Brivanib

Cat. No.: HY-10337

CAS No.: 649735-46-6

Molecular Formula: $C_{19}H_{19}FN_4O_3$

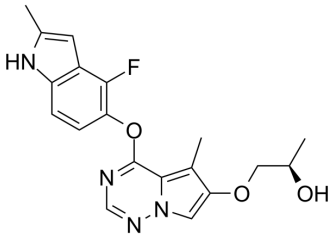
Molecular Weight: 370.38

Target: VEGFR; Autophagy

Pathway: Protein Tyrosine Kinase/RTK; Autophagy

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (135.00 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6999 mL	13.4996 mL	26.9993 mL
	5 mM	0.5400 mL	2.6999 mL	5.3999 mL
	10 mM	0.2700 mL	1.3500 mL	2.6999 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (5.62 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.62 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.62 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Brivanib (BMS-540215) is an ATP-competitive inhibitor against VEGFR2 with an IC_{50} of 25 nM, and has moderate potency against VEGFR-1 and FGFR-1, but >240-fold against PDGFR-β[1].

IC_{50} & Target

VEGFR2

25 nM (IC_{50})

In Vitro	Brivanib inhibits VEGFR1 and FGFR-1 with IC_{50} of 0.38 μM and 0.148 μM. Brivanib is not sensitive to PDGFRβ, EGFR, LCK, PKC α or JAK-3 with IC_{50} all above 1900 nM. Brivanib could inhibit the proliferation of VEGF-stimulated HUVECs with IC_{50} of 40 nM, compared to 276 nM in FGF-stimulated HUVECs. On the other hand, brivanib exhibits low activity to tumor cell lines[1]. Brivanib doses ≤20 μM paradoxically enhances FGF-induced LX-2 cell proliferation, whereas higher brivanib doses (≥30 μM) inhibits LX-2 cell proliferation. The inhibitory effect of brivanib on liver fibrosis is not through inhibition of TGF-β1-induced stellate cell activation, and is possibly through inhibition of PDGF-BB-induced stellate cell activation[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Brivanib displays antitumor activities in H3396 xenograft in athymic mice. At a dose of 60 and 90 mg/kg (p.o.), brivanib completely inhibits the tumor growth, with TGI of 85% and 97%, respectively[1]. Moreover, brivanib significantly suppresses tumor growth in Hepatocellular carcinoma (HCC) xenografts, which due to the decrease in phosphorylation of VEGFR2. The results show that the tumor weights in 06-0606 xenograft mice are 55% and 13%, compared with the controls at a dose of 50 mg/kg and 100 mg/kg. Brivanib is suggested to be efficient in treatment of HCC[2]. Brivanib (50 mg/kg, p.o.) attenuates liver fibrosis and stellate cell activation induced by BDL in mice. Brivanib inhibits growth factor and growth factor receptor mRNA expression in sham control animals but shows variable effects in bile duct ligated animals[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [3]	Viability is measured in LX-2 cells using the Cell Counting Kit-8 (CCK-8). Using 96-well plates with 2,000 cells per well, HSCs are incubated in 10% FBS-supplemented DMEM for 24 hours, followed by starvation in serum-free media. After 24 hours of starvation, brivanib is added at different doses. Two hours later, 5 ng/mL PDGF-BB is added. The cells are incubated for an additional 72 hours and cell viability is measured. Each experiment is performed in three replicates at least four times. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Male mice 4-6 weeks of age are treated 3 times a week with a total of 12 intraperitoneal (i.p.) injections of 150 mL/kg TAA. At the onset of TAA treatment, placebo or brivanib (25 or 50 mg/kg) is administered orally on 5 consecutive days with weekend breaks. The animals are sacrificed 4 weeks after the start of the injections. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Cell Rep. 2023 Mar 20;42(3):112275.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Bhide RS, et al. Discovery and preclinical studies of (R)-1-(4-(4-fluoro-2-methyl-1H-indol-5-yloxy)-5- methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy)propan- 2-ol (BMS-540215), an in vivo active potent VEGFR-2 inhibitor. J Med Chem, 2006, 49 (7), 2143-2146.

[2]. Huynh H, et al. Brivanib alaninate, a dual inhibitor of vascular endothelial growth factor receptor and fibroblast growth factor receptor tyrosine kinases, induces growth inhibition in mouse models of human hepatocellular carcinoma. Clin Cancer Res, 2008,

[3]. Nakamura I, et al. Correction: Brivanib Attenuates Hepatic Fibrosis In Vivo and Stellate Cell Activation In Vitro by Inhibition of FGF, VEGF and PDGF Signaling. PLoS One. 2015 Nov 3;10(11):e0142355.

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

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