Rucaparib phosphate

Cat. No.: HY-10617

CAS No.: 459868-92-9

Molecular Formula: $C_{19}H_{21}FN_3O_5P$

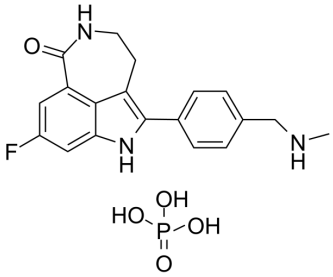
Molecular Weight: 421.36

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 : ≥ 33 mg/mL (78.32 mM)

H_2O : 5 mg/mL (11.87 mM; ultrasonic and warming and heat to 60°C)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3733 mL	11.8663 mL	23.7327 mL
5 mM	0.4747 mL	2.3733 mL	4.7465 mL
10 mM	0.2373 mL	1.1866 mL	2.3733 mL

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

In Vivo

1. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (5.93 mM); Clear solution
2. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.93 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.17 mg/mL (5.15 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.17 mg/mL (5.15 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.17 mg/mL (5.15 mM); Clear solution
6. Add each solvent one by one: 1% DMSO >> 99% saline
   Solubility: ≥ 0.5 mg/mL (1.19 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Rucaparib (AG014699) phosphate 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 phosphate is a modest hexose-6-phosphate dehydrogenase (H6PD) inhibitor. Rucaparib phosphate 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) phosphate is a possible N-demethylation metabolite of AG14644[1].
Rucaparib (0.1, 1, 10, 100 μM; 24 hours) phosphate 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 phosphate is due to downstream inhibition of activation of NF-κB, and is independent of SSB repair inhibition. Rucaparib phosphate 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 phosphate 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) phosphate and AG14584 significantly increase Temozolomide toxicity. Rucaparib (1 mg/kg) phosphate significantly increases Temozolomide-induced body weight loss. Rucaparib (0.1 mg/kg) phosphate 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) phosphate 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) phosphate has greatest antitumor effect with three complete regressions[2].
Rucaparib phosphate 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 athymic nude mice, implanted SW620 colorectal tumor cells (1×10^7 cells per animal) s.c.[1]
Dosage:	0.1 mg/kg in combination with Temozolomide (p.o., 200 mg/kg), 0.05, 0.15, and 0.5 mg/kg in combination with Temozolomide (p.o., 68 mg/kg) or 10 mg/kg
Administration:	IP, single dose for 0.1 mg/kg and 10 mg/kg, five daily doses for 0-0.5 mg/kg
Result:	Significantly increased Temozolomide toxicity, showed outstanding chemosensitization potency and caused enhancement of Temozolomide-induced tumor growth delay

Animal Model:	CD-1 nude mice bearing established Capan-1 xenografts[2]
Dosage:	10 mg/kg or 50, 100 and 150 mg/kg
Administration:	IP for 10 mg/kg; PO for 50, 100 and 150 mg/kg, single dose (Pharmacokinetics)
Result:	Parent drug was detectable in the plasma only at 30 min after 10 mg/kg i.p and up to 4 h for 50–150 mg/kg p.o.. Was still detectable in most mice receiving oral rucaparib at 3 days. Does not easily cross the plasma membrane.

Animal Model:	CD-1 nude mice bearing established Capan-1 xenografts[2]
Dosage:	10 mg/kg i.p. daily for 5 days per week for 6 weeks, 50 or 150 mg/kg p.o. daily × five weekly × six, 150 mg/kg p.o. once per week for 6 weeks or three times per week for 6

	weeks, or 150 mg/kg p.o. daily for five days every 3 weeks
Administration:	IP or PO
Result:	10 mg/kg i.p. significantly inhibited the growth of the tumor, daily oral administration at 150 mg/kg had an equivalent effect on tumor growth to 10 mg/kg i.p.. The schedule with the greatest antitumor effect was oral administration of 150 mg/kg on a once weekly schedule with three complete regressions.

Animal Model:	CD-1 nude mice, NB1691 and SHSY5Y xenografts[6]
Dosage:	1 mg/kg
Administration:	IP, daily for 5 d in combination with Temozolomide (orally daily ×5 at a dose of 68 mg/kg)
Result:	Enhanced the antitumor activity of Temozolomide and indicated complete and sustained tumor regression.

CUSTOMER VALIDATION

- Nat Methods. 2023 Jul 20.
- Sci Immunol. 2024 Mar 15;9(93):eadj7238.
- Sci Immunol. 2024 Mar 15.
- Sci Transl Med. 2021 May 26;13(595):eabe8226.
- Sci Adv. 2022 Feb 18;8(7):eabl9794.

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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]. 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.

[6]. 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.

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