For Research Use Only

Bemcentinib

www.ptgcn.com

Catalog Number: CM06603

产品信息

Catalog Number:
CM06603

CAS号:
1037624-75-1

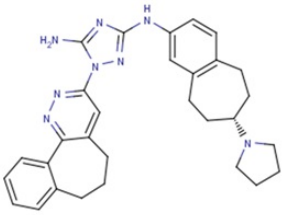
分子式:
$C_{30}H_{34}N_8$

主要靶点:
TAM Receptor

主要通路:
蛋白酪氨酸激酶

分子量:
506.64

溶解度:
DMSO:5.07 mg/mL (10 mM);Ethanol:< 1 mg/mL (insoluble or slightly soluble);H2O:< 1 mg/mL (insoluble or slightly soluble)



靶点活性

Axl:14 nM (cell free)

体外活性

Bemcentinib （R428） activity was limited to the tyrosine kinase subfamily. Of the 133 kinases, Axl was most potently inhibited by R428. With the exception of Tie-2, Ftl-1, Flt-3, Ret, and Abl, kinase inhibition by R428 was at least 10 times lower than observed for Axl. R428 dose-dependently suppressed invasion of both human MDA-MB-231 and murine 4T1 breast cancer cell lines [1]. Addition of R428 (50 nM-1 μM) resulted in a dose-dependent inhibition of differentiation of 3T3-F442A preadipocytes into mature adipocytes. Oil Red O staining ranged between 84 and 35% of that of DMSO control at R428 concentrations between 50 nM and 1 μM. Inhibition of Axl signaling by R428 in differentiating preadipocytes was confirmed by the Axl cell-based assay, yielding lower values (A450) for phospho-Akt activity upon treatment with 1 μM R428 compared with medium control or DMSO control [2]. The Axl inhibitor R428 showed a mean IC50 dose of ~ 2.0 μM for the primary CLL B cells after 24 hours of treatment and normal B-, T- and natural killer (NK) cells showed no significant amount of cell death at this dose of R428 (2.5 μM) under similar experimental conditions [3].

体内活性

R428 treatment reduced lung metastasis. R428 (7 mg/kg twice daily) significantly suppressed both total metastatic burden and the number of larger metastases. R428 suppressed both tumor angiogenesis and vascular endothelial growth factor (VEGF)–induced corneal neovascularization in vivo [1]. At day 35, the last day of HFD feeding, the body weight in both groups treated with R428 (75 mg/kg/day or 25 mg/kg twice daily, p.o.) was significantly lower than in the corresponding vehicle-treated groups. Compared with the start of the experiment, body weights at the end were significantly increased in both vehicle-treated groups, but not in R428-treated groups [2].

动物实验

Female BALB/c mice were inoculated in the mammary fat pad with 0.5 × 10^6 4T1 cells. Forty-eight hours after inoculation, mice were randomized into treatment groups (n = 10). Oral dosing with R428 (7–75 mg/kg twice daily) or vehicle continued until days 19 to 21. Cisplatin (1.2 or 4 mg/kg) was administered i.v. once weekly. Body weight and tumor size were measured thrice per week. Lungs were exposed postmortem. Total number and size of surface lung macrometastases were measured (small, <2 mm; medium, ≥2 mm and <3 mm; large, ≥3 mm). Half of each primary tumor was snap frozen in liquid nitrogen. The other half, and the livers were fixed in paraformaldehyde/lysine/periodate solution, paraffin embedded and sectioned (5 μm thick). Two H&E-stained liver sections per animal were examined microscopically for micrometastases in three view fields. Synergism was determined using Clark's synergy calculation [1].

细胞实验

MDA-MB-231 or 4T1 cells (1 × 10^5) were allowed to migrate through Matrigel toward 20% FCS in an 8- μm pore 24-well Transwell plate at 37°C for 16 to 24 h. Noninvaded cells and Matrigel were removed by swabbing. Invaded cells were fixed in 4% formaldehyde, stained with 1% crystal violet, and quantified as for Axl cell-based assay. Cells were preincubated with R428 for 3 h. R428 was added to both upper and lower Transwell chambers [1].

储存

store at low temperature | Powder: -20°C for 3 years | In solvent: -80°C for 1 year | Shipping with blue ice.