Rucaparib monocamsylate

Cat. No.: HY-102003

CAS No.: 1859053-21-6

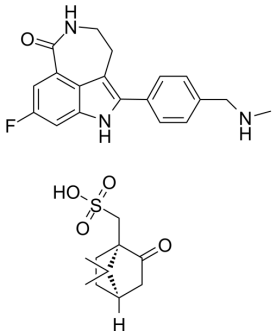
Molecular Formula: $C_{29}H_{34}FN_3O_5S$

Molecular Weight: 555.66

Target: PARP

Pathway: Cell Cycle/DNA Damage; Epigenetics

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (89.98 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7997 mL	8.9983 mL	17.9966 mL
	5 mM	0.3599 mL	1.7997 mL	3.5993 mL
	10 mM	0.1800 mL	0.8998 mL	1.7997 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: ≥ 2.08 mg/mL (3.74 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.74 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.74 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Rucaparib (AG014699) monocamsylate 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 monocamsylate is a modest hexose-6-phosphate dehydrogenase (H6PD) inhibitor. Rucaparib monocamsylate 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) monocamsylate is a possible N-demethylation metabolite of AG14644[1].
Rucaparib (0.1, 1, 10, 100 μM; 24 hours) monocamsylate 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 monocamsylate is due to downstream inhibition of activation of NF-κB, and is independent of SSB repair inhibition. Rucaparib monocamsylate 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 monocamsylate 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) monocamsylate and AG14584 significantly increase Temozolomide toxicity. Rucaparib (1 mg/kg) monocamsylate significantly increases Temozolomide-induced body weight loss. Rucaparib (0.1 mg/kg) monocamsylate 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) monocamsylate 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) monocamsylate has greatest antitumor effect with three complete regressions[2].
Rucaparib monocamsylate 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 or 50, 150 mg/kg
Administration:	10 mg/kg for i.p. or 50, 150 mg/kg for p.o.
Result:	Significantly inhibited the growth of the tumor.

CUSTOMER VALIDATION

- J Med Chem. 2023 Mar 6.
- J Mol Med (Berl). 2019 Aug;97(8):1183-1193.

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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.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA