Buparlisib

Cat. No.: HY-70063

CAS No.: 944396-07-0

Molecular Formula: $C_{18}H_{21}F_3N_6O_2$

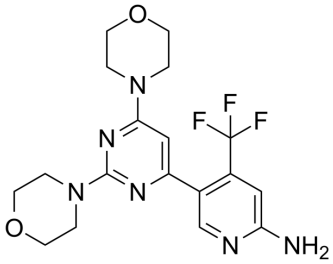
Molecular Weight: 410.39

Target: PI3K; Apoptosis

Pathway: PI3K/Akt/mTOR; Apoptosis

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 : 100 mg/mL (243.67 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4367 mL	12.1835 mL	24.3671 mL
5 mM	0.4873 mL	2.4367 mL	4.8734 mL
10 mM	0.2437 mL	1.2184 mL	2.4367 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 (6.09 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.09 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.09 mM); Clear solution
4. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (6.09 mM); Clear solution
5. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.09 mM); Clear solution
6. Add each solvent one by one: 50% PEG300 >> 50% saline
   Solubility: 2.08 mg/mL (5.07 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description	Buparlisib (BKM120; NVP-BKM120) is a pan-class I PI3K inhibitor, with IC_{50}s of 52, 166, 116 and 262 nM for p110α, p110β, p110δ and p110γ, respectively.			
IC_{50} & Target	p110α 52 nM (IC_{50})	p110α-H1047R 58 nM (IC_{50})	p110α-E545K 99 nM (IC_{50})	p110δ 116 nM (IC_{50})
	p110β 166 nM (IC_{50})	p110γ 262 nM (IC_{50})	Vps34 2.4 μM (IC_{50})	mTOR 4.6 μM (IC_{50})
In Vitro	Buparlisib (NVP-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 (NVP-BKM120) induces multiple myeloma (MM) cell apoptosis in both dose- and time-dependent manners. Buparlisib (NVP-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 (NVP-BKM120) and 24-h treatment are chose in in the following experiments if not stated otherwise. Buparlisib (NVP-BKM120) treatment results in a dose-dependent growth inhibition in all tested MM cell lines. Buparlisib (NVP-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, NVP-BKM120 treatment results in MM cell growth inhibition and apoptosis in dose- and time-dependent manners[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.			
In Vivo	In A2780 xenograft tumors, oral dosing of Buparlisib (NVP-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 (NVP-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, NVP-BKM120 treatment significantly prolongs the survival of tumor-bearing mice ($P<0.05$)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.			

PROTOCOL

Cell Assay [1]	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 (NVP-BKM120) supplied in DMSO (20 mM) are diluted further into DMSO (7.5 uL of 20 mM Buparlisib (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 (NVP-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 37°C for 3 days and developed using Cell Titer Glo. Inhibition of cell proliferation is determined by luminescence read using Trilux[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	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 (NVP-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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Med. 2016 Jul;22(7):723-6.
- Nature. 2022 Dec;612(7940):555-563.
- Nature. 2018 Aug;560(7719):499-503.
- Cancer Discov. 2020 Aug;10(8):1226-1239.
- Cancer Discov. 2019 Sep;9(9):1306-1323.

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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. J Mol Med (Berl). 2012 Jun;90(6):695-706.

[3]. Ni J, et al. Combination inhibition of PI3K and mTORC1 yields durable remissions in mice bearing orthotopic patient-derived xenografts of HER2-positive breast cancer brain metastases. Nat Med. 2016 Jul;22(7):723-6.

[4]. Liu H, et al. Identifying and Targeting Sporadic Oncogenic Genetic Aberrations in Mouse Models of Triple Negative Breast Cancer. Cancer Discov. 2018 Mar;8(3):354-369.

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