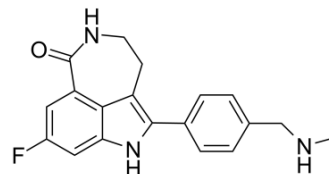


Rucaparib

Cat. No.:	HY-10617A		
CAS No.:	283173-50-2		
Molecular Formula:	C ₁₉ H ₁₈ FN ₃ O		
Molecular Weight:	323.36		
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 : 50 mg/mL (154.63 mM; Need ultrasonic)					
		Solvent Concentration	Mass	1 mg	5 mg	10 mg
	Preparing Stock Solutions	1 mM		3.0925 mL	15.4626 mL	30.9253 mL
		5 mM		0.6185 mL	3.0925 mL	6.1851 mL
		10 mM		0.3093 mL	1.5463 mL	3.0925 mL
Please refer to the solubility information to select the appropriate solvent.						
In Vivo	<ol style="list-style-type: none"> Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 2.08 mg/mL (6.43 mM); Clear solution Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.08 mg/mL (6.43 mM); Clear solution Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.08 mg/mL (6.43 mM); Clear solution 					

BIOLOGICAL ACTIVITY

Description	Rucaparib (AG014699) is an orally active and potent inhibitor of PARP with K _i of 1.4 nM for PARP1 in a cell-free assay. Rucaparib shows binding affinity to eight other PARP domains ^[1] .
IC₅₀ & Target	PARP-1 1.4 nM (K _i)
In Vitro	Rucaparib is the most potent PARP inhibitor in enzyme assays (K _i , 1.4 nM), and a possible N-demethylation metabolite of

AG14644^[1]. The radio-sensitization by Rucaparib is due to downstream inhibition of activation of NF- κ B, and is independent of SSB repair inhibition. Rucaparib could target NF- κ B activated by DNA damage and overcome toxicity observed with classical NF- κ B inhibitors without compromising other vital inflammatory functions^[2]. Rucaparib inhibits PARP-1 activity by 97.1% at a concentration of 1 μ M in permeabilised D283Med cells^[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Rucaparib and AG14584 significantly ($P < 0.05$) increases 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 is not toxic but significantly enhances temozolomide-induced TGD in the DNA repair protein-competent D384Med xenografts. Pharmacokinetics studies also show that Rucaparib is detected in the brain tissue, which indicates that Rucaparib has potential in intra-cranial malignancy therapy^[3]. Rucaparib significantly potentiates the cytotoxicity of topotecan and temozolomide in NB-1691, SH-SY-5Y, and SKNBE (2c) cells. Rucaparib enhances the antitumor activity of temozolomide and indicates complete and sustained tumor regression in NB1691 and SHSY5Y xenografts^[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay ^[1]

Inhibition of PARP activity in 5×10^3 D283Med cells is measured using various concentrations of Rucaparib (0-1 μ M), compared with DMSO-only. Maximally stimulated PARP activity is measured in samples of permeabilised cells by immunologica.

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Cell Assay ^[1]

Medulloblastoma cell lines are seeded in 96-well plates at a density of 1×10^3 , 3×10^3 and 3×10^3 , respectively. At 24 hours (D384Med) or 48 hours (D283Med and D425Med) after seeding, the cells are exposed to various concentrations of temozolomide in the presence or absence of 0.4 μ M Rucaparib. After 3 days (D425Med and D384Med) or 5 days (D283Med) of culture, cell viability is evaluated by a XTT cell proliferation kit assay. Cell growth is expressed as a percentage in relation to DMSO or 0.4 μ M Rucaparib-alone controls. The concentration of temozolomide, alone or in combination with Rucaparib that inhibited growth by 50% (GI_{50}) is calculated. The potentiation factor 50 (PF50) is defined as the ratio of the GI_{50} of temozolomide in the presence of Rucaparib to the GI_{50} of temozolomide alone.

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Animal Administration ^[1]

A single dose of temozolomide is administered p.o. as a suspension in saline at 200 mg/kg either alone or in combination with a single i.p. administration of PARP inhibitor administered at 0.1 [Rucaparib and MS-AG14644 (equivalent to 0.078 mg/kg free AG14644 only)], 1.0, and 10 mg/kg (for the mesylate salts equivalent to 0.79 and 7.9 mg/kg free AG14451 and AG14452 and 0.78 and 7.8 free AG14531 and AG14644). Control animals are treated with either normal saline p.o. and i.p. or normal saline p.o and PARP inhibitor 10 mg/kg i.p.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Clin Cancer Res. 2017 Feb 15;23(4):1001-1011.
- Theranostics. 2020 Jul 25;10(21):9477-9494.
- Sens Actuators B Chem. 2018 Nov 10; 273:1047-1053.
- Sens Actuators B Chem. 2018, 259: 565-572.
- Talanta. 2018 Apr 1;180:127-132.

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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- κ B mediates radio-sensitization by the PARP-1 inhibitor, AG-014699. *Oncogene*, 2012, 31(2), 251-264.
- [3]. Daniel RA, et al. Central nervous system penetration and enhancement of temozolomide activity in childhood medulloblastoma models by poly(ADP-ribose) polymerase inhibitor AG-014699. *Br J Cancer*, 2010, 103(10), 1588-1596.
- [4]. 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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Caution: Product has not been fully validated for medical applications. For research use only.