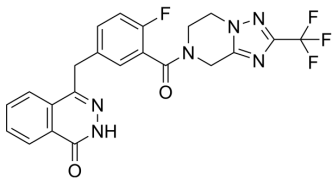
Fluzoparib

Cat. No.:	HY-114778
CAS No.:	1358715-18-0
Molecular Formula:	$C_{22}H_{16}F_4N_6O_2$
Molecular Weight:	472.4
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 : 33.33 mg/mL (70.55 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1169 mL	10.5843 mL	21.1685 mL
	5 mM	0.4234 mL	2.1169 mL	4.2337 mL
	10 mM	0.2117 mL	1.0584 mL	2.1169 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: ≥ 2.08 mg/mL (4.40 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.40 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Fluzoparib (SHR3162) is a potent and orally active PARP1 inhibitor (IC_{50}=1.46±0.72 nM, a cell‐free enzymatic assay) with superior antitumor activity. Fluzoparib selectively inhibits the proliferation of homologous recombination repair (HR)‐deficient cells, and sensitizes both HR‐deficient and HR‐proficient cells to cytotoxic agents. Fluzoparib exhibits good pharmacokinetic properties in vivo and can be used for BRCA1/2-mutant relapsed ovarian cancer research[1].

IC_{50} & Target

PARP-1
1.46±0.72 nM (IC_{50})

In Vitro

Fluzoparib (30?μM; 24 hour) increases the levels of γH2AX in a concentration‐dependent manner in both?BRCA2‐deficient V‐C8 cells and?BRCA1‐deficient MDA‐MB‐436 cells, but not in?BRCA‐proficient V‐C8#13‐5 cells[1].

	Fluzoparib (10?μM; 24 hour) increases levels of both pCDK1 and cyclin B, indicating activation of the G2/M checkpoint in MDA ⊠MB⊠436 cells[1]. Fluzoparib (10?μM; 72 hour) increases the processing of caspase⊠3, ⊠8, and ⊠9 concentration⊠dependently, it induces G2/M arrest and apoptosis in HR⊠deficient?MDA⊠MB⊠436 cells?cells[1]. Fluzoparib is preferentially efficacious against HR⊠deficient cells, such as BRCA1⊠deficient (UWB1.289), MDA⊠MB⊠436, BRCA2⊠deficient (V⊠C8), BRCA1⊠deficientBRCA2⊠mutated (MX⊠1) and BRCA1?hypermethylated (OVCAR⊠8) cells with IC_{50} values of 0.51?μM, 1.57?μM, 0.053?μM, 1.57?μM, and 1.43?μM, respectively. The IC_{50} values for HR⊠proficient cells (V⊠C8#13 ⊠5 and UWB1.289 BRCA1) are both >10?μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Fluzoparib (oral gavage; 0.3, 1, or 3?mg/kg; single dose) exhibits a good pharmacokinetic profile in Female Balb/cA nude mice (5⊠6 weeks old) mice bearing MDA⊠MB⊠436. After a single oral dose, fluzoparib is rapidly absorbed and rapidly cleared from blood at all dose levels; plasma concentrations of fluzoparib quickly reaches maximum within 2?hours. In contrast, concentrations of fluzoparib in tumor remains at high levels even at 24?hours after dosing (57.9?ng/g , 39.3 ng/g, and 85.6?ng/g for doses of 0.3, 1, and 3?mg/kg, respectively)[1]. Fluzoparib (oral gavage; 30 mg/kg; 21 days) apparently inhibits the growth of tumor with an inhibition rate of 59% (day 21) at 30?mg/kg, and it does not cause significant loss of body weight in Nude mice bearing?MDA⊠MB⊠436 ?(BRCA1⊠ deficient)?model[1]. Fluzoparib (3mg/kg) combines with Cisplatin, Paclitaxel, or Apatinib (oral gavage; BID; 21 days) causes growth inhibition with rates of 61.4%, 55.3%, and 72.8%, respectively. Fluzoparib, Cisplatin, and Apatinib combination or Fluzoparib, Paclitaxel, and Apatinib combination can cause growth inhibition with rates of 84.9% and 75.6% (day 21), respectively in vivo. The 2⊠drug combination of Fluzoparib with cisplatin and The 3⊠drug Fluzoparib, Cisplatin, and Apatinib combination lead to loss of body weight, whereas no apparent toxicity was observed in other combinations[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Molecules. 2022, 27(19), 6219.

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REFERENCES

[1]. Lei Wang, et al. Pharmacologic characterization of fluzoparib, a novel poly(ADP-ribose) polymerase inhibitor undergoing clinical trials. Cancer Sci. 2019 Mar;110(3):1064-1075.

[2]. Huiping Li, et al. Phase I dose-escalation and expansion study of PARP inhibitor, fluzoparib (SHR3162), in patients with advanced solid tumors. Chin J Cancer Res. 2020 Jun;32(3):370-382.

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