Talazoparib tosylate

Cat. No.: HY-108413

CAS No.: 1373431-65-2

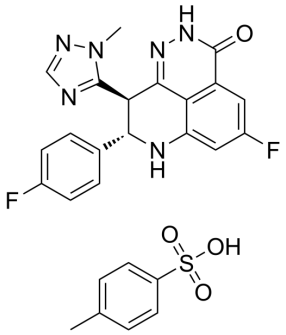
Molecular Formula: $C_{26}H_{22}F_2N_6O_4S$

Molecular Weight: 552.55

Target: PARP

Pathway: Cell Cycle/DNA Damage; Epigenetics

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 108 mg/mL (195.46 mM)
H_2O : < 0.1 mg/mL (insoluble)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8098 mL	9.0490 mL	18.0979 mL
	5 mM	0.3620 mL	1.8098 mL	3.6196 mL
	10 mM	0.1810 mL	0.9049 mL	1.8098 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 (4.52 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.52 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Talazoparib tosylate (BMN 673ts) is a novel, potent and orally available PARP1/2 inhibitor with an IC_{50} of 0.57 nM for PARP1.

IC_{50} & Target

IC50: 0.57 nM (PARP1)[1]

In Vitro

Talazoparib is a potent PARP1/2 inhibitor (PARP1 IC_{50}=0.57 nM), it has no effect on PARG activity at concentrations up to 1 μM. Talazoparib binds to PARP1 with a dissociation constant (K_D) of 0.29 nM. Talazoparib inhibits PARP1 and -2 to a similar extent, with K_is of 1.20 and 0.85 nM, respectively. Talazoparib selectively targets tumor cells with BRCA1, BRCA2, or PTEN gene defects with 20- to more than 200-fold greater potency than existing PARP1/2 inhibitors. Talazoparib targets tumor cells with homologous recombination gene defects. Tumor models that are either BRCA1-deficient (MX-1 and SUM149) or

	BRCA2-deficient (Capan-1) are profoundly sensitive to Talazoparib. Talazoparib induces nuclear γ-H2AX foci at concentrations as low as 100 pM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Talazoparib is readily orally bioavailable, with more than 40% absolute oral bioavailability in rats when dosed in carboxylmethyl cellulose. Oral administration of Talazoparib elicits remarkable antitumor activity; xenografted tumors that carry defects in DNA repair due to BRCA mutations or PTEN deficiency are profoundly sensitive to oral Talazoparib treatment at well-tolerated doses in mice. Synergistic or additive antitumor effects are also found when Talazoparib is combined with temozolomide, SN38, or platinum drugs[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	LoVo cells are treated with Talazoparib (10, 40 nM) and temozolomide (TMZ) either alone or in combination for 5 days. Surviving fraction is determined using CellTiter-Glo assay.[1] MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] In single-agent studies, olaparib (100 mg/kg), Talazoparib (0.33 or 0.1 mg/kg/d), or vehicle (10% DMAc, 6% Solutol, and 84% PBS) is administered by oral gavage (per os), once daily or Talazoparib (0.165 mg/kg) twice daily for 28 consecutive days. Mice are continuously monitored for 10 more days after last day of dosing[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Cell. 2020 Dec 14;38(6):844-856.e7.
- Nat Genet. 2022 Dec;54(12):1983-1993.
- Cancer Discov. 2022 May 12;candisc.1181.2021.
- Cancer Discov. 2017 Sep;7(9):984-998.
- Nat Cancer. 2022 Oct;3(10):1211-1227.

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REFERENCES

[1]. Shen Y, et al. BMN 673, a novel and highly potent PARP1/2 inhibitor for the treatment of human cancers with DNA repair deficiency. Clin Cancer Res. 2013 Sep 15;19(18):5003-15.

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