Adavosertib

Cat. No.: HY-10993

CAS No.: 955365-80-7

Molecular Formula: $C_{27}H_{32}N_8O_2$

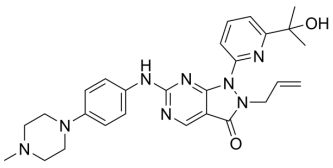
Molecular Weight: 501

Target: Wee1

Pathway: Cell Cycle/DNA Damage

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	1 year
	-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (249.50 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9960 mL	9.9800 mL	19.9601 mL
	5 mM	0.3992 mL	1.9960 mL	3.9920 mL
	10 mM	0.1996 mL	0.9980 mL	1.9960 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 0.5% Methylcellulose/saline water
   Solubility: 5 mg/mL (9.98 mM); Suspension solution; Need ultrasonic
2. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.87 mg/mL (5.73 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.15 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.15 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.15 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Adavosertib (AZD-1775; MK-1775) is a potent Wee1 inhibitor with an IC_{50} of 5.2 nM.

IC_{50} & Target

IC50: 5.2 nM (Wee1)

In Vitro	Adavosertib (MK-1775) enhances the cytotoxic effects of 5-FU in p53-deficient human colon cancer cells. Adavosertib (MK-1775) inhibits CDC2 Y15 phosphorylation in cells, abrogates DNA damaged checkpoints induced by 5-FU treatment, and causes premature entry of mitosis determined by induction of Histone H3 phosphorylation[1]. Adavosertib (MK-1775) abrogates the radiation-induced G2 block in p53-defective cells but not in p53 wild-type lines[2]. The combination of NSC 613327 with Adavosertib (MK-1775) produces robust anti-tumor activity and remarkably enhances tumor regression response (4.01 fold) compared to NSC 613327 treatment in p53-deficient tumors[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In vivo, Adavosertib (MK-1775) potentiates the anti-tumor efficacy of 5-FU at tolerable doses[1]. Adavosertib (MK-1775) (60 mg/kg twice daily, p.o.) enhances H1299 xenograft tumor response to fractionated radiotherapy [2]. Adavosertib (MK-1775) (30 mg/kg. p.o.) regresses tumor growth in PANC198, PANC215 and PANC185 as compared to GEM treated mice[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Total protein is extracted from the cell pellet using a lysis solution containing 50 mM HEPES (pH 7.9), 0.4 mol/L NaCl, and 1 mM EDTA and fortified with 10 µL/mL phosphatase inhibitor cocktail 1, 10 µL/mL phosphatase inhibitor cocktail 2, 10 µL/mL protease inhibitor, and 1% NP-40. Protein concentration of the lysates is determined by the Bio-Rad protein assay. Equal amounts of protein are separated by 12% SDS-PAGE and transferred to an Immobilon membrane. Nonspecific binding sites on the membrane are blocked in 5% nonfat dry milk in Tris (20 mM)-buffered saline (150 mM, pH 7.4) with 0.1% Tween (TBS-T). Protein signals are detected by incubating the membrane in primary antibody in 5% nonfat dry milk overnight at 4°C, followed by a 45-min incubation in the appropriate peroxidase-conjugated secondary antibody. The membrane is then developed by enhanced chemiluminescence with ECL plus Western Blotting Detection Reagents on a Typhoon 9400 scanner. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Tumor xenografts are produced in the leg by im inoculation of 1×10^6 Calu-6 cells in 10 µL. Irradiation and Adavosertib (MK-1775) treatment are started when tumors reach 8 mm diameter and continue for 5 days. Gamma-rays are delivered locally to the tumor-bearing legs of unanesthetized mice using a small-animal irradiator consisting of two parallel-opposed ^{137}Cs sources, at a dose rate of 5 Gy/min. Tumors are irradiated twice daily separated by 6 h. Adavosertib (MK-1775) is given by gavage in 0.1 mL volumes 1 h before and 2 h after the first daily radiation dose. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Cell. 2022 Dec 20;S1535-6108(22)00565-7.
- J Hematol Oncol. 2018 Aug 1;11(1):99.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Sci Adv. 2021 Apr 30;7(18):eabd4676.
- Blood Cancer J. 2021 Jul 31;11(7):137.

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REFERENCES

[1]. Hirai H, et al. MK-1775, a small molecule Wee1 inhibitor, enhances anti-tumor efficacy of various DNA-damaging agents, including 5-FU. Cancer Biol Ther. 2010 Apr;9(7):514-22.

[2]. 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. Epub 2011 Jul 28.

[3]. Rajeshkumar NV, et al. MK-1775, a potent Wee1 inhibitor, synergizes with NSC 613327 to achieve tumor regressions, selectively in p53-deficient pancreatic cancer xenografts.Clin Cancer Res. 2011 May 1;17(9):2799-806. Epub 2011 Mar 9.

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