BMS-599626 Hydrochloride

Cat. No.: HY-12010

CAS No.: 873837-23-1

Molecular Formula: $C_{27}H_{28}ClFN_8O_3$

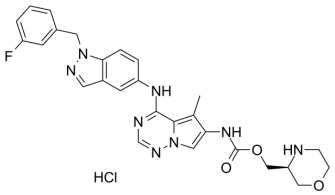
Molecular Weight: 567.01

Target: EGFR

Pathway: JAK/STAT Signaling; Protein Tyrosine Kinase/RTK

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (176.36 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7636 mL	8.8182 mL	17.6364 mL
	5 mM	0.3527 mL	1.7636 mL	3.5273 mL
	10 mM	0.1764 mL	0.8818 mL	1.7636 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: ≥ 2.5 mg/mL (4.41 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.41 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.41 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BMS-599626 Hydrochloride (AC480 Hydrochloride) is a selective and orally bioavailable HER1 and HER2 inhibitor, with IC_{50}s of 20 and 30 nM, respectively. BMS-599626 Hydrochloride displays ~8-fold less potent to HER4 (IC_{50}=190 nM), >100-fold to VEGFR2, c-Kit, Lck, MEK. BMS-599626 Hydrochloride inhibits tumor cell proliferation, and has potential to increase tumor response to radiotherapy[1][2].

In Vitro

BMS-599626 Hydrochloride inhibits the proliferation of tumor cells that are dependent on HER1/HER2 signaling.BMS-599626 Hydrochloride (0.03-8 μM; 1 huors) results in the inhibition of receptor autophosphorylation, as well as MAPK phosphorylation, with IC_{50}s of 0.3 and 0.22 μM, respectively, in Sal2 cells which express a CD8HER2 fusion protein[1]. BMS-599626 Hydrochloride abrogates HER1 and HER2 signaling and inhibited the proliferation of tumor cell lines that are

dependent on these receptors, with IC_{50}s in the range of 0.24 to 1 μM.In GEO cells, HER1 phosphorylation is stimulated by treatment with EGF and is inhibited by BMS-599626 Hydrochloride (IC_{50}=0. 75 μM).There is also nearly complete inhibition of EGF-dependent MAPK (0. 8 μM) but only partial inhibition of AKT signaling.The latter likely reflects the activation of AKT by multiple upstream signals.Treatment of N87 cells with BMS-599626 Hydrochloride leads to the inhibition of HER2 (0. 38 μM), which is expressed to a high level because of gene amplification, as well as MAPK and AKT phosphorylation (0.35 μM for both)[1].

At the molecular level, in HN-5 cells the agent (BMS-599626 Hydrochloride) inhibits the expression of pEGFR, pHER2, cyclins D and E, pRb, pAkt, pMAPK, pCDK1 and 2, CDK 6, and Ku70 proteins. BMS-599626 Hydrochloride also induced accumulation of cells in the G1 cell cycle phase, inhibited cell growth, enhanced radiosensitivity, and prolonged the presence of γ-H AX foci up to 24 h after radiation[2].

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

In Vivo

BMS-599626 Hydrochloride (60-240 mg/kg; p.o.; daily for 14 days) results in a dose-dependent inhibition of Sal2 tumor growth[1].

BMS-599626 Hydrochloride treatment results in the inhibition of GEO xenograft tumor growth when given once daily for 14 days. In addition to efficacy in the Sal2, GEO, and KPL4 models, BMS-599626 has similar antitumor activity in other HER2 amplified xenograft models including the BT474 breast and N87 gastric tumors, as well as other HER1-overexpressing non-small-cell lung tumors (A549 and L2987)[1].

BMS-599626 Hydrochloride given before and during irradiation improved the radioresponse of HN5 tumors in vivo[2].

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

Animal Model:	Athymic female nude mice (nu/nu mice, Sal2 tumor model)[1]
Dosage:	60, 120, 240 mg/kg
Administration:	Oral; daily for 14 days
Result:	Resulted in a dose-dependent inhibition of Sal2 tumor growth.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Life Sci. 2021 Dec 16;289:120231.
- BMC Pulm Med. 2023 May 11;23(1):162.

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REFERENCES

[1]. Wong TW, et al. Preclinical antitumor activity of BMS-599626, a pan-HER kinase inhibitor that inhibits HER1/HER2 homodimer and heterodimer signaling. Clin Cancer Res. 2006 Oct 15;12(20 Pt 1):6186-93.

[2]. Torres MA, et al. AC480, formerly BMS-599626, a pan Her inhibitor, enhances radiosensitivity and radioresponse of head and neck squamous cell carcinoma cells in vitro and in vivo. Invest New Drugs. 2011 Aug;29(4):554-61.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA