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产品名称：Fruquintinib
产品别名：呋喹替尼；HMPL-013

生物活性：

Description	Fruquintinib (HMPL-013) is a highly potent and selective VEGFR 1/2/3 inhibitor with IC50s of 33, 0.35, and 35 nM, respectively.		
IC_{50} & Target	VEGFR1	VEGFR2	VEGFR3
	33 nM (IC_{50})	35 nM (IC_{50})	0.5 nM (IC_{50})
In Vitro	Fruquintinib demonstrates potent inhibition on VEGF-A dependent KDR phosphorylation in HEK293-KDR cells and VEGF-A induced proliferation in primary HUVECs with IC50s of 0.6±0.2 nM and 1.7 nM, respectively. Similarly, potent VEGFR3 attenuation by fruquintinib is observed in primary HLECs, with IC50s of 1.5 nM and 4.2 nM for VEGF-C stimulated VEGFR3 phosphorylation and proliferation, respectively. Fruquintinib suppresses the tube branching, tube length and area in a concentration-dependent manner. The tubule length of primary HUVECs decreased by 74% and 94% at 0.03 and 0.3 μM of fruquintinib, respectively. Fruquintinib inhibits HUVEC tubule growth and CAM angiogenesis. Tube formation is suppressed significantly after treatment with fruquintinib at 0.3 μM for 18 hours[1].		
In Vivo	Gastric cancer BGC-823 model is found to be most sensitive to fruquintinib. In this model, fruquintinib inhibits tumor growth by 62.3% and 95.4~98.6%, at 0.5 and 2 mg/kg once daily dosing, respectively. When the dose is elevated to 5 mg/kg and 20 mg/kg, the tumors regress by 24.1% and 48.6%, respectively. The level of anti-tumor growth activity of fruquintinib varies in different tumor xenograft models. Fruquintinib significantly decreases the micro-vessel density even at the lowest dose of 0.8 mg/kg[1].		

Solvent&Solubility

In Vitro:

DMSO : 5.88 mg/mL (14.95 mM; Need ultrasonic)

	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	2.5420 mL	12.7100 mL	25.4201 mL
	5 mM	0.5084 mL	2.5420 mL	5.0840 mL
	10 mM	0.2542 mL	1.2710 mL	2.5420 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: ≥ 0.59 mg/mL (1.50 mM); Clear solution

	此方案可获得 ≥ 0.59 mg/mL (1.50 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 5.8999996 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: ≥ 0.59 mg/mL (1.50 mM); Clear solution 此方案可获得 ≥ 0.59 mg/mL (1.50 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 5.8999996 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: ≥ 0.59 mg/mL (1.50 mM); Clear solution 此方案可获得 ≥ 0.59 mg/mL (1.50 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 5.8999996 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Sun Q, et al. Discovery of fruquintinib, a potent and highly selective small molecule inhibitor of VEGFR 1, 2, 3 tyrosine kinases for cancer therapy. Cancer Biol Ther. 2014;15(12):1635-45.

实验参考：

Cell Assay	Primary HUVECs or HLECs in exponential phase are suspended in 100 μL of RPMI-1640 media containing 0.5% FBS, and seeded at 5000 cell/well in 96-well plates pre-coated with 0.2% gelatin or fibronectin, and incubated overnight in a 5% CO_2, 37°C incubator. Fruquintinib and VEGF-A165 or VEGF-C (50 ng/mL) are added and incubated for 48 hours. Viability of the cells is determined using CCK-8 assay format[1].
Animal Administration	Mice: The patient derived xenograft models are established after the primary tumor adopted serial passages in vivo. Once tumors have grown to 100-300 mm^3, the animals are randomly assigned with 6-8 animals per group. The mice are treated orally with the vehicle (control group) or fruquintinib at a dose range of 0.5-20 mg/kg suspended in the vehicle (treated group) once daily for 3 weeks. In combination studies, docetaxel (Taxotere, 5 mg/kg) or oxaliplatin (10 mg/kg) is administered to nude mouse via intravenous injection, once a week. Tumor size and body weights are measured 3 times a week. Tumor volumes (TV) are calculated[1].
References	[1]. Sun Q, et al. Discovery of fruquintinib, a potent and highly selective small molecule inhibitor of VEGFR 1, 2, 3 tyrosine kinases for cancer therapy. Cancer Biol Ther. 2014;15(12):1635-45.