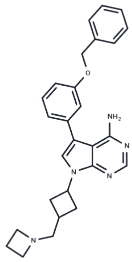
Data Sheet (Cat.No.T6080)

TargetMol

NVP-AEW541

Chemical Properties

CAS No. :	475489-16-8
Formula:	C27H29N5O
Molecular Weight:	439.55
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	NVP-AEW541 (AEW541), a potent inhibitor of IGF-1R(IC50=150 nM) and InsR(IC50=140 nM), exhibits excellent efficiency and specificity for IGF-1R in a cell-based assay.
Targets(IC50)	FLT,Autophagy,IGF-1R,Tyrosine Kinases
In vitro	NVP-AEW541 also inhibits InsR, Tek, Flt1 and Flt3 with IC50 of 140 nM, 530 nM, 600 nM and 420 nM in purified kinases/recombinant kinase domains assay. NVP-AEW541 is more selective and shows 27-fold more potent than InsR at the cellular level. NVP-AEW541 suppresses the IGF-I-mediated survival, soft agar and proliferation of MCF-7 cells with IC50 of 0.162 μM, 0.105 μM and 1.64 μM, respectively. NVP-AEW541 also reduces the level of phospho-IGF-1R and phospho-PKB in NWT-21 cells. [1] NVP-AEW541 shows growth inhibitory effect on TC-71 musculoskeletal sarcoma cells in low-serum medium as well as in 10% FBS-containing medium. NVP-AEW541 inhibits cell cycle progression and induces specific G1 arrest in sarcoma cell lines (TC-71, SK-N-MC, SaoS-2, RD/18 and RH4). [2] NVP-AEW541 could inhibit the growth of human neuroblastoma cells with IC50 of 0.4-6.8 μM. An increase in the hypodiploid fraction and the depletion of the S and G2-M compartments could be detected in these cell lines. NVP-AEW541-driven inhibition of IGF-1R causes a reduction of phosphorylation of Akt, but not of Erk1 and Erk2 in neuroblastoma cells. [3] NVP-AEW541 inhibits glioma cell growth and disrupts the autocrine loop initiated by HIF1α stabilization. [4] A recent study shows that NVP-AEW541 suppresses the proliferation and viability of PC3, DU145, and 22Rv1 prostate cancer cells, without necessarity of associated cell death. NVP-AEW541 decreases phospho-Akt levels in 22Rv1 and DU415 cells but not PC3 cells, without affecting total Akt levels, which shows that PTEN status could determine the effectiveness of NVP-AEW541 with essential Akt. NVP-AEW541-induced radiosensization is dependent on Akt activation status. NVP-AEW541 could increase the H2AX phosphorylation (a measure of DSBs) in PC3, DU145, and 22Rv1 cells. [5]
In vivo	NVP-AEW541 (50 mg/kg, p.o.) results in abrogation of basal and IGF-I-induced receptor, and PKB and MAPK phosphorylation, with T/C value of 14% in the NWT-21 tumor xenograft. [1] NVP-AEW541 (50 mg/kg) causes tumor shrinkage in both HTLA-230 and SK-N-BE2c xenografts, without signs of systemic toxicity. NVP-AEW541 could inhibit tumor invasion both in Matrigel-coated chambers and in HTLA-230 xenografts. [3]
Kinase Assay	In vitro kinase assays: NVP-AEW541 is dissolved in DMSO (10 mM) and stored at -20 °C. Dilutions are freshly made in DMSO/water 1:1. The final concentration of DMSO in the

Kinase Assay	enzyme assays is <0.5 %. The protein kinase assays are carried out in 96-well plates at RT and terminated by the addition of 20 μL of 125 mM EDTA. Subsequently, 30 μL (c-Abl, c-Src, IGF-1R) of the reaction mixture are transferred onto Immobilon-PVDF presoaked for 5 min with methanol, rinsed with water, then soaked for 5 min with 0.5 % H3PO4 and mounted on vacuum manifold. After spotting all samples, vacuum is connected and each well rinsed with 200 μL 0.5 % H3PO4. Membranes are removed and washed 4× on a shaker with 1.0 % H3PO4, once with ethanol. After drying, mounting in Packard TopCount 96-well frame, and adding of 10 μL/well of Microscint, membranes are counted. IC50 values are calculated by linear regression analysis of the percentage inhibition of NVP-AEW541 in duplicate, at four concentrations (usually 0.01, 0.1, 1, and 10 μM). One unit of protein kinase activity is defined as 1 nmol of 33P transferred from [γ33P]ATP to the substrate protein per minute per mg of protein at 37 °C.
Cell Research	Between 3 × 103 and 6 × 103 cells/well are seeded in 96-well plates with a total media volume of 100 μL/well. Increasing concentrations of NVP-AEW541 is added 24 hours thereafter in quadruplicate. 72 hours later, cells are fixed by addition of 25 μL/well Glutaraldehyde (20%) and incubation for 10 min at RT. Cells are then washed 2× with 200 μL/well Water and 100 μL Methylene Blue (0.05%) is added. After incubation for 10 min at RT, cells are washed 3× with 200 μL/well Water. 200 μL/well HCl (3%) is added, and following incubation for 30 min at RT on a plate shaker, absorbance is measured at 650 nm.(Only for Reference)

Solubility Information

Solubility	DMSO: 51 mg/mL (116.03 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (4.55 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	2.2751 mL	11.3753 mL	22.7505 mL
5 mM	0.455 mL	2.2751 mL	4.5501 mL
10 mM	0.2275 mL	1.1375 mL	2.2751 mL
50 mM	0.0455 mL	0.2275 mL	0.455 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

García-Echeverría C, et al. Cancer Cell. 2004, 5(3), 231-239.
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Tanno B, et al. Clin Cancer Res. 2006, 12(22), 6772-6780.
Gariboldi MB, et al. Biochem Pharmacol, 2010, 80(4), 455-462.
Isebaert SF, et al. Int J Radiat Oncol Biol Phys, 2011, 81(1), 239-247.

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