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产品名称：BMS-599626 (Hydrochloride)
产品别名：AC480 Hydrochloride

生物活性：

Description	BMS-599626 Hydrochloride (AC480 Hydrochloride) is a selective and orally bioavailable HER1 and HER2 inhibitor, with IC50s of 20 and 30 nM, respectively. BMS-599626 Hydrochloride displays ~8-fold less potent to HER4 (IC50=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 IC50s 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 IC50s 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 (IC50=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].
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]

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.

In Vitro:

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

	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
Preparing	1 mM	1.7636 mL	8.8182 mL	17.6364 mL

<table>
<tr><td rowspan="3">Solvent&Solubility</td><td rowspan="2">Stock Solutions</td><td>5 mM</td><td>0.3527 mL</td><td>1.7636 mL</td><td>3.5273 mL</td></tr>
<tr><td>10 mM</td><td>0.1764 mL</td><td>0.8818 mL</td><td>1.7636 mL</td></tr>
<tr><td colspan="5">*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。
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。
In Vivo:
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：
——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
1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline
Solubility: ≥ 2.5 mg/mL (4.41 mM); Clear solution
此方案可获得 ≥ 2.5 mg/mL (4.41 mM，饱和度未知) 的澄清溶液。
以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)
Solubility: ≥ 2.5 mg/mL (4.41 mM); Clear solution
此方案可获得 ≥ 2.5 mg/mL (4.41 mM，饱和度未知) 的澄清溶液。
以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。

3.请依序添加每种溶剂： 10% DMSO →90% corn oil
Solubility: ≥ 2.5 mg/mL (4.41 mM); Clear solution
此方案可获得 ≥ 2.5 mg/mL (4.41 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。
以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。</td></tr>
<tr><td>References</td><td colspan="5">[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.</td></tr>
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