Olaparib

Cat. No.: HY-10162

CAS No.: 763113-22-0

Molecular Formula: $C_{24}H_{23}FN_4O_3$

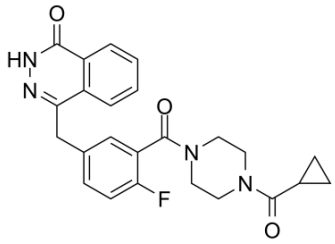
Molecular Weight: 434.46

Target: PARP; Autophagy; Mitophagy

Pathway: Cell Cycle/DNA Damage; Epigenetics; Autophagy

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 : ≥ 33.33 mg/mL (76.72 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
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

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.75 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.75 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.75 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Olaparib (AZD2281; KU0059436) is a potent and orally active PARP inhibitor with IC_{50}s of 5 and 1 nM for PARP1 and PARP2, respectively. Olaparib is an autophagy and mitophagy activator[1][2][3][4].

IC_{50} & Target

PARP-2 1 nM (IC_{50})	PARP-1 5 nM (IC_{50})	tankyrase-1 1.5 μM (IC_{50})	Autophagy
Mitophagy			

In Vitro	Olaparib (AZD2281) is a single digit nanomolar inhibitor of both PARP-1 and PARP-2 that shows standalone activity against BRCA1-deficient breast cancer cell lines. Olaparib is applied to SW620 cell lysates, and identified the IC_{50} for PARP-1 inhibition to be around 6 nM and the total ablation of PARP-1 activity to be at concentrations of 30−100 nM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Animals bearing SW620 xenografted tumors are treated with Olaparib (10 mg/kg, p.o.) in combination with NSC 362856 (TMZ) (50 mg/kg, p.o.) once daily for 5 consecutive days, after which the tumors are left to grow out[1]. Olaparib increases vascular perfusion in Calu-6 tumors established in a DWC model. Administration of olaparib(50 mg/kg, p.o.) as a single agent (top panel) or in combination with radiation (bottom panel) results in an increase in fluorescence intensity in the Calu-6 tumors[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	This assay determined the ability of Olaparib to inhibit PARP-1 enzyme activity. PARP-2 activity inhibition is measured by using a variation of the PARP-1 assay in which PARP-2 protein (recombinant) is bound down by a PARP-2 specific antibody in a 96-well white-walled plate. PARP-2 activity is measured following ^{3}H-NAD^+ DNA additions. After washing, scintillant is added to measure ^{3}H-incorporated ribosylations. For tankyrase-1, an AlphaScreen assay is developed in which HIS-tagged recombinant TANK-1 protein is incubated with biotinylated NAD^+ in a 384-well ProxiPlate assay. Alpha beads are added to bind the HIS and biotin tags to create a proximity signal, whereas the inhibition of TANK-1 activity is directly proportional to the loss of this signal. All experiments are repeated at least three times[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	The PF_{50} value is the potentiation factor, which is calculated as the ratio of the IC_{50} of the control growth with alkylating agent methylmethane sulfonate (MMS) divided by the IC_{50} of the MMS combined with the PARP inhibitor. HeLa B cells are used, and Olaparib is tested at a fixed 200 nM concentration for screening with MMS. For the testing of Olaparib on the SW620 colorectal cell line, the concentrations that are used are 1, 3, 10, 100 and 300 nM. Cell growth is assessed by the use of the sulforhodamine B (SRB) assay[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice[2] Mice bearing 220-250 mm^3 tumors are randomized into 4 treatment groups (n=5): A; vehicle control (10% DMSO in PBS/10% 2-hydroxy-propyl-β-cyclodextrin daily for 5 days by oral gavage), B; Olaparib (50 mg/kg daily for 5 days by oral gavage), C; 10 Gy fractionated radiotherapy (2 Gy daily for 5 days), D; Olaparib and 10 Gy (5×2 Gy) fractionated radiotherapy (with olaparib given 30 min prior to each daily 2 Gy dose of radiation). Tumor volume measurements are determined daily until they reached 1000 mm^3. The number of days for each individual tumor to quadruple in size from the start of the treatment (relative tumor volume×4; RTV4) is calculated for the individual tumors in each group. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nature. 2018 Nov;563(7729):131-136.
- Cell. 2019 Jan 24;176(3):505-519.e22.
- Cancer Discov. 2020 Jul 15;CD-20-0026.
- Cancer Discov. 2018 Mar;8(3):354-369.
- Cancer Discov. 2017 Sep;7(9):984-998.

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REFERENCES

[1]. Menear KA, et al. 4-[3-(4-cyclopropanecarbonylpiperazine-1-carbonyl)-4-fluorobenzyl]-2H-phthalazin-1-one: a novel bioavailable inhibitor of poly(ADP-ribose) polymerase-1. J Med Chem. 2008 Oct 23;51(20):6581-91

[2]. Senra JM, et al. Inhibition of PARP-1 by olaparib (AZD2281) increases the radiosensitivity of a lung tumor xenograft.Mol Cancer Ther. 2011 Oct;10(10):1949-58.

[3]. Yasukawa M, et al. Synergetic Effects of PARP Inhibitor AZD2281 in Oral Squamous Cell Carcinoma in Vitro and in Vivo. Int J Mol Sci. 2016 Feb 24;17(3):272.

[4]. Bian X, et al. PTEN deficiency sensitizes endometrioid endometrial cancer to compound PARP-PI3K inhibition but not PARP inhibition as monotherapy. Oncogene. 2018 Jan 18;37(3):341-351.

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