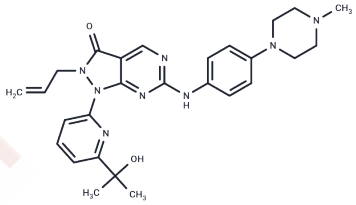
Data Sheet (Cat.No.T2077)

TargetMol

Adavosertib

Chemical Properties



CAS No. : 955365-80-7

Formula: C27H32N8O2

Molecular Weight: 500.6

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	Adavosertib (MK-1775) is a small molecule inhibitor of the checkpoint kinase WEE1 (IC50: 5.2 nM). It hinders the G2 DNA damage checkpoint.
Targets(IC50)	Wee1
In vitro	MK-1775 (Adavosertib) inhibits phosphorylation of CDC2 at Tyr15 (CDC2Y15), a direct substrate of Wee1 kinase in cells. MK-1775 abrogates G(2) DNA damage checkpoint, leading to apoptosis in combination with DNA-damaging chemotherapeutic agents such as gemcitabine, carboplatin, and cisplatin selectively in p53-deficient cells [1]. Nanomolar concentrations of MK-1775 radiosensitized p53-defective human lung, breast, and prostate cancer cells but not similar lines with wild-type p53. Consistent with its ability to radiosensitize, MK-1775 abrogated the radiation-induced G? block in p53-defective cells but not in p53 wild-type lines [2].
In vivo	Gemcitabine was administered to nude rats bearing WiDr (human colorectal) tumors at a dose of 50 mg/kg (i.v., bolus). Twenty-four hours later, MK-1775 was p.o. administered at a dose of 5, 10, or 20 mg/kg. Gemcitabine alone only moderately inhibited tumor growth. Cotreatment with MK-1775 significantly enhanced the antitumor effects in a dose-dependent manner and was well tolerated [1]. MK-1775 also significantly enhanced the antitumor efficacy of radiation in vivo as shown in tumor growth delay studies, again for p53-defective tumors [2].
Kinase Assay	Kinase reaction was conducted with 10 μmol/L ATP, 1.0 μCi of [γ-33P]ATP, and 2.5 μg of poly(Lys, Tyr) as a substrate at 30°C for 30 min. Radioactivity incorporated into the substrate was trapped on MultiScreen-PH plates and was counted on a liquid scintillation counter [1].
Cell Research	Tumor cells were cultured in 96-well plates and incubated with DNA-damaging agents for 24 h, then with MK-1775 and nocodazole for additional 8 h. For p-CDC2Y15 assay, cells were lysed and subjected in a colorimetric ELISA to determine the amounts of p-CDC2Y15 (1:100) and total CDC2 (1:200). For phospho-histone H3 (pHH3), cells were fixed with methanol, stained with anti-pHH3 specific antibody and bound antibody was stained with Alexa Fluor 488 goat anti-rabbit antibody. Images were acquired with an INCell Analyzer 1000 [1].
Animal Research	Subcutaneous xenograft tumors were formed by injection of the human cancer cell lines in the hind flank of immunodeficient nude rats (F344/NJcl-rnu). To facilitate tumor formation, cells were injected in medium containing Matrigel, a solubilized basement

Animal Research	membrane preparation extracted from the Engelbreth-Holm-Swarm mouse sarcoma. Gemcitabine, carboplatin, and cisplatin were dissolved or diluted in saline and were dosed i.v. MK-1775 was prepared in a vehicle of 0.5% methylcellulose solution and was dosed p.o. 24 h after dosing DNA-damaging agents. For efficacy studies, tumor volumes were measured with a caliper every 3 d and body weights were determined each weekday. Statistical analysis was done using repeated-measure ANOVA followed by Dunnett's test for relative tumor volume. T/C (%) was calculated as (ΔT/ΔC) × 100 if ΔT > 0 or (ΔT/TI) × 100 if ΔT < 0. ΔT was the change in mean tumor volume to the initial tumor volume for the treatment group, and ΔC was the change in mean tumor volume to the initial tumor volume for the vehicle control group. Ti was the initial tumor volume of the treatment group [1].

Solubility Information

Solubility	DMSO: 240 mg/mL (479.42 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: 7.4 mg/mL (14.78 mM),Solution. *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	1.9976 mL	9.988 mL	19.976 mL
5 mM	0.3995 mL	1.9976 mL	3.9952 mL
10 mM	0.1998 mL	0.9988 mL	1.9976 mL
50 mM	0.040 mL	0.1998 mL	0.3995 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

Hirai H, et al. Small-molecule inhibition of Wee1 kinase by MK-1775 selectively sensitizes p53-deficient tumor cells to DNA-damaging agents. Mol Cancer Ther. 2009 Nov;8(11):2992-3000.

Al-Jamaei A A H, de Visscher J G A M, Ramadugula V S, et al. WEE1 kinase inhibitor MK-1775 sensitizes oral tongue squamous cell carcinoma cells to radiation irrespective of TP53 status. Oral Diseases. 2022

Gao X, Ren X, Wang F, et al.Immunotherapy and drug sensitivity predictive roles of a novel prognostic model in hepatocellular carcinoma.Scientific Reports.2024, 14(1): 9509.

Bridges KA, et al. MK-1775, a novel Wee1 kinase inhibitor, radiosensitizes p53-defective human tumor cells. Clin Cancer Res. 2011 Sep 1;17(17):5638-48.

Esposito E, Marra G, Catalano R, et al.Therapeutic potential of targeting the FLNA-regulated Wee1 kinase in adrenocortical carcinomas.International Journal of Cancer.2024

Tel:781-999-4286 E_mail:info@targetmol.com Address:34 Washington Street,Wellesley Hills,MA 02481