Opaganib

Cat. No.: HY-16015

CAS No.: 915385-81-8

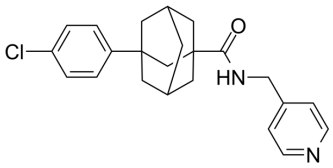
Molecular Formula: $C_{23}H_{25}ClN_2O$

Molecular Weight: 380.91

Target: SphK

Pathway: Immunology/Inflammation

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (262.53 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6253 mL	13.1265 mL	26.2529 mL
	5 mM	0.5251 mL	2.6253 mL	5.2506 mL
	10 mM	0.2625 mL	1.3126 mL	2.6253 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 (6.56 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.56 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.56 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Opaganib (ABC294640) is a selective, competitive sphingosine kinase 2 (SK2) inhibitor with K_i of 9.8 μM.

IC_{50} & Target

Ki: 9.8 μM (SK2)[1]

In Vitro

Using recombinant human SK1 and SK2, Opaganib demonstrates dose-dependent inhibition of SK2 with an IC_{50} of approximately 60 μM without affecting the activity of SK1 at concentrations up to at least 100 μM. In contrast, N,N-dimethylsphingosine (DMS) inhibits both SK1 and SK2 with IC_{50} values of approximately 60 and 20 μM, respectively. Kinetic analyses of varying concentrations of Opaganib (ABC294640) in the presence of 2.5 to 25 μM sphingosine indicated a K_i of 9.8±1.4 μM for the inhibition of SK2. Opaganib (ABC294640) decreases [^{3}H]S1P formation in a dose-dependent fashion with

	an IC_{50} value of 26 μM[1]. IC_{50} values for Opaganib (ABC294640) are approximately 50 and 60 μM for A-498 and Bxpc-3 cells, respectively; whereas the IC_{50} values for Opaganib (ABC294640) are approximately 20 and 40 μM for these cells[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Opaganib induces a transient minor decrease in the hematocrit of rats. Hematology studies indicate decreases in red blood cell number and hematocrit of approximately 20% in animals given either 100 or 250 mg/kg/day; and a slight increase in neutrophils and decrease in basophils in the treated rats[1]. Mice are gavaged with Opaganib (50 mg/kg), a selective inhibitor of sphingosine kinase-2 (SK2), 1 h before surgery and subjected to 1 h-warm ischemia to ~70% of the liver followed by reperfusion. Opaganib-treatment largely prevented the increase of sphingosine-1-phosphate (S1P) after ischemia-reperfusion (IR) in vivo[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	To determine the effects of the test compounds (e.g., Opaganib (ABC294640)) on proliferation, cells are plated into 96-well microtiter plates and allowed to attach for 24 h. Varying concentrations of Opaganib are added to individual wells and the cells are incubated for an additional 72 h. At the end of this period, the number of viable cells is determined by use of the sulforhodamine-binding assay. The percentage of cells killed is calculated as the percentage decrease in sulforhodamine-binding compare with control cultures. Regression analyses of inhibition curves are performed by use of GraphPad Prism[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1][3]	Rats[1] Sprague-Dawley male rats (7-8 weeks old) are orally dosed with 0, 100, or 250 mg of ABC294640•HCl/kg in 0.375% Polysorbate-80 in PBS daily for 7 days. The animals are observed daily for viability, signs of gross toxicity, and behavioral changes, and a battery of detailed observations are performed on study days 1 and 7. Blood is sampled from all animals on day 8 of the study for hematology, clinical biochemistry, and serology assessments, and the animals are sacrificed. Gross necropsies are performed on all study rats, and selected organs and tissues are evaluated in the control and high-dose level groups. Mice[3] Male C57BL/6 (8-9 weeks) mice are gavaged with 50 mg/kg of Opaganib (ABC294640), or an equivalent volume of vehicle (0.375% Tween 80 in phosphate buffered saline, pH 7.1) 1 h before surgery. Under ether anesthesia, ischemia to 70% of the total liver is induced for 1 h. After opening the vascular clamp, the non-ischemic liver lobes are removed, and mice are observed 7 days for survival. Sham operation included equivalent anesthesia and laparotomy without ischemia. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- FASEB J. 2019 Mar;33(3):3636-3646.
- Biochim Biophys Acta Mol Basis Dis. 2018 Nov;1864(11):3824-3836.
- Channels. 2020 Dec;14(1):216-230.
- Arch Med Res. 2018 Jul;49(5):335-341.
- Oncotarget. 2016 Mar 29;7(13):16663-75.

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REFERENCES

[1]. French KJ, et al. Pharmacology and antitumor activity of ABC294640, a selective inhibitor of sphingosine kinase-2. J Pharmacol Exp Ther. 2010 Apr;333(1):129-39.

[2]. Beljanski V, et al. Combined anticancer effects of sphingosine kinase inhibitors and sorafenib. Invest New Drugs. 2011 Dec;29(6):1132-42.

[3]. Shi Y, et al. Sphingosine kinase-2 inhibition improves mitochondrial function and survival after hepatic ischemia-reperfusion. J Hepatol. 2012 Jan;56(1):137-45.

[4]. Liu Q, et al. Inhibition of sphingosine kinase-2 suppresses inflammation and attenuates graft injury after liver transplantation in rats. PLoS One. 2012;7(7):e41834.

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