras/MAPK signaling respectively. The corresponding residues of Her-2, tyrosine residues 877 and 1248 are dephosphorylated significantly by CI-1033 at a concentration of 3 μM or higher. CI could block EGFR internalization and increase the rate of apoptosis in primary osteosarcoma cells in a titratable fashion. [5] In addition, CI-1033 inhibits the proliferation of TT, TE2, TE6 and TE10 cells significantly at 0.1 nM. [6]
In vivo	Canertinib shows impressive activity against A431 xenografts in nude mice at 5 mg/kg of body weight. [1] Canertinib (20 to 80 mg/kg/d) achieves a high degree of tumor regressions in H125 xenograft models. [3] Oral administration of Canertinib causes a marked inhibition of growth in TT, TE6 and TE10 xenografts in nude mice, without animal death and <10% weight loss. [6]
Kinase Assay	Tyrosine Kinase Assays: Enzyme assays for determination of IC50 are performed in 96-well filter plates in a total volume of 0.1 mL, containing 20 mM Hepes, pH 7.4, 50 mM sodium vanadate, 40 mM magnesium chloride, 10 μM adenosine triphosphate (ATP)

	containing 0.5 mCi of [32P]ATP, 20 mg of polyglutamic acid/tyrosine, 10 ng of EGFR tyrosine kinase, and appropriate dilutions of CI-1033. All components except the ATP are added to the well and the plate is incubated with shaking for 10 min at 25 °C. The reaction is started by adding [32P]ATP, and the plate is incubated at 25 °C for another 10 min. The reaction is terminated by addition of 0.1 mL of 20% trichloroacetic acid (TCA). The plate is kept at 4 °C for at least 15 min to allow the substrate to precipitate. The wells are then washed five times with 0.2 mL of 10% TCA and 32P incorporation determined with a Wallac β plate counter.
Cell Research	Cells (1 × 104) are seeded in each well of a 24-well plastic culture plate and left overnight in DMEM or RPMI-1640 supplemented with 10% FBS. The next morning, the cells are treated with the indicated concentrations of CI-1033 (0.1-5.0 nM) for varying periods (1, 3, 5 and 7 days). After treatment, the cells are counted using a Coulter counter. The percent of cell proliferation is calculated by this formula: treatment cell number/control cell number × 100 for each time period.(Only for Reference)

Solubility Information

Solubility	DMSO: 4.86 mg/mL (10 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.0579 mL	10.2893 mL	20.5787 mL
5 mM	0.4116 mL	2.0579 mL	4.1157 mL
10 mM	0.2058 mL	1.0289 mL	2.0579 mL
50 mM	0.0412 mL	0.2058 mL	0.4116 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

Smaill JB et al. J Med Chem. 2000; 43(7): 1380-1397.
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Slichenmyer WJ et al. Semin Oncol. 2001; 28(5 Suppl 16): 80-85.
Citri A et al. EMBO J. 2002; 21(10): 2407-2417.
Hughes DP et al. Pediatr Blood Cancer. 2006; 46(5): 614-623.