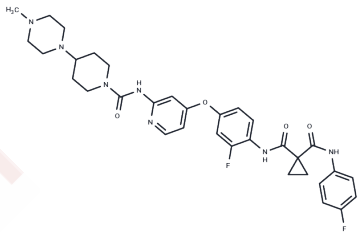
Data Sheet (Cat.No.T6517)

TargetMol

Golvatinib

Chemical Properties



CAS No. : 928037-13-2

Formula: C33H37F2N7O4

Molecular Weight: 633.69

Appearance: no data available

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

Biological Description

Description	Golvatinib (E-7050) is an orally bioavailable dual kinase inhibitor of c-Met (hepatocyte growth factor receptor) and VEGFR-2 (vascular endothelial growth factor receptor-2) tyrosine kinases with potential antineoplastic activity. c-Met/VEGFR kinase inhibitor E7050 binds to and inhibits the activities of both c-Met and VEGFR-2, which may inhibit tumor cell growth and survival of tumor cells that overexpress these receptor tyrosine kinases. c-Met and VEGFR-2 are upregulated in a variety of tumor cell types and play important roles in tumor cell growth, migration and angiogenesis.
Targets(IC50)	c-Met/HGFR,VEGFR
In vitro	In vitro studies indicate that E7050 potently inhibits phosphorylation of both c-Met and VEGFR-2. E7050 also potently represses the growth of both c-met amplified tumor cells and endothelial cells stimulated with either HGF or VEGF. [1] E7050 circumvents resistance to all of the reversible, irreversible, and mutant-selective EGFR-TKIs induced by exogenous and/or endogenous HGF in EGFR mutant lung cancer cell lines, by blocking the Met/Gab1/PI3K/Akt pathway in vitro. E7050 also prevents the emergence of gefitinib-resistant HCC827 cells induced by continuous exposure to HGF. [2]
In vivo	In vivo studies using E7050 shows inhibition of the phosphorylation of c-Met and VEGFR-2 in tumors, and strong inhibition of tumor growth and tumor angiogenesis in xenograft models. Treatment of some tumor lines containing c-met amplifications with high doses of E7050 (50–200 mg/kg) induces tumor regression and disappearance. In a peritoneal dissemination model, E7050 shows an antitumor effect against peritoneal tumors as well as a significant prolongation of lifespan in treated mice. [1] In another xenograft model research, tumors produced by HGF-transfected Ma-1 (Ma-1/HGF) cells are more angiogenic than vector control tumors and shows resistance to ZD1839. E7050 alone inhibits angiogenesis and retards growth of Ma-1/HGF tumors. E7050 combined with ZD1839 induces marked regression of tumor growth. [3]
Kinase Assay	Western blot analysis: The phosphorylation status of c-Met and VEGFR-2 is detected by Western blot analysis. For c-Met, MKN45 cells are incubated with a serial dilution of E7050 in complete medium at 37 °C for 2 h. For VEGFR-2, HUVEC are starved with human endothelial serum free medium containing 0.5% FBS for 24 h. Subsequently HUVEC are incubated with a serial dilution of E7050 for 1 h and then incubated with 20 ng/mL of human VEGF for 5 min. Cells are lysed by lysis buffer (50 mM HEPES [pH 7.4], 150 mM NaCl, 10% glycerol, 1% Triton X-100, 1.5 mM MgCl2, 1 mM EDTA [pH 8.0], 100 mM NaF, 1 mM phenylmethylsulfonyl fluoride 1 mM sodium orthovanadate, 10 μg/mL aprotinin, 50

	μg/mL leupeptin, and 1 μg/mL pepstatin A). The resected tumor samples are homogenized with lysis buffer containing 25 mM β-glycerophosphate and 0.5% (v/v) phosphatase inhibitor cocktail 2 at 4 °C. Cellular debris is removed by centrifugation at 17 860 g for 20 min at 4 °C. Aliquots of the supernatants containing 5-20 μg of protein are subjected to SDS-PAGE under reducing conditions. The proteins are then transferred onto PVDF membranes, blocked with TBS containing 0.05% Tween-20 and either 5% skim milk or 5% BSA. The membranes are probed with the following antibodies: anti-c-Met polyclonal antibody (C-28) and anti-VEGFR-2 polyclonal antibody (C-20); mouse anti-phosphotyrosine clone 4 g10; and anti-VEGFR-2 polyclonal antibody, anti-phospho-VEGFR-2 (Tyr996) polyclonal antibody, and anti-phospho-c-Met (Tyr1234/1235) polyclonal antibody. Detection is performed using a Super Signal enhanced chemiluminescence kit. Immunoreactive bands are visualized by chemiluminescence with an Image Master-VDS-CL detection system. The intensity of each band is measured by using an image analyzer.
Cell Research	Cells (1-3 × 103 cells/100 μL/well) are seeded on 96-well culture plates with various concentrations of E7050 and cultured for 3 days. Then, 10 μL of WST-8 reagent is added to each well, and absorbance is measured at 450 nm compared with a reference measurement at 660 nm using a MTP-500 microplate reader. HUVEC (2 × 103 cells/well) are cultured for 3 days in medium containing HGF (30 ng/mL), VEGF (20 ng/mL), or basic fibroblast growth factor (bFGF) (20 ng/mL) together with serially diluted E7050.(Only for Reference)

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: < 1 mg/mL (insoluble or slightly soluble), DMSO: 100 mg/mL (157.81 mM) (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.5781 mL	7.8903 mL	15.7806 mL
5 mM	0.3156 mL	1.5781 mL	3.1561 mL
10 mM	0.1578 mL	0.789 mL	1.5781 mL
50 mM	0.0316 mL	0.1578 mL	0.3156 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

Nakagawa T et al. Cancer Sci, 2010, 101(1), 210-215.
Wang W et al. Clin Cancer Res, 2012, 18(6), 1663-1671.
Takeuchi S et al. Am J Pathol, 2012, 181(3), 1034-1043.