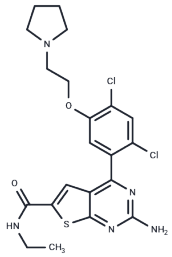
Data Sheet (Cat.No.T2114)

TargetMol

VER-82576

Chemical Properties



CAS No. : 847559-80-2

Formula: C21H23Cl2N5O2S

Molecular Weight: 480.41

Storage: 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	VER-82576 (NVP-BEP800), a synthetic HSP90β inhibitor (IC50: 58 nM), exhibits >70-fold selectivity against Hsp90 family members Trap-1 and Grp94.
Targets(IC50)	HSP
In vitro	In the A375 malignant melanoma transplantation tumor model, NVP-BEP800 (15 or 30 mg/kg/day, p.o.) treatment for 15 days dose-dependently decreased the levels of B-Raf and Akt phosphorylation and showed anticancer activity, with T/C values of 53% and 6% with NVP-BEP800 (15 and 30 mg/kg/day) treatment and almost total tumor inhibition with 30 mg/kg/day. 30 mg/kg inhibited almost all tumors. In BT-474 breast cancer transplantation tumors, NVP-BEP800 treatment increased the dissociation of Hsp90-p23 complex and decreased the levels of stable ErbB2, p-Akt and p-S6 in a dose-dependent manner, and NVP-BEP800 (30 mg/kg/day) treatment resulted in 38% tumor regression. Treatment with 15 mg/kg/day resulted in a T/C of 36%.
In vivo	NVP-BEP800 effectively inhibited the proliferation of various tumor cell lines including A375 cells (GI50: 38 nM) and PC3 cells (GI50: 1.05 μM). In A2058 and A549 cells, NVP-BEP800 (5-fold of GI50) increased the G2-M phase percentage. In BT-474 cells, NVP-BEP800 induced Akt and ErbB2 dephosphorylation, ErbB2 degradation, and Hsp70 induction in a concentration-dependent manner (IC50: 218/39.5/137/207 nM).At a concentration of 10 μM of Hsp70, the effects of NVP-BEP800 on the closely related GHKL ATPase, topoisomerase II, and structurally unrelated ATPases were observed. II and structurally unrelated ATPases were not significantly inhibited.
Kinase Assay	Competitive binding fluorescent polarization assay: Recombinant Hsp90β, TAMRA-radicicol, or various concentrations of NVP-BEP800 is added in assay buffer (50 mM TRIS pH 7.4, 5 mM MgCl2, 150 mM KCl, and 0.1% CHAPS), mixed, and incubated at room temperature for 30 to 45 minutes prior to reading. The 2D-FIDA-based HTS assay based on confocal technologies monitors the decreased fluorescence polarization on displacement of the high affinity ligand TAMRA-radicicol from Hsp90β by NVP-BEP800. The concentration of NVP-BEP800 which inhibits Hsp90β by 50% is determined from the competition curve.
Cell Research	Cells are exposed to NVP-BEP800 for 24 hours. Cell proliferation is determined using either sulforhodamine B for adherent cells or MTS assay for suspension cells or those showing low adherence. Cell death is determined using a ToxiLight nondestructive cytotoxicity bioassay kit. Cell cycle progression is determined by RNase A/propidium

Cell Research	iodide staining following fixation in 70% ethanol. Caspase-3/7 activity is determined using a homogeneous caspase activity kit.(Only for Reference)

Solubility Information

Solubility	DMSO: 1 mg/mL (2.08 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.0816 mL	10.4078 mL	20.8156 mL
5 mM	0.4163 mL	2.0816 mL	4.1631 mL
10 mM	0.2082 mL	1.0408 mL	2.0816 mL
50 mM	0.0416 mL	0.2082 mL	0.4163 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

Massey AJ, et al. Mol Cancer Ther, 2010, 9(4), 906-919.