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产品名称: **BMS-690514**  
产品别名: **BMS-690514**

生物活性:

|                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                     |              |             |              |
|--------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|--------------|-------------|--------------|
| Description        | BMS-690514 is a potent and orally active inhibitor of EGFR and VEGFR; has IC50s of 5, 20 and 60 nM for EGFR, HER 2 and HER 4, respectively.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                     |              |             |              |
| IC50 & Target      | EGFR                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | HER2                                | HER4         |             |              |
|                    | 5 nM (IC50)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 20 nM (IC50)                        | 60 nM (IC50) |             |              |
| In Vitro           | BMS-690514 targets several critical signaling pathways: human epidermal growth factor receptor (HER)/ErbB, angiogenesis signaling through VEGFR2, lymphangiogenesis through VEGFR3, and also shows activity against VEGFR1, Flt-3, and Lck. Permeability of BMS-690514 in Caco-2 cells is in the intermediate range with a moderate potential to be a P-gp substrate <sup>[2]</sup> . BMS-690514 inhibits members of the VEGFR family with IC50 values in the range of 25 to 50 nM. Non-small cell lung tumor cells with exon 19 deletion (HCC4006, HCC827, and PC9) are highly sensitive to BMS-690514, which inhibits their proliferation with IC50 values of 2 to 35 nM. Tumor cell lines with EGFR gene amplification (DiFi, NCI-H2073, A431) are also highly sensitive to inhibition by BMS-690514. Tumor cell lines that are dependent on HER2 signaling are also found to be highly sensitive to BMS-690514. Breast and gastric tumor cell lines that have HER2 gene amplification (N87, SNU-216, AU565, BT474, KPL4, and HCC202) are inhibited with IC50 values of 20 to 60 nM <sup>[1]</sup> . |                                     |              |             |              |
| In Vivo            | BMS-690514 has been shown to be efficacious in a broad spectrum of tumor xenografts. At doses that are efficacious and well tolerated in the animal models, BMS-690514 inhibits tumor cell proliferation and tumor blood flow[1]. The oral bioavailability of BMS-690514 is 78% in mice, 100% in rats, 8% in monkeys, and 29% in dogs. BMS-690514 is able to cross the blood-brain barrier with a brain-to-plasma ratio of 1. The preclinical ADME properties of BMS-690514 suggest good oral bioavailability in humans and metabolism by multiple pathways including oxidation and glucuronidation[2].                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                     |              |             |              |
| Solvent&Solubility | <b>In Vitro:</b><br><b>DMSO : ≥ 25 mg/mL (67.86 mM)</b><br><br>* "≥" means soluble, but saturation unknown.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                     |              |             |              |
|                    | <b>Preparing Stock Solutions</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | <div>SolventMassConcentration</div> | <b>1 mg</b>  | <b>5 mg</b> | <b>10 mg</b> |
|                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 1 mM                                | 2.7142 mL    | 13.5711 mL  | 27.1422 mL   |
|                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 5 mM                                | 0.5428 mL    | 2.7142 mL   | 5.4284 mL    |
|                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 10 mM                               | 0.2714 mL    | 1.3571 mL   | 2.7142 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。<br><br>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。<br><br><b>In Vivo:</b><br><br>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:<br><br>——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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                     |              |             |              |



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|-----------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                       | <p>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</p> <p>1.请依序添加每种溶剂: 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline</p> <p>Solubility: <math>\geq 2.5</math> mg/mL (6.79 mM); Clear solution</p> <p>此方案可获得 <math>\geq 2.5</math> mg/mL (6.79 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 400 <math>\mu</math>L PEG300 中, 混合均匀向上述体系中加入 50 <math>\mu</math>L Tween-80, 混合均匀; 然后继续加入 450 <math>\mu</math>L 生理盐水定容至 1 mL。</p> <p>2.请依序添加每种溶剂: 10% DMSO→ 90% (20% SBE-<math>\beta</math>-CD in saline)</p> <p>Solubility: <math>\geq 2.5</math> mg/mL (6.79 mM); Clear solution</p> <p>此方案可获得 <math>\geq 2.5</math> mg/mL (6.79 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 20% 的 SBE-<math>\beta</math>-CD 生理盐水水溶液中, 混合均匀。</p> <p>3.请依序添加每种溶剂: 10% DMSO →90% corn oil</p> <p>Solubility: <math>\geq 2.5</math> mg/mL (6.79 mM); Clear solution</p> <p>此方案可获得 <math>\geq 2.5</math> mg/mL (6.79 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。</p> <p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 玉米油中, 混合均匀。</p>                                                                                                                                                                                                                                                                                                                                                                               |
| References            | <p>[1]. Wong TW, et al. Antitumor and antiangiogenic activities of BMS-690514, an inhibitor of human EGF and VEGF receptor kinase families. Clin Cancer Res. 2011 Jun 15;17(12):4031-41.</p> <p>[2]. Marathe P, et al. Preclinical pharmacokinetics and in vitro metabolism of BMS-690514, a potent inhibitor of EGFR and VEGFR2. J Pharm Sci. 2010 Aug;99(8):3579-93.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| 实验参考:                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Animal Administration | <p>Rats: BMS-690514 is administered to male Sprague–Dawley rats as a 10 min infusion intraarterially (IA) (1 mg/kg) or orally by gavage (10mg/kg). Vehicles used for dosing are: IA, 10mM acetate buffer (pH 5.0, 1 mL/kg) and PO, PEG400/10mM acetate buffer (pH 5.0, 2 mL/kg) (10:90). Serial plasma samples are obtained predose and at 0.17 (or 0.25 for PO), 0.5, 0.75, 1, 2, 4, 6, 8, 12, and 24 h postdose. Rats are fasted overnight and fed 4 h postdose. The brain uptake of BMS-690514 is investigated after the last dose in a 2-week toxicology study (3, 10, and 30 mg/kg/day). Brain samples are weighed and homogenized in 3 volumes of ice-chilled water. Concentrations of BMS-690514 in plasma and brain homogenates are determined by LC/MS/MS[2].</p> <p>Mice: The pharmacokinetics of BMS-690514 is investigated in male balb-c mice. A total of 18 mice are divided into two groups to receive BMS-690514 as a single dose of 1mg/kg IV bolus or 5 mg/kg orally by gavage. The vehicle used for both IV (0.1mL/mouse) and PO (0.2mL/mouse) dose is Tween-80/PG/water (10:40:50). Serum concentrations of BMS-690514 are measured at 0.05 (or 0.25 for PO), 0.5, 1, 3, 6, 8, and 24 h postdose. The mice are fasted overnight and fed 6 h after dosing. Three blood samples are taken from each mouse by retro-orbital bleeding and there are three mice per time point. At the 24h time point only one sample is taken from each of the three mice. Composite serum concentration–time profiles are constructed for pharmacokinetic analysis[2].</p> |



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#### References

- [1]. Wong TW, et al. Antitumor and antiangiogenic activities of BMS-690514, an inhibitor of human EGF and VEGF receptor kinase families. Clin Cancer Res. 2011 Jun 15;17(12):4031-41.
- [2]. Marathe P, et al. Preclinical pharmacokinetics and in vitro metabolism of BMS-690514, a potent inhibitor of EGFR and VEGFR2. J Pharm Sci. 2010 Aug;99(8):3579-93.



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