Rucaparib acetate

Cat. No.: HY-10617D

CAS No.: 773059-23-7

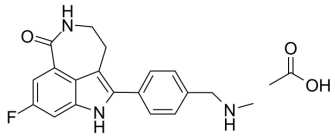
Molecular Formula: $C_{21}H_{22}FN_3O_3$

Molecular Weight: 383.42

Target: PARP

Pathway: Cell Cycle/DNA Damage; Epigenetics

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Rucaparib (AG014699) acetate is an orally active, potent inhibitor of PARP proteins (PARP-1, PARP-2 and PARP-3) with a K_i of 1.4 nM for PARP1. Rucaparib acetate is a modest hexose-6-phosphate dehydrogenase (H6PD) inhibitor. Rucaparib acetate has the potential for castration-resistant prostate cancer (CRPC) research[1][2][3][4].		
IC_{50} & Target	PARP-1 1.4 nM (Ki)	PARP-2	PARP-3
In Vitro	Rucaparib (AG014699) acetate is a possible N-demethylation metabolite of AG14644[1]. Rucaparib (0.1, 1, 10, 100 μM; 24 hours) acetate is cytotoxic and has the LC_{50} being 5 μM in Capan-1 (BRCA2 mutant) cells and only 100 nM in MX-1 (BRCA1 mutant) cells[2]. The radio-sensitization by Rucaparib acetate is due to downstream inhibition of activation of NF-κB, and is independent of SSB repair inhibition. Rucaparib acetate can target NF-κB activated by DNA damage and overcome toxicity observed with classical NF-κB inhibitors without compromising other vital inflammatory functions[5]. Rucaparib acetate inhibits PARP-1 activity by 97.1% at a concentration of 1 μM in permeabilised D283Med cells[6]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.		
In Vivo	Rucaparib (AG014699) acetate and AG14584 significantly increase Temozolomide toxicity. Rucaparib (1 mg/kg) acetate significantly increases Temozolomide-induced body weight loss. Rucaparib (0.1 mg/kg) acetate esults in a 50% increase in the temozolomide-induced tumor growth delay[1]. Rucaparib (10 mg/kg for i.p. or 50, 150 mg/kg for p.o.; daily for 5 days per week for 6 weeks) acetate significantly inhibits the growth of the tumor, and there is one complete tumor regression and two persistent partial regressions[2]. Rucaparib (150 mg/kg; p.o.; once per week for 6 weeks or three times per week for 6 weeks) acetate has greatest antitumor effect with three complete regressions[2]. Rucaparib acetate enhances the antitumor activity of temozolomide and indicates complete and sustained tumor regression in NB1691 and SHSY5Y xenografts[6]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.		

CUSTOMER VALIDATION

- Sci Transl Med. 2021 May 26;13(595):eabe8226.

- Clin Cancer Res. 2017 Feb 15;23(4):1001-1011.
- Theranostics. 2020 Jul 25;10(21):9477-9494.
- Talanta. 2018 Apr 1;180:127-132.
- Am J Cancer Res. 2020 Aug 1;10(8):2649-2676.

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REFERENCES

[1]. Thomas HD, et al. Preclinical selection of a novel poly(ADP-ribose) polymerase inhibitor for clinical trial. Mol Cancer Ther, 2007, 6(3), 945-956.

[2]. J Murray, et al. Tumour cell retention of rucaparib, sustained PARP inhibition and efficacy of weekly as well as daily schedules. Br J Cancer. 2014 Apr 15;110(8):1977-84.

[3]. Matt Shirley, et al. Rucaparib: A Review in Ovarian Cancer. Target Oncol. 2019 Apr;14(2):237-246.

[4]. Jianneng Li, et al. Hexose-6-phosphate dehydrogenase blockade reverses prostate cancer drug resistance in xenograft models by glucocorticoid inactivation. Sci Transl Med. 2021 May 26;13(595):eabe8226.

[5]. Hunter JE, et al. NF-κB mediates radio-sensitization by the PARP-1 inhibitor, AG-014699. Oncogene, 2012, 31(2), 251-264.

[6]. Daniel RA, et al. Inhibition of poly(ADP-ribose) polymerase-1 enhances temozolomide and topotecan activity against childhood neuroblastoma. Clin Cancer Res, 2009, 15(4), 1241-1249.

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