For Research Use Only

Volasertib

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Catalog Number: CM06042

产品信息

Catalog Number:
CM06042

CAS号:
755038-65-4

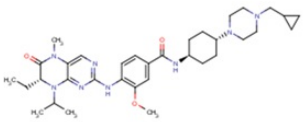
分子式:
$C_{34}H_{50}N_8O_3$

主要靶点:
Apoptosis|PLK

主要通路:
细胞周期|凋亡

分子量:
618.81

溶解度:
H2O:<1 mg/mL,DMSO:16 mg/mL (25.9 mM),Ethanol:<1 mg/mL



靶点活性

PLK1:0.87 nM (cell free)|PLK2:5 nM (cell free)|PLK3:56 nM (cell free)

体外活性

Volasertib (BI 6727) potently inhibited Plk1 as well as the two closely related kinases Plk2 and Plk3 (IC50 values 0.87, 5, and 56 nmol/L, respectively). BI 6727 inhibited proliferation of multiple cell lines derived from various cancer tissues, including carcinomas of the colon (HCT 116, EC50 = 23 nmol/L) and lung (NCI-H460, EC50 = 21 nmol/L), melanoma (BRO, EC50 = 11 nmol/L), and hematopoietic cancers (GRANTA-519, EC50 = 15 nmol/L; HL-60, EC50 = 32 nmol/L) with EC50 values of 11 to 37 nmol/L [1]. BI 6727 showed nanomolar activity on NB TICs, with an EC50 of 21 nmol/L, and an excellent selectivity profile, with an EC50 of 2.8 μmol/L on SKPs [2]. Volasertib inhibited proliferation in all 40 cell lines tested, with a mean half-maximal growth inhibitory concentration of 313 nmol/l (range: 4-5000 nmol/l) [3].

体内活性

BI 6727 has physicochemical and pharmacokinetic properties that allow in vivo testing of i.v. as well as oral formulations, adding flexibility to dosing schedules. Finally, BI 6727 shows marked antitumor activity in multiple cancer models, including a model of taxane-resistant colorectal cancer [1]. Volasertib was highly active against RMS-1 alveolar rhabdomyosarcoma xenografts, resulting in 100% tumor regression. Activity was associated with complete and prolonged G2/M arrest and subsequent apoptotic cell death. Volasertib showed synergistic activity with vincristine but antagonistic effects with etoposide [3].

动物实验

Female BomTac:NMRI-Foxn1nu mice were grafted s.c. with 2 × 10^6 HCT 116 human colon carcinoma cells (ATCC CCL-247), 1 × 10^6 NCI-H460 non–small cell lung cancer cells (ATCC HTB-177), or CXB1 human colon carcinoma tumor pieces derived from patient material by serial transplantation in nude mice. When tumors had reached a volume of ~50 to 100 mm^3, animals were randomized into treatment and control groups of 10 mice each. BI 6727 was formulated in hydrochloric acid (0.1 N), diluted with 0.9% NaCl, and injected i.v. into the tail vein at the indicated dose and schedule. For oral treatment, BI 6727 was resuspended in 0.5% Natrosol 250 hydroxyethyl-cellulose and given intragastrally via gavage needle. An administration volume of 10 mL per kilogram of body weight was used for both administration routes. Tumor volumes were determined thrice a week using a caliper. The results were converted to tumor volume (mm^3) by the formula length × width2 × π/6. The weight of the mice was determined as an indicator of tolerability on the same days. Median tumor volumes on the last day of the experiment were used to calculate treated versus control values (= tumor volume treated mice × 100/tumor volume control mice) [1].

细胞实验

Cell proliferation assays were done by incubating cells in the presence of various concentrations of BI 6727 for 72 h and cell growth was assessed by measuring Alamar blue dye conversion in a fluorescence spectrophotometer. Effective concentrations at which cellular growth was inhibited by 50% (EC50) were extrapolated from the dose-response curve fit [1].

描述

Volasertib (BI-6727) is a potent inhibitor of PLK1 (IC50: 0.87 nM), inducing mitotic arrest and apoptosis. It also inhibits PLK2/PLK3 (IC50s: 5/56 nM).

储存

Powder: -20°C for 3 years | In solvent: -80°C for 1 year