S49076

Cat. No.: HY-12965

CAS No.: 1265965-22-7

Molecular Formula: $C_{22}H_{22}N_4O_4S$

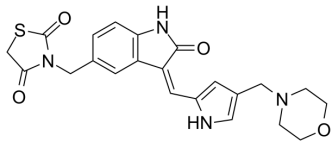
Molecular Weight: 438.5

Target: FGFR; c-Met/HGFR

Pathway: Protein Tyrosine Kinase/RTK

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 31 mg/mL (70.70 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2805 mL	11.4025 mL	22.8050 mL
5 mM	0.4561 mL	2.2805 mL	4.5610 mL
10 mM	0.2281 mL	1.1403 mL	2.2805 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.70 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.70 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

S49076 is a novel, potent inhibitor of MET, AXL/MER, and FGFR1/2/3 with IC_{50} values below 20 nM.

IC_{50} & Target

FGFR1 18 nM (IC_{50})	FGFR1^{V561M} 23 nM (IC_{50})	FGFR2 17 nM (IC_{50})	FGFR2^{N549H} 19 nM (IC_{50})
FGFR3 15 nM (IC_{50})	AXL 7 nM (IC_{50})	MER 2 nM (IC_{50})	

In Vitro

S49076 potently blocks cellular phosphorylation of MET, AXL, and FGFRs and inhibits downstream signaling. S49076 inhibits

	the proliferation of MET- and FGFR2-dependent gastric cancer cells, blocks MET-driven migration of lung carcinoma cells, and inhibits colony formation of hepatocarcinoma cells expressing FGFR1/2 and AXL. Total inhibition of MET phosphorylation is seen after 2 hours of incubation with 10 nM S49076 and an with an IC_{50} of 2 nM. S49076 inhibits MET phosphorylation on this site in GTL-16 gastric carcinoma cells with an IC_{50} value of 3 nM. The IC_{50} for AXL inhibition by S49076 is 56 nM. S49076 inhibits AXL signaling via AKT with an IC_{50} of 33 nM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In tumor xenograft models, a good pharmacokinetic/pharmacodynamic relationship for MET and FGFR2 inhibition following oral administration of S49076 is established and correlated well with impact on tumor growth. MET, AXL, and the FGFRs have all been implicated in resistance to VEGF/VEGFR inhibitors such as bevacizumab. Combination of S49076 with bevacizumab in colon carcinoma xenograft models leads to near total inhibition of tumor growth. S49076 alone caused tumor growth arrest in bevacizumab-resistant tumors[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	For GTL-16 and SNU-16 viability assays, cells are seeded in 96-well microplates at the appropriate density in media containing 10% FCS and supplemented 48 hours later with serial dilutions of S49076 in a final volume of 150 µL per well. After 96 hours (GTL-16) or 120 hours (SNU-16) incubation (corresponding to 4 doubling times), 15 µL of a solution of 5 mg/mL MTT is added to each well and the plates are incubated for 4 hours at 37°C. The formazan metabolite is solubilized in SDS for SNU-16 and, following removal of the MTT solution, in DMSO for GTL-16. Global cell viability is estimated by measurement of optical density at 540 nm[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: Female balb/c and swiss nu/nu mice are used in the study. The hydrochloride salt of S49076 is administered orally to mice in 1% (w/v) hydroxyethylcellulose in ammonium acetate buffer pH 4.5 in a volume of 200 µL per 20 g body weight. The maximal tolerated dose of S49076 in these mice is determined to be 100 mg/kg/d (5 days a week for at least 3 weeks). Bevacizumab is dissolved in PBS and administered intraperitoneally in a volume of 200 µL per 20 g body weight[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Commun. 2019 Apr 18;10(1):1812

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REFERENCES

[1]. Burbridge MF, et al. S49076 is a novel kinase inhibitor of MET, AXL, and FGFR with strong preclinical activity alone and in association with bevacizumab. Mol Cancer Ther. 2013 Sep;12(9):1749-62.

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