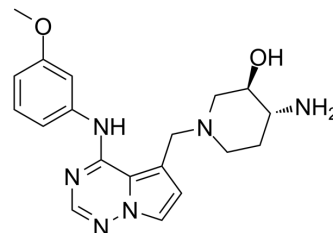


BMS-690514

Cat. No.:	HY-10333		
CAS No.:	859853-30-8		
Molecular Formula:	C ₁₉ H ₂₄ N ₆ O ₂		
Molecular Weight:	368.43		
Target:	EGFR; VEGFR		
Pathway:	JAK/STAT Signaling; Protein Tyrosine Kinase/RTK		
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 : ≥ 25 mg/mL (67.86 mM)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
 Solubility: ≥ 2.5 mg/mL (6.79 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
 Solubility: ≥ 2.5 mg/mL (6.79 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
 Solubility: ≥ 2.5 mg/mL (6.79 mM); Clear solution

BIOLOGICAL ACTIVITY

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 5 nM (IC ₅₀)	HER2 20 nM (IC ₅₀)	HER4 60 nM (IC ₅₀)
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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^[2]. 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^[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration ^[2]

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].

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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Science. 2017 Dec 1;358(6367):eaan4368.
- Technical University of Munich. 24.01.2018.

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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.

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

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