PARP1/BRD4-IN-2

Cat. No.: HY-150613

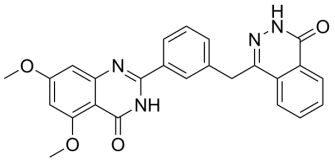
Molecular Formula: $C_{25}H_{20}N_4O_4$

Molecular Weight: 440.45

Target: Epigenetic Reader Domain; PARP; Apoptosis

Pathway: Epigenetics; Cell Cycle/DNA Damage; Apoptosis

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

PARP1/BRD4-IN-2 is a potent and selective PARP1 and BRD4 inhibitor with IC_{50} values of 197 nM and 238 nM, respectively. PARP1/BRD4-IN-2 inhibits DNA damage repair, arrests G0/G1 transition and induces apoptosis. PARP1/BRD4-IN-2 has anti-tumor activity in MDA-MB-468 xenograft mouse model. PARP1/BRD4-IN-2 can be used for researching triple-negative breast cancer (TNBC)[1].

IC_{50} & Target

BRD4	PARP1
238 nM (IC_{50})	197 nM (IC_{50})

In Vitro

PARP1/BRD4-IN-2 (compound BP44) can directly bind to BRD4 and PARP1 in MDA-MB-468 cells and improve their thermal stability[1].

PARP1/BRD4-IN-2 has antiproliferative activity against MDA-MB-231 and MDA-MB-468 with IC_{50}s of 6.61±0.58 μM and 3.01±0.83 μM, respectively[1].

PARP1/BRD4-IN-2 (5, 10, and 20 μM) down-regulates Bcl-2 and up-regulates Bax and cleaved caspase3 at 20 μM; inhibits colony formation and promotes cell apoptosis in MDA-MB-468 cells[1].

PARP1/BRD4-IN-2 (5, 10, and 20 μM) down-regulates DNA damage-related proteins CtIP, Mre11, Rad51, and p-RPA32 dose-dependently; causes DNA damage repair defects by down-regulating Rad51 and p-RPA32[1].

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

In Vivo

PARP1/BRD4-IN-2 (40 and 80 mg/kg; IG, for 16 days) significantly inhibits tumor growth in xenograft mice and without significant toxicities, and significantly down-regulates the expression of CtIP, c-Myc, PAR, and Rad51 in tumor tissues[1].

Pharmacokinetic Parameters of PARP1/BRD4-IN-2 in Sprague-Dawley rats[1].

	IV (1 mg/kg)	PO (10 mg/kg)
$T_{1/2}$ (h)	3.02 ± 0.57	3.33 ± 0.71
C_{max} (ng/mL)	258 ± 11	242 ± 6
AUC_{0-t} (ng/mL·h)	629 ± 49	1489 ± 130
$AUC_{0-\infty}$ (ng/mL·h)	642 ± 36	1530 ± 146

V_Z (L/kg)	21.1 ± 2.6	
CL (mL/min/kg)	33.7 ± 1.5	
F (%)		23.8 ± 1.3

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

Animal Model:	Female BALB/c nude mice (implanted subcutaneously with MDA-MB-468 tumor cells)[1]
Dosage:	40 and 80 mg/kg
Administration:	IG, for 16 days
Result:	Significantly inhibited tumor growth and exhibits no significant toxicities; and significantly down-regulated the expression of CtIP, c-Myc, PAR, and Rad51 in tumor tissues.

REFERENCES

[1]. Zhang J, et al. Discovery of 4-Hydroxyquinazoline Derivatives as Small Molecular BET/PARP1 Inhibitors That Induce Defective Homologous Recombination and Lead to Synthetic Lethality for Triple-Negative Breast Cancer Therapy. J Med Chem. 2022 May 12;65(9):6803-6825.

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