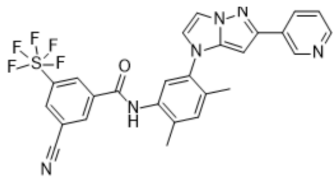
BAY-826

Cat. No.:	HY-100756
CAS No.:	1448316-08-2
Molecular Formula:	$C_{26}H_{19}F_5N_6OS$
Molecular Weight:	558.53
Target:	Discoidin Domain Receptor; Tie
Pathway:	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 : 100 mg/mL (179.04 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7904 mL	8.9521 mL	17.9041 mL
	5 mM	0.3581 mL	1.7904 mL	3.5808 mL
	10 mM	0.1790 mL	0.8952 mL	1.7904 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: ≥ 1 mg/mL (1.79 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1 mg/mL (1.79 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1 mg/mL (1.79 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BAY-826 is a selective and potent TIE-2 inhibitor with a K_d of 1.6 nM, respectively.

IC_{50} & Target

Tie2
1.6 nM (Kd)

In Vitro

BAY-826 is a selective and potent inhibitor of TIE-2 (dissociation constant = 1.6 nM) and binds with similar high affinity to only 4 of 456 tested kinases, namely, TIE-1, DDR1, DDR2, and Serine/threonine-protein kinase 10 (LOK) (dissociation

	constant = 0.9, 0.4,1.3, and 5.9 nM).The high biochemical affinity for TIE-2 translates into very potent cellular mechanistic activity with an EC50 of about 1.3 nM for inhibition of TIE-2 autophosphorylation in human umbilical vein endothelial cells. The TIE-2 inhibitor BAY-826 is tested for its acute growth inhibitory as well as anti-clonogenic properties in all four mouse glioma cell lines. BAY-826 is highly selective against other angiogenic kinases, such as VEGFR, fibroblast growth factorreceptor (FGFR), or Platelet-derived growth factor receptor (PDGFR), and affects VEGF-stimulated proliferation of HUVEC only atμM concentrations, respectively. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	BAY-826 (oral gavage; 25 mg/kg,50 mg/kg,100 mg/k) potently inhibits ANG-1-stimulated TIE-2 autophosphorylation in murine lungs in female CB17/scid mice[1]. BAY-826 improves tumor control in syngeneic mouse glioma models. Co-treatment with BAY-826 and irradiation is ineffective in one model (SMA-497), but provided synergistic prolongation of survival in another (SMA-560) cell. TIE- 2 inhibition may improve tumor response to treatment in highly vascularized tumors such as glioblastoma[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay	Murine SMA-497, SMA-540, SMA-560, and GL-261 glioma cells are used.The cells are commonly cultured as adherent monolayers in Dulbecco`s modified Eagle medium supplemented with 10% heatinactivated fetal calf serum and 2 mM glutamine. Cells are irradiated in a Coradiation source at 1, 3, and 9 Gy. The cells are pre-incubated for 10 min in the 37°C incubator either with 0.1% DMSO as control or 1μM BAY-826. TIE-2 autophosphorylation is induced for 20 min with either 4 mM Na_3VO_4 or with 400 ng/mL COMP-ANG-1 in the presence of either 0.1% DMSO or 1 μM BAY-826[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration	Following anesthesia, a burr hole is drilled in the skull 2 mm lateral to the bregma. The needle of a Hamilton syringe is introduced to a depth of 3 mm. A volume of 2 μL of a single cell suspension in PBS is slowly injected into the right striatum. In female and male VM/Dk mice (in-house husbandry) 5×10^3 SMA glioma cells are implanted, whereas in female C57Bl/6 mice (Charles River) 2×10^4 GL-261 cells are implanted (n =10 per group). The mice employed have body weights >20 g. Systemic treatment with BAY-826 is performed by oral gavage (100 mg/kg body weight daily) or the solvent (10% Ethanol/40% Solutol/50% Aqua dest), respectively [1] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Schneider H, et al. J Neurochem. 2017 Jan; 140(1):170-182. doi: 10.1111/jnc.13877. Epub 2016 Dec 12.Novel TIE-2 inhibitor BAY-826 displays in vivo efficacy in experimental syngeneic murine glioma models.

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