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产品名称：NVP-BKM120 (Hydrochloride)
产品别名：布帕尼西盐酸盐；Buparlisib Hydrochloride；BKM120 (Hydrochloride)

生物活性：

Description

Buparlisib Hydrochloride (BKM120 Hydrochloride) is a pan-class I PI3K inhibitor, with IC50 of 52 nM/166 nM/116 nM/262 nM for p110α/p110β/p110δ/p110γ, respectively.

IC_{50} & Target

p110α	p110α-H1047R	p110α-E545K	p110δ	p110β
52 nM (IC_{50})	58 nM (IC_{50})	99 nM (IC_{50})	116 nM (IC_{50})	166 nM (IC_{50})
p110γ	Vps34	mTOR		
262 nM (IC_{50})	2.4 μM (IC_{50})	4.6 μM (IC_{50})		

In Vitro

Buparlisib (BKM120) exhibits 50-300 nM activity for class I PI3K's, including the most common p110α mutants. Additionally, NVP-BKM120 exhibits lower potency against class III and class IV PI3K's, where 2, 5, >5, and >25 μM biochemical activity is observed for inhibition of VPS34, mTOR, DNAPK, and PI4K, respectively[1]. Buparlisib (BKM120) induces multiple myeloma (MM) cell apoptosis in both dose- and time-dependent manners. Buparlisib (BKM120) at concentrations ≥10 μM induces significant apoptosis in all tested MM cell lines at 24 h (P<0.05, compares with control). Therefore, 10 μM Buparlisib (BKM120) and 24-h treatment are chose in in the following experiments if not stated otherwise. Buparlisib (BKM120) treatment results in a dose-dependent growth inhibition in all tested MM cell lines. Buparlisib (BKM120) IC_{50} varies among tested MM cells. At 24 h treatment, IC_{50} for ARP-1, ARK, and MM.1R is between 1 and 10 μM, while IC_{50} for MM.1S is <1 μM, and IC_{50} for U266 is between 10 and 100 μM. In summary, Buparlisib (BKM120) treatment results in MM cell growth inhibition and apoptosis in dose- and time-dependent manners[2].

In Vivo

In A2780 xenograft tumors, oral dosing of Buparlisib (BKM120) at 3, 10, 30, 60, and 100 mg/kg results in a dose dependent modulation of $pAKT^{Ser473}$. Partial inhibition of $pAKT^{Ser473}$ is observed at 3 and 10 mg/kg, and near complete inhibition is observed at doses of 30, 60, or 100 mg/kg, respectively. Inhibition of pAKT (normalized to total AKT) tracked well with both plasma and tumor drug exposure[1]. Mice receiving Buparlisib (BKM120) (5 μM per kg per day for 15 days) treatment has significantly smaller tumor burdens as compare with control mice, which are measured as tumor volume (P<0.05) and level of circulating human kappa chain (P<0.05). In addition, Buparlisib (BKM120) treatment significantly prolongs the survival of tumor-bearing mice (P<0.05)[2].

In Vitro:

DMSO : ≥ 50 mg/mL (111.89 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2379 mL	11.1894 mL	22.3789 mL
5 mM	0.4476 mL	2.2379 mL	4.4758 mL
10 mM	0.2238 mL	1.1189 mL	2.2379 mL

*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

Solvent&Solubility	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： 0.5% CMC-Na/saline water Solubility: 10 mg/mL (22.38 mM); Precipitated solution; Need ultrasonic 2.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.5 mg/mL (5.59 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.59 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。 3.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (5.59 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.59 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。 4.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.59 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.59 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。
References	[1]. Burger MT, et al. Identification of NVP-BKM120 as a Potent, Selective, Orally Bioavailable Class I PI3 Kinase Inhibitor for Treating Cancer. ACS Med Chem Lett. 2011 Aug 26;2(10):774-9. [2]. Zheng Y, et al. Novel phosphatidylinositol 3-kinase inhibitor NVP-BKM120 induces apoptosis in myeloma cells and shows synergistic anti-myeloma activity with dexamethasone. J Mol Med (Berl). 2012 Jun;90(6):695-706.

实验参考：

Cell Assay	A2780 cells are cultured in DMEM supplemented with 10% FBS. L-glutamine, sodium pyruvate, and antibiotics. Cells are plated in the same medium at a density of 1000 cells per well, 100 uL per well into black-walled-clear-bottom plates and incubated for 3-5 hours. Buparlisib (BKM120) supplied in DMSO (20 mM) are diluted further into DMSO (7.5 uL of 20 mM NVP-BKM120 in 22.5 uL DMSO. Mix well, transfer 10 uL to 20 uL DMSO, repeat until 9 concentrations have been made). The diluted

	Buparlisib (BKM120) solution (2 uL), is then added to cell medium (500 uL) cell medium. Equal volumes of this solution (100 uL) are added to the cells in 96 well plates and incubated at 37ºC for 3 days and developed using Cell Titer Glo. Inhibition of cell proliferation is determined by luminescence read using Trilux[1].
Animal Administration	Mice[2] Six- to eight-week-old female severe combined immunodeficiency (SCID) mice are used. SCID mice are subcutaneously inoculated in the right flank with 1 million ARP-1 or MM.1S cells suspended in 50 μL phosphate-buffered saline (PBS). After palpable tumor developed (tumor diameter ≥5 mm), mice are treated with intraperitoneal injection of DMSO/PBS or Buparlisib (BKM120) (5 μM per kg per day) for 15 days. Tumor sizes are measured every 5 days, and blood samples are collected at the same period. Tumor burdens are evaluated by measuring tumor size and detecting circulating human kappa chain or lambda chain.
References	[1]. Burger MT, et al. Identification of NVP-BKM120 as a Potent, Selective, Orally Bioavailable Class I PI3 Kinase Inhibitor for Treating Cancer. ACS Med Chem Lett. 2011 Aug 26;2(10):774-9. [2]. Zheng Y, et al. Novel phosphatidylinositol 3-kinase inhibitor NVP-BKM120 induces apoptosis in myeloma cells and shows synergistic anti-myeloma activity with dexamethasone. J Mol Med (Berl). 2012 Jun;90(6):695-706.