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产品名称：3-(4-氯苯基)-N-(4-吡啶基甲基)金刚烷-1-甲酰胺
产品别名：Opaganib ； ABC294640

生物活性：

Description	Opaganib (ABC294640) is a selective, competitive sphingosine kinase 2 (SK2) inhibitor with Ki 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 IC50 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 IC50 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 Ki 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 IC50 value of 26 μM[1]. IC50 values for Opaganib (ABC294640) are approximately 50 and 60 μM for A-498 and Bxpc-3 cells, respectively; whereas the IC50 values for Opaganib (ABC294640) are approximately 20 and 40 μM for these cells[2].
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].
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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (6.56 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (6.56 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (6.56 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.56 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (6.56 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.56 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.

实验参考：

Cell Assay	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].
Animal Administration	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.
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.