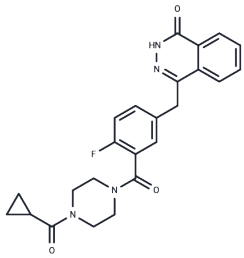
Data Sheet (Cat.No.T3015)

TargetMol

Olaparib

Chemical Properties



CAS No. : 763113-22-0

Formula: C24H23FN4O3

Molecular Weight: 434.46

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	Olaparib (KU0059436) is a small molecule inhibitor of PARP1/PARP2 (IC50=5/1 nM), with weak inhibitory activity against PARP tankyrase-1 (IC50=1.5 μM), and is selective and orally active. Olaparib exhibits autophagy and mitochondrial autophagy activation activity.
Targets(IC50)	Mitophagy,Autophagy,PARP
In vitro	**METHODS**: Human cervical cancer cells SiHa and ME180 were treated with Olaparib (5-10 μM) and cisplatin (1-30 μM) for 72 h. Cell growth inhibition was detected by MTT. **RESULTS**: Olaparib and cisplatin co-treatment showed significant cell growth inhibition compared to cells treated with a single drug. [1] **METHODS**: Human endometrial cancer cells HEC-6 and HEC-6-PTEN were treated with Olaparib (10 μM) for 72 h. The cell cycle was analyzed by Flow Cytometry. **RESULTS**: Olaparib induced a significant increase in the sub-G1 population of HEC-6 and HEC-6-PTEN cells. [2] **METHODS**: Chicken lymphoma cells DT40 were treated with Olaparib (0.01-10 μM) for 30 min, and the expression levels of target proteins were detected by Western Blot. **RESULTS**: Olaparib dose-dependently inhibited the expression level of PARylation and the activation of PARP. [3]
In vivo	**METHODS**: To detect anti-tumor activity in vivo, Olaparib (10 mg/kg) and TMZ (50 mg/kg) were orally administered to mice bearing human colorectal cancer tumor SW620 once daily for five days. **RESULTS**: Significant suppression of tumor volume was observed in the TMZ plus Olaparib combination treatment group compared to the TMZ group alone. [4] **METHODS**: To investigate the therapeutic effects of Olaparib on asthma, Olaparib (1-10 mg/kg) was administered intraperitoneally once daily for three days to an OVA-based asthmatic C57BL/6 mouse model. **RESULTS**: Olaparib significantly reduced airway eosinophilia, mucus production, and hyperresponsiveness. The protective effects of Olaparib were associated with inhibition of the Th2 cytokines eotaxin, IL-4, IL-5, IL-6, IL-13, and M-CSF, as well as ovalbumin-specific IgE, and an increase in the Th1 cytokine IFN-γ. Olaparib is a potential candidate for clinical trials in human asthma. [5]
Kinase Assay	This assay determined the ability of test compounds to inhibit PARP-1 enzyme activity. The method that was used was as reported. We measured PARP-2 activity inhibition by using a variation of the PARP-1 assay in which PARP-2 protein (recombinant) was bound

Kinase Assay	down by a PARP-2 specific antibody in a 96-well white-walled plate. PARP-2 activity was measured following 3H-NAD+ DNA additions. After washing, scintillant was added to measure 3 H-incorporated ribosylations. For tankyrase-1, an AlphaScreen assay was developed in which HIS-tagged recombinant TANK-1 protein was incubated with biotinylated NAD+ in a 384-well ProxiPlate assay. Alpha beads were added to bind the HIS and biotin tags to create a proximity signal, whereas the inhibition of TANK-1 activity was directly proportional to the loss of this signal. All experiments were repeated at least three times [1].
Cell Research	HSC-2, Ca9-22, and SAS oral carcinoma cells were seeded in 24-well plates at a density of 2 × 104 cells/well. After overnight incubation, the culture medium was replaced with fresh medium containing various concentrations of PARP inhibitor AZD228 or cisplatin. After 24 h of treatment, the number of viable cells was assessed using an MTT assay as reported previously. Briefly, one-tenth of the fluid volume of 5 mg/mL MTT in RPMI-1640 medium was added to each well, followed by incubation for 4 h at 37 °C. After incubation, the medium was carefully removed and an adequate volume of 0.1 N HCl in isopropanol was added to each well and the resultant formazan crystals was dissolved. Absorbance was determined at 570 nm by microplate reader in 96-well assay plates. All experiments were performed in triplicate [2].
Animal Research	Once the tumor diameter had reached 7 mm, the mice were randomly assigned to the following groups: (a) control (200 μL saline); (b) cisplatin (2 mg/kg per body weight, dissolved in 200 μL sterilized water); (c) AZD2281 (25 mg/kg per body weight, dissolved in 200 μL sterilized water); or (d) combination (both cisplatin and AZD2281). The chemicals were administered intraperitoneally every three days, five times. Although AZD2281 is administered orally in the clinic, intraperitoneal injection was recommended by the manufacturer because of easier manipulation and the ethical constraints associated with oral gavage administration to mice. Tumor size and body weight were measured at the time of administration. The tumor volume was calculated using following equation. Tumor volume = verticality × width × height × 0.5236. Three days after the last administration, all surviving mice were sacrificed [2].

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble) DMSO: 82.5 mg/mL (189.89 mM),Sonication is recommended. Ethanol: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 8 mg/mL (18.41 mM),Solution. *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	2.3017 mL	11.5085 mL	23.0171 mL
5 mM	0.4603 mL	2.3017 mL	4.6034 mL
10 mM	0.2302 mL	1.1509 mL	2.3017 mL
50 mM	0.046 mL	0.2302 mL	0.4603 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

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