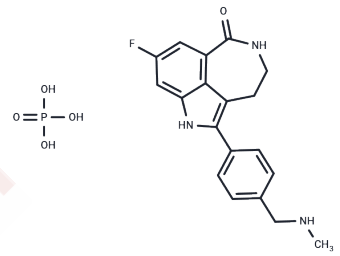
Data Sheet (Cat.No.T6127)

TargetMol

Rucaparib Phosphate

Chemical Properties



CAS No. : 459868-92-9

Formula: C19H18FN3O·H3PO4

Molecular Weight: 421.36

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Rucaparib Phosphate (PF-01367338 phosphate) is an inhibitor of PARP (Ki: 1.4 nM for PARP1) that is used in clinical therapy to sensitize cancer cells to chemotherapy.
Targets(IC50)	PARP
In vitro	AG14447 (the phosphate salt of Rucaparib) is the most potent PARP inhibitor in enzyme assays (Ki: 1.4 nmol/L) [1]. In permeabilised D283Med cells, Rucaparib (AG-014699), at concentrations of 0.1, 0.4 and 1?μ inhibited PARP-1 activity by 81.1, 96.8 and 97.1%, respectively [2]. AG014699 (≤10 μM) was cytotoxic to cells with mutated BRCA1/2 or XRCC3 and to UACC3199 cells with epigenetically silenced BRCA1 but not to cells without BRCA1/2 or XRCC3 mutations or that were heterozygous for BRCA2 mutation [3].
In vivo	When 10 mg/kg Rucaparib was administered in combination with temozolomide, body weight loss was observed at days 4 to 13 posttreatment with the nadir body weight ranging from 83% to 96% of the starting weight. At a dose of 1 mg/kg, Rucaparib also significantly increased temozolomide-induced body weight loss [1]. At 1mg/kg daily five times, AG-014699 alone did not cause any marked toxicity or affect tumour growth compared with vehicle-only controls. Co-administration of AG-014699 with temozolomide also resulted in complete tumour regressions in all mice, of which three out of five were sustained throughout the experiment. The MMR-defective D283Med xenografts grew very rapidly and showed very little response to temozolomide alone (TGD of only 2 days) with no regressions observed in any mice [2].
Kinase Assay	We measured inhibition of human full-length recombinant PARP-1 by [32P]NAD+ incorporation as described previously. The [32P]ADP-ribose incorporated into acid insoluble material was quantified using a PhosphorImager. Kis were calculated by nonlinear regression analysis [1].
Cell Research	Inhibition of PARP activity in 5000 exponentially growing D283Med cells was measured following treatment with a range of AG-014699 concentrations (0–1?μ), in comparison with DMSO-only controls. Maximally stimulated PARP activity was measured in replicate samples (n?3) of permeabilised cells by immunological detection of the amount of poly (ADP-ribose) (PAR) formed, using 10H anti-PAR antibody, during a 6-min incubation with NAD+ and oligonucleotide (substrate and activator) by reference to a PAR standard curve using a GCLP-validated assay described previously [2].

Animal Research	One or four daily doses of PARP inhibitor AG-014699 (1?mg/kg intraperitoneally (i.p.)) were given to CD-1 nude mice bearing established D283Med xenografts. At 0.5, 2, 6 and 24?h after the initial or fourth daily dose of AG-014699, three animals per time point were bled by cardiac puncture under general anaesthesia, and then killed. Plasma was separated from the blood samples using standard methods and stored at ?80°C. The brains and tumours were removed, snap frozen in liquid nitrogen and stored at ?80°C before analysis. Blood, tumour and brain tissue were removed from three untreated control animals and processed in the same way [2].

Solubility Information

Solubility	Ethanol: < 1 mg/mL (insoluble or slightly soluble), H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 78 mg/mL (185.11 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (4.75 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
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
50 mM	0.0475 mL	0.2373 mL	0.4747 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

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.
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.
Drew Y, et al. Therapeutic potential of poly(ADP-ribose) polymerase inhibitor AG014699 in human cancers with mutated or methylated BRCA1 or BRCA2. J Natl Cancer Inst. 2011 Feb 16;103(4):334-46.