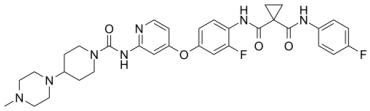
Data Sheet

Product Name:	Golvatinib
Cat. No.:	CS-0595
CAS No.:	928037-13-2
Molecular Formula:	C33H37F2N7O4
Molecular Weight:	633.69
Target:	c-Met/HGFR; VEGFR
Pathway:	Protein Tyrosine Kinase/RTK
Solubility:	DMSO : 50 mg/mL (78.90 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

Golvatinib (E-7050) is a potent dual inhibitor of both **c-Met** and **VEGFR2** kinases with **IC_{50}**s of 14 and 16 nM, respectively. IC50 & Target: IC50: 14 nM (c-Met), 16 nM (VEGFR2)[1] **In Vitro:** Golvatinib (E-7050) potently inhibits phosphorylation of both c-Met and VEGFR-2. Golvatinib also potently represses the growth of both c-met amplified tumor cells and endothelial cells stimulated with either HGF or VEGF.

Golvatinib strongly inhibits the growth of MKN45, EBC-1, Hs746T, and SNU-5 tumor cells with IC_{50} values of 37, 6.2, 23, and 24 nM, respectively. The growth of A549, SNU-1 and 0MKN74 tumor cells is inhibited by Golvatinib with much higher IC_{50} values[1].

Golvatinib 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.

Golvatinib also prevents the emergence of gefitinib-resistant HCC827 cells induced by continuous exposure to HGF[2]. **In Vivo:** Golvatinib (E-7050) 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 Golvatinib (50-200 mg/kg) induced tumor regression and disappearance. In a peritoneal dissemination model, Golvatinib shows an antitumor effect against peritoneal tumors as well as a significant prolongation of lifespan in treated mice[1].

Golvatinib (E7050) plus Gefitinib results in marked regression of tumor growth associated with inhibition of Akt phosphorylation in cancer cells[2].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [1]Cells (1000-3000 cells/100 μL/well) are seeded on 96-well culture plates with various concentrations of Golvatinib 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[1]. **Animal Administration:** [1]Mice: Nude mice bearing MKN45, Hs746T, SNU-5, or EBC-1 tumors are administered Golvatinib (25, 50, 100, 200 mg/kg) or vehicle only as a control, once a day. Tumor volume is measured using calipers on the indicated days (0-15 days)[1].

References:

[1]. Nakagawa T et al. E7050: a dual c-Met and VEGFR-2 tyrosine kinase inhibitor promotes tumor regression and prolongs survival in mouse xenograft models. Cancer Sci, 2010, 101(1), 210-215.

[2]. Wang W et al. Met kinase inhibitor E7050 reverses three different mechanisms of hepatocyte growth factor-induced tyrosine kinase inhibitor resistance

in EGFR mutant lung cancer. Clin Cancer Res, 2012, 18(6), 1663-1671.

CAIndexNames:

1,1-Cyclopropanedicarboxamide, N-[2-fluoro-4-[[2-[[[4-(4-methyl-1-piperazinyl)-1-piperidinyl]carbonyl]amino]-4-pyridinyl]oxy]phenyl]-N'-(4-fluorophenyl)-

SMILES:

O=C(NC1=CC=C(C=C1F)OC2=CC(NC(N3CCC(CC3)N4CCN(CC4)C)=O)=NC=C2)C5(CC5)C(NC6=CC=C(C=C6)F)=O

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 732-484-9848 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA