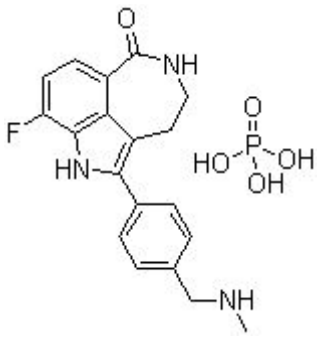
Product Introduction

Rucaparib (AG-014699,PF-01367338)

Rucaparib (AG-014699, PF-01367338) is an inhibitor of **PARP** with K_i of 1.4 nM for PARP1, also showing binding affinity to eight other PARP domains. Phase 1/2.

Technical Data:

Molecular Weight (MW):	421.36	
Formula:	$C_{19}H_{18}FN_3O.H_3PO_4$	
Solubility (25°C) *** <1 mg/ml means slightly soluble or insoluble:**	DMSO 84 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	459868-92-9	

Biological Activity

Rucaparib is a potent inhibitor of purified full-length human PARP-1 and shows higher inhibition of cellular PARP in LoVo and SW620 cells. Besides, Rucaparib binds detectably to eight other PARP domains, including PARP2, 3, 4, 10, 15, 16, TNKS1 and TNKS2. [1] [2] The radio-sensitization by Rucaparib is due to downstream inhibition of activation of NF-κB, and is independent of SSB repair inhibition. Rucaparib could target NF-κB activated by DNA damage and overcome toxicity observed with classical NF-κB inhibitors without compromising other vital inflammatory functions. [3] Rucaparib inhibits PARP-1 activity by 97.1%

at a concentration of 1 μM in permeabilised D283Med cells. [4]

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. [4]

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. [5]

The first PARP inhibitor used in clinical trials combined with temozolomide.

References

[1] Thomas HD, et al. Mol Cancer Ther, 2007, 6(3), 945-956.

[2] Kotz, J. SciBX 5(13); doi:10.1038/scibx.2012.323.

[3] Hunter JE, et al. Oncogene, 2012, 31(2), 251-264.

[4] Daniel RA, et al. Br J Cancer, 2010, 103(10), 1588-1596.

[5] Daniel RA, et al. Clin Cancer Res, 2009, 15(4), 1241-1249.

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