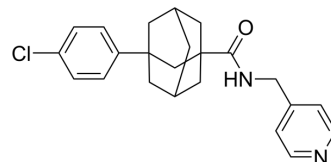


Opaganib

Cat. No.:	HY-16015		
CAS No.:	915385-81-8		
Molecular Formula:	C ₂₃ H ₂₅ ClN ₂ O		
Molecular Weight:	380.91		
Target:	SphK		
Pathway:	Immunology/Inflammation		
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 : 100 mg/mL (262.53 mM; Need ultrasonic)			
		Solvent Concentration	Mass	
			1 mg	5 mg
			10 mg	
Preparing Stock Solutions	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	<ol style="list-style-type: none"> 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 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 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.
IC₅₀ & 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 $9.8 \pm 1.4 \mu\text{M}$ for the inhibition of SK2. Opaganib (ABC294640) decreases [^3H]S1P formation in a dose-dependent fashion with an IC_{50} value of $26 \mu\text{M}$ ^[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

- Arch Med Res. 2018 Jul;49(5):335-341.
- Biochim Biophys Acta Mol Basis Dis. 2018 Nov;1864(11):3824-3836.
- FASEB J. 2019 Mar;33(3):3636-3646.
- Neurocrit Care. 2021 Sep 10.
- Channels. 2020 Dec;14(1):216-230.

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

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