Sitravatinib

Cat. No.: HY-16961

CAS No.: 1123837-84-2

Molecular Formula: $C_{33}H_{29}F_2N_5O_4S$

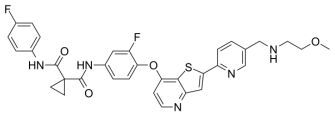
Molecular Weight: 629.68

Target: VEGFR; c-Kit; FLT3; Discoidin Domain Receptor; Trk Receptor

Pathway: Protein Tyrosine Kinase/RTK; Neuronal Signaling

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 32 mg/mL (50.82 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.5881 mL	7.9405 mL	15.8811 mL
	5 mM	0.3176 mL	1.5881 mL	3.1762 mL
	10 mM	0.1588 mL	0.7941 mL	1.5881 mL

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

In Vivo

1. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 2.75 mg/mL (4.37 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.5 mg/mL (3.97 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (3.97 mM); Suspended solution; Need ultrasonic
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.97 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Sitravatinib (MGCD516) is an orally bioavailable receptor tyrosine kinase (RTK) inhibitor with IC_{50}s of 1.5 nM, 2 nM, 2 nM, 5 nM, 6 nM, 6 nM, 8 nM, 0.5 nM, 29 nM, 5 nM, and 9 nM for Axl, MER, VEGFR3, VEGFR2, VEGFR1, KIT, FLT3, DDR2, DDR1, TRKA, TRKB, respectively[1]. Sitravatinib shows potent single-agent antitumor efficacy and enhances the activity of PD-1 blockade through promoting an antitumor immune microenvironment[2].

IC_{50} & Target				
	Axl 1.5 nM (IC_{50})	MER 2 nM (IC_{50})	VEGFR3 2 nM (IC_{50})	VEGFR2 5 nM (IC_{50})
	VEGFR1 6 nM (IC_{50})	TrkA 5 nM (IC_{50})	TrkB 9 nM (IC_{50})	KIT 6 nM (IC_{50})
	FLT3 8 nM (IC_{50})	DDR2 0.5 nM (IC_{50})	DDR1 29 nM (IC_{50})	

In Vitro

Sitravatinib (0.01 nM-10 μM; 14 days) reduces colony formation in a dose-dependent manner in KLN205 and E0771 cell lines [2].

Sitravatinib (0.001-10 μM; 5 days) inhibits tumor cell viability with IC_{50}s of approximately 1 μM in KLN205, E0771 and CT1B-A5 cell lines[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[2]

Cell Line:	KLN205, E0771, CT1B-A5 cells
Concentration:	0.001, 0.01, 0.1, 1, 10 μM
Incubation Time:	5 days
Result:	Inhibited KLN205, E0771, CT1B-A5 cells with IC_{50}s of approximately 1 μM.

In Vivo

Sitravatinib (20 mg/kg; p.o.; once per day for 6 days) significantly inhibits tumor progression and induces tumor regression in C57BL/6 mice bearing CT1B-A5 cells model[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	6-week-old C57BL/6 mice (bearing CT1B-A5 cells) [2]
Dosage:	20 mg/kg
Administration:	Oral administration; once per day for 6 days
Result:	Significantly inhibited tumor progression and induced tumor regression.

REFERENCES

[1]. Patwardhan PP et al. Significant blockade of multiple receptor tyrosine kinases by MGCD516 (Sitravatinib), a novel small molecule inhibitor, shows potent anti-tumor activity in preclinical models of sarcoma. Oncotarget, 2016 Jan 26;7(4):4093-109.

[2]. Du W, et al. Sitravatinib potentiates immune checkpoint blockade in refractory cancer models. JCI Insight. 2018 Nov 2;3(21). pii: 124184.

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