**BIOLOGICAL ACTIVITY:**

Buparlisib (NVP-BKM120) is a pan-class I PI3K inhibitor, with IC50s of 52, 166, 116 and 262 nM for p110α, p110β, p110δ and p110γ, respectively. IC50 & Target: IC50: 52 nM (p110α), 166 nM (p110β), 116 nM (p110δ), 262 nM (p110γ). 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. 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 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) IC50 varies among tested MM cells. At 24 h treatment, IC50 for ARP-1, ARK, and MM.1R is between 1 and 10 μM, while IC50 for MM.1S is <1 μM, and IC50 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.

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.

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).

**PROTOCOL (Extracted from published papers and Only for reference)**

**Cell Assay:** NVP-BKM120 is dissolved in DMSO and stored, and then diluted with appropriate media before use. 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 μL 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 μL of 20 mM Buparlisib (NVP-BKM120) in 22.5 μL DMSO). Mix well, transfer 10 μL to 20 μL DMSO, repeat until 9 concentrations have been made. The diluted Buparlisib (NVP-BKM120) solution (2 μL), is then added to cell medium (500 μL) cell medium. Equal volumes of this solution (100 μL) 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.

**Animal Administration:** NVP-BKM120 is dissolved in DMSO/PBS (Mice). A 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.

References:


CAIndexNames:
2-Pyridinamine, 5-(2,6-di-4-morpholinyl-4-pyrimidinyl)-4-(trifluoromethyl)-

SMILES:
FC(F)(C1=C(C=C(N3CCOC3)=NC(N4CCOC4)=N2)C=NC(N)=C1)F

Caution: Product has not been fully validated for medical applications. For research use only.

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