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产品名称：BGB-283
产品别名：Lifirafenib

生物活性：

Description	Lifirafenib (BGB-283) is a novel and potent Raf Kinase and EGFR inhibitor with IC_{50} values of 23 and 29 nM for recombinant $BRaf^{V600E}$ and EGFR, respectively.

IC_{50} & Target	EGFR	$BRaf^{V600E}$	$EGFR^{L858R/T790M}$
	29 nM (IC_{50})	23 nM (IC_{50})	495 nM (IC_{50})

In Vitro	Lifirafenib (BGB-283) potently inhibits $BRaf^{V600E}$-activated ERK phosphorylation and cell proliferation. It demonstrates selective cytotoxicity and preferentially inhibits proliferation of cancer cells harboring $BRaf^{V600E}$ and EGFR mutation/amplification. In $BRaf^{V600E}$ colorectal cancer cell lines, Lifirafenib (BGB-283) effectively inhibits the reactivation of EGFR and EGFR-mediated cell proliferation[1].
In Vivo	Lifirafenib (BGB-283) treatment leads to dose-dependent tumor growth inhibition accompanied by partial and complete tumor regressions in both cell line-derived and primary human colorectal tumor xenografts bearing $BRaf^{V600E}$ mutation[1].

Solvent&Solubility

In Vitro:

DMSO： ≥ 100 mg/mL (209.02 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	**1 mg**	**5 mg**	**10 mg**
	1 mM	2.0902 mL	10.4511 mL	20.9021 mL
	5 mM	0.4180 mL	2.0902 mL	4.1804 mL
	10 mM	0.2090 mL	1.0451 mL	2.0902 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 (5.23 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.23 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% corn oil

Solubility: ≥ 2.5 mg/mL (5.23 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (5.23 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]. Tang Z, et al. BGB-283, a Novel RAF Kinase and EGFR Inhibitor, Displays Potent Antitumor Activity in BRAF-Mutated Colorectal Cancers. Mol Cancer Ther. 2015 Oct;14(10):2187-97.

实验参考：

Cell Assay	Melanoma, colon, breast, and lung cancer cells are left to attach for 16 hours and then treated with a 10-point dilution series in duplicate. CellTiter-Glo reagent is added in each well. Mixture is mixed on an orbital shaker for 2 minutes to allow cell lysing, followed by 10 minutes incubation at room temperature to allow development and stabilization of luminescent signal. Luminescent signal is measured using PHERAstar FS reader. EC_{50} values for cell viability are determined[1].
Animal Administration	Mice: When the average tumor size reaches 110 to 200 mm^3, mice are randomized to treatment groups and treated twice per day or once daily by oral gavage (p.o.) with vehicle alone or 2.5 to 30 mg/kg of BGB-283. As control, mice are treated with erlotinib (100 mg/kg qd) or cetuximab (40 mg/kg twice weekly). Lifirafenib (BGB-283) and erlotinib are formulated at the desired concentration as a homogenous suspension in 0.5% (w/v) methylcellulose in purified water. Cetuximab is formulated by diluting the injection solution with saline before dosing[1].
References	[1]. Tang Z, et al. BGB-283, a Novel RAF Kinase and EGFR Inhibitor, Displays Potent Antitumor Activity in BRAF-Mutated Colorectal Cancers. Mol Cancer Ther. 2015 Oct;14(10):2187-97.