

Product Data Sheet

Product Name: Sitravatinib

Cat. No.: GC19332

Chemical Properties

Cas. No. 1123837-84-2

SMILES O=C(C1(C(NC2=CC=C(F)C=C2)=O)CC1)NC3=CC=C(OC4=C5C(C=C(C6=NC=C(CNCOC)C=C6)S5)=NC=C4)C(F)=C3

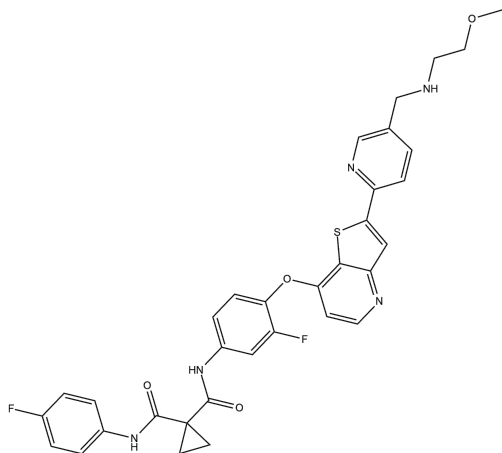
Formula $C_{33}H_{29}F_2N_5O_4S$ M.Wt 629.68

Solubility DMSO : ≥ 32 mg/mL (50.82 mM) Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines Sunitinib and axitinib-resistant (SuR/AxR) human LM2-4 and mouse RENCA or 4T1 cells

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Preparation Method	5x10³ and 1x10³ cells/well (for human and mouse SuR/AxR cell lines, respectively) were plated in 96-well plates in growth media. The next day, growth media was removed and replaced with media containing various concentrations of sitravatinib or cabozantinib. Sitravatinib concentrations ranged between 1 and 10μM for human and 0.02 and 10μM for mouse cell lines, and cabozantinib concentrations ranged between 0.01 and 10μM for mouse cell lines. Preliminary studies were conducted using multiple concentration ranges to arrive at optimal concentrations for IC₅₀ determination. After 72 hours, MTS was added to the cells and, after 2 hours, measured at a wavelength of 490nm using a spectrophotometer.
Reaction Conditions	1 and 10μM for human and 0.02 and 10μM for mouse cell lines; 72 hours
Applications	Sitravatinib drug concentrations needed to reach 50% inhibition (IC ₅₀) was consistently less in SuR/AxR cells.

Animal experiment [2]:

Animal models	SW620 and SW620/Ad300 cells transplanted nude mice
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Preparation Method	SW620 and SW620/Ad300 cells were harvested and washed twice with PBS. Then, both cell lines (1×10^7 cells in 0.1 mL PBS) were injected subcutaneously under armpits of the nude mice. Once the tumor volume reached 500mm^3, the mice were euthanized, and the tumor tissues were dissected. Each tumor tissue, except the necrotic part, was cut into $2 \times 2\text{mm}$ in size. The small tumor pieces were implanted subcutaneously under armpits of the nude mice. When the tumor reached approximately 100mm^3, the mice were randomly assigned to the following four groups. Sitravatinib was prepared in a final concentration of 0.5% hydroxypropyl methylcellulose (HPMC) and 0.1% Tween-80 solution (pH 1.4) (vehicle A), while vincristine was prepared in autoclaved water (vehicle B). Group 1 mice received vehicle A (administered orally) 1h prior to vehicle B (administered intraperitoneally). Group 2 mice received sitravatinib (prepared in vehicle A, 2mg/kg, administered orally) 1h prior to vehicle B (administered intraperitoneally). Group 3 mice received vehicle A (administered orally) 1h prior to vincristine (prepared in vehicle B, 0.4mg/kg, administered intraperitoneally). Group 4 mice received sitravatinib 1h prior to vincristine at indicated dosages. All treatments were given every other day for 14 days.
Dosage form	2mg/kg; oral; every other day for 14 days.
Applications	Sitravatinib alone had 37% inhibitory effect on tumor volume (IRV) and 28% inhibitory effect on tumor weight (IRW) compared with the control group treated with vehicle only in the SW620 mice. The growth of xenograft tumors was significantly inhibited by combination of sitravatinib and vincristine with 76% IRV and 89% IRW.
References:	[1]. Dolan, Melissa, et al. "Enhanced efficacy of sitravatinib in metastatic models of antiangiogenic therapy resistance." PloS one 14.8 (2019): e0220101. [2]. Yang, Yuqi, et al. "Modulating the function of ABCB1: in vitro and in vivo characterization of sitravatinib, a tyrosine kinase inhibitor." Cancer Communications 40.7 (2020): 285-300.

Background

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Sitravatinib is a tyrosine kinase inhibitor (TKI) that targets the TYRO3, AXL, and MERTK (TAM) receptors, the vascular endothelial growth factor receptor (VEGFR) family, c-Kit, and c-MET^[1,2].

In vitro, Sitravatinib treatment decreased MET, EphA2, EphA3, or AXL protein phosphorylation levels in sunitinib and axitinib-resistant (SuR/AxR) human LM2-4 and mouse RENCA or 4T1 cells after 3 hours, enhanced effect in resistant cell lines^[2]. The IC₅₀ values for the three sensitive cell lines (DDL5, MPNST and LS141) ranged between 250–750nM, IC₅₀ values for the less sensitive cell lines (A673 and Saos2) ranged between 1.5–2.0mM^[3].

In vivo, Sitravatinib (2mg/kg; oral; every other day for 14 days) alone had 37% inhibitory effect on tumor volume (IRV) and 28% inhibitory effect on tumor weight (IRW) in the SW620 mice^[4]. Sitravatinib (p.o.; 20mg/kg; once per day for 24 days) significantly inhibited tumor progression and induced tumor regression in immunocompetent mice bearing KLN205, CT1B-A5, or E0771 tumors^[5].

References:

- [1] Msaouel, Pavlos, et al. "Sitravatinib in combination with nivolumab plus ipilimumab in patients with advanced clear cell renal cell carcinoma: a phase 1 trial." *Nature communications* 16.1 (2025): 578.
- [2] Dolan, Melissa, et al. "Enhanced efficacy of sitravatinib in metastatic models of antiangiogenic therapy resistance." *PloS one* 14.8 (2019): e0220101.
- [3] Patwardhan, Parag P., 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* 7.4 (2015): 4093.
- [4] Yang, Yuqi, et al. "Modulating the function of ABCB1: in vitro and in vivo characterization of sitravatinib, a tyrosine kinase inhibitor." *Cancer Communications* 40.7 (2020): 285-300.
- [5] Du, Wenting, et al. "Sitravatinib potentiates immune checkpoint blockade in refractory cancer models." *JCI insight* 3.21 (2018): e124184.

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