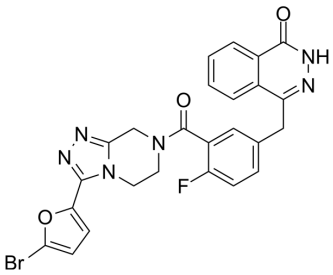
YCH1899

Cat. No.:	HY-155993
CAS No.:	3032451-66-1
Molecular Formula:	$C_{25}H_{18}BrFN_6O_3$
Molecular Weight:	549.35
Target:	PARP
Pathway:	Cell Cycle/DNA Damage; Epigenetics
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

YCH1899 is an orally active PARP inhibitor, with an IC_{50}< 0.001 nM for PARP1/2. YCH1899 exhibits distinct antiproliferation activity against Olaparib (HY-10162)-resistant and Talazoparib (HY-16106)-resistant Capan-1 cells (Capan-1/OP and Capan-1/TP cells) , with IC_{50} values of 0.89 and 1.13 nM, respectively. YCH1899 has acceptable pharmacokinetic properties in rats[1].

IC_{50} & Target

PARP-1 <0.001 nM (IC_{50})	PARP-2 <0.001 nM (IC_{50})	PARP3 1.1 nM (IC_{50})	PARP4 1.0 nM (IC_{50})
TNKS1 3.8 nM (EC50)	TNKS2 12.4 nM (IC_{50})	PARA6 9.5 nM (IC_{50})	PARP-7 7.3 nM (IC_{50})
ARTD10/PARP10 10.8 nM (IC_{50})	PARA11 2.166 μM (IC_{50})	human PARP12 14.1 nM (IC_{50})	PARP14 35.914 μM (IC_{50})
PARP15 51.623 nM (IC_{50})			

In Vitro

YCH1899 (7 days) shows obvious anti-proliferation activity on Capan-1, Capan-1/OP and Capan-1/TP cells, with IC_{50} of 0.10, 0.89 and 1.13 nM, respectively.[1].

YCH1899 (0.001-1 μM, 4 h) stabilizes PARP1-DNA complexes and suppresses PARP formation[1].

YCH1899 (3.5 h) inhibits the proliferation of BRCA mutant/wild-type cells (V-C8, V79, HCT-15, HCC1937) with IC_{50}s ranging from 1.19-44.24 nM[1].

YCH1899 (1 μM, 24 h) causes a large increase in the number of γH2AX foci in Capan-1、Capan-1/OP、Capan-1/TP cells[1].

YCH1899 (1 μM, 48 h) induces a dramatic decrease in HR (Homologous Recombination) repair activity in U2OS-DR-GFP cells [1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	HCC1937, HCT-15, MDA-MB-436, UWB1.289, UWB1.289+BRCA1, V–C8, V79 cells
Concentration:	0-1 μM approximately
Incubation Time:	24 h
Result:	Inhibited the proliferation of BRCA-Deficient/Wild-Type Cells and IC_{50}s value were 4.54,

	44.24, 0.52, 0.02, 0.34, 1.19, 29.32nM, respectively.

Immunofluorescence[1]

Cell Line:	Capan-1, Capan-1/OP cells, Capan-1/TP cells
Concentration:	0.01, 0.1, 1 μM
Incubation Time:	24 h
Result:	Increased γH2AX level in a dose-dependent manner.

Western Blot Analysis[1]

Cell Line:	Capan-1 and Capan-1/OP cells
Concentration:	1, 10, 100 nM
Incubation Time:	4 h
Result:	Improved stability of PARP1-DNA complexes and induced chromatin-bound PARP1 accumulation in the presence of MMS (methanesulfonate). Inhibited PARP formation in the presence of 0.1% H_2O_2.

In Vivo

YCH1899 (5 mg/kg, intravenous injection) has a moderate clearance rate in rats[1].
YCH1899 overcomes acquired Talazoparib resistance and has a significant regression of tumor volume in MDA-MB-436/OP (6.25, 12.5, and 25 mg/kg, orally, once a day for 27 days) and Capan-1/R-in vivo xenografts (12.5 and 25 mg/kg, orally, once a day for 21 days) [1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	MDA-MB-436/OP xenografts and Capan-1/R-in vivo xenografts mice[1]
Dosage:	12.5 and 25 mg/kg
Administration:	Oral administration
Result:	Inhibited MDA-MB-436/OP xenografts tumor growth with T/C of 36.74% and 15.29% at 12.5 and 25 mg/kg Inhibited Capan-1/R xenografts tumor growth with T/C of 48.92% and 13.87% at 12.5 and 25 mg/kg.

Animal Model:	rats[1]
Dosage:	5 mg/kg
Administration:	Intravenous injection
Result:	Had a moderate clearance rate (24.5 mL/min/kg) and half-life (3.25 h).

REFERENCES

[1]. Sun Y, et al. YCH1899, a Highly Effective Phthalazin-1(2H)-one Derivative That Overcomes Resistance to Prior PARP Inhibitors. J Med Chem. 2023 Aug 21.

Caution: Product has not been fully validated for medical applications. For research use only.

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