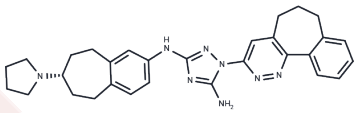
Data Sheet (Cat.No.T6269)

TargetMol

Bemcentinib

Chemical Properties



CAS No. : 1037624-75-1

Formula: C30H34N8

Molecular Weight: 506.64

Storage: Store at low temperature
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Bemcentinib (R428) is a selective inhibitor of Axl (IC50: 14 nM) and has been investigated for the treatment of NSCLC.
Targets(IC50)	TAM Receptor
In vitro	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 ~ 2.0μM 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 (2.5μM) under similar experimental conditions [3].
In vivo	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].
Kinase Assay	A five-point R428 dose titration was performed in radiometric in vitro kinase assays on 133 kinases at the Km(ATP) for each kinase. Axl, Mer, and Tyro3 assays were also performed using a fluorescence polarization protocol. HER2 activity was determined by Z'-LYTE assay [1].
Cell Research	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

Cell Research	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].
Animal Research	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].

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: < 1 mg/mL (insoluble or slightly soluble), DMSO: 23.4 mg/mL (46.19 mM),Sonication and heating are recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween-80+45% Saline: 1 mg/mL (1.97 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.9738 mL	9.8689 mL	19.7379 mL
5 mM	0.3948 mL	1.9738 mL	3.9476 mL
10 mM	0.1974 mL	0.9869 mL	1.9738 mL
50 mM	0.0395 mL	0.1974 mL	0.3948 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Holland SJ, et al. R428, a selective small molecule inhibitor of Axl kinase, blocks tumor spread and prolongs survival in models of metastatic breast cancer. Cancer Res. 2010 Feb 15;70(4):1544-54.
Huang M, Liu M, Huang D, et al. Tumor perivascular cell-derived extracellular vesicles promote angiogenesis via the Gas6/Axl pathway. Cancer Letters. 2021
Yuan Y, Guo Y, Guo Z W, et al.Marsdenia tenacissima extract induces endoplasmic reticulum stress-associated immunogenic cell death in non-small cell lung cancer cells through targeting AXL.Journal of Ethnopharmacology. 2023: 116620.
Lijnen HR, et al. Growth arrest-specific protein 6 receptor antagonism impairs adipocyte differentiation and adipose tissue development in mice. J Pharmacol Exp Ther. 2011 May;337(2):457-64.
Ghosh AK, et al. The novel receptor tyrosine kinase Axl is constitutively active in B-cell chronic lymphocytic leukemia and acts as a docking site of nonreceptor kinases: implications for therapy. Blood. 2011 Feb 10;117(6): 1928-37.