Rucaparib

Cat. No.: HY-10617A

CAS No.: 283173-50-2

Molecular Formula: $C_{19}H_{18}FN_3O$

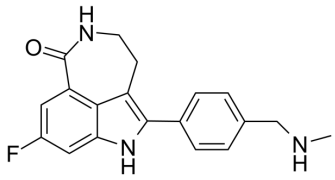
Molecular Weight: 323

Target: PARP

Pathway: Cell Cycle/DNA Damage; Epigenetics

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (77.40 mM; ultrasonic and adjust pH to 4 with HCl)

H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.0960 mL	15.4799 mL	30.9598 mL
5 mM	0.6192 mL	3.0960 mL	6.1920 mL
10 mM	0.3096 mL	1.5480 mL	3.0960 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (7.74 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.74 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.74 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Rucaparib (AG014699) 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 is a modest hexose-6-phosphate dehydrogenase (H6PD) inhibitor. Rucaparib has the potential for castration-resistant prostate cancer (CRPC) research[1][2][3][4].

IC_{50} & Target

PARP-1	PARP-2	PARP-3
1.4 nM (Ki)		

In Vitro	Rucaparib (AG014699) is a possible N-demethylation metabolite of AG14644[1]. Rucaparib (0.1, 1, 10, 100 μM; 24 hours) 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 is due to downstream inhibition of activation of NF-κB, and is independent of SSB repair inhibition. Rucaparib 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 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) and AG14584 significantly increase Temozolomide toxicity. Rucaparib (1 mg/kg) significantly increases Temozolomide-induced body weight loss. Rucaparib (0.1 mg/kg) results 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) 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) has greatest antitumor effect with three complete regressions[2]. Rucaparib 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.

Animal Model:	Female CD-1 nude mice aged 10-12 weeks with Capan-1 cells[2]
Dosage:	10 mg/kg for i.p. or 50, 150 mg/kg for p.o.
Administration:	IP or PO
Result:	Significantly inhibited the growth of the tumor.

CUSTOMER VALIDATION

- Nat Methods. 2023 Jul 20.
- Sci Transl Med. 2021 May 26;13(595):eabe8226.
- Sci Adv. 2022 Feb 18;8(7):eabl9794.
- Theranostics. 2020 Jul 25;10(21):9477-9494.
- Clin Cancer Res. 2017 Feb 15;23(4):1001-1011.

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

[3]. 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.

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

[5]. 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.

[6]. 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.

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