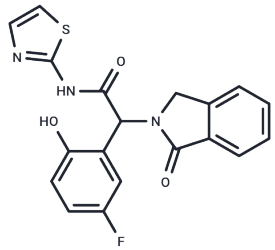
Data Sheet (Cat.No.T6824)

TargetMol

EAI045

Chemical Properties



CAS No. : 1942114-09-1

Formula: C19H14FN3O3S

Molecular Weight: 383.4

Appearance: no data available

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

Biological Description

Description	EAI045, an allosteric inhibitor, targets towards drug-resistant EGFR mutants but avoids the wild-type receptor.
Targets(IC50)	EGFR
In vitro	EAI045 potently inhibits EGFR Y1173 phosphorylation in H1975 cells (half maximal effective concentration (EC50)=2 nM) but not in HaCaT cells, which have wild-type EGFR. It shows no anti-proliferative effect in H1975 and H3255 cell lines even at concentrations up to 10 μM[1]. EAI045 inhibits the L858R/T790M mutant with an IC50 of 3 nM but does not completely abolish EGFR autophosphorylation in H1975 NSCLC cells harboring this mutant. Dimerization-defective/independent mutants are more sensitive to EAI045, suggesting activity against one subunit of an EGFR heterodimer/asymmetric dimer[2].
In vivo	Mouse pharmacokinetic studies with EAI045 reveals a maximal plasma concentration of 0.57 μM, a half-life of 2.15 h, and oral bioavailability of 26% after dosing at 20 mg/kg[1]. When combined with cetuximab that blocks EGFR dimerization, EAI045 markedly reduces tumor growth in a mouse model of L858R/T790M-mutant-driven lung cancer. The mice treated alone with EAI045 do not respond. EAI045 in combination with cetuximab also induces marked tumor shrinkage in the mouse model carrying L858R/T790M/C797S, a mutant known to be resistant to all third-generation EGFR TKIs. EAI045 and cetuximab exhibits mechanistic synergy[2].
Kinase Assay	ERK dimerization assay: Compound screening is performed in HEK293T cells treated with the potential inhibitors (10 μM) for 30 min before EGF stimulation. Cellular lysates are tested for ERK dimerization by native PAGE and p-ERK evaluation of the potential positives. In vitro ERK dimerization is assayed using GST-MEK1 ΔN EE purified from bacteria, bound to glutathione sepharose beads, and incubated with 25 μg/ml of purified His-ERK2 plus increasing concentrations of DEL-22379. Western blotting, kinase assays, and luciferase assays are also performed. In silico docking of the DEL-22379 compound is carried out with the modeling tools provided by the OpenEye package (v. 2.1).
Cell Research	H1975, H3255 and HaCaT cell lines are plated in solid white 384-well plates at 500 cells per well in 10% FBS RPMI penicillin/streptomycin media. Using a Pin Tool, 50 nl of serial diluted compounds are transferred to the cells. After 3?days, cell viability is measured. (Only for Reference)

Solubility Information

Solubility	DMSO: 16.67 mg/mL (43.48 mM),Sonication is recommended. Ethanol: < 1 mg/mL (insoluble or slightly soluble), H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.6082 mL	13.0412 mL	26.0824 mL
5 mM	0.5216 mL	2.6082 mL	5.2165 mL
10 mM	0.2608 mL	1.3041 mL	2.6082 mL
50 mM	0.0522 mL	0.2608 mL	0.5216 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

Jia Y, et al. Nature. 2016, 534(7605):129-32.
Wang S, et al. J Hematol Oncol. 2016, 9(1):59.