Polθ/PARP-IN-1

Cat. No.: HY-161302

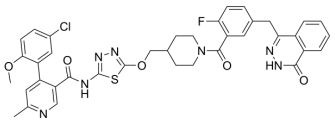
Molecular Formula: $C_{38}H_{33}ClFN_7O_5S$

Molecular Weight: 754.23

Target: Apoptosis; DNA/RNA Synthesis; PARP

Pathway: Apoptosis; Cell Cycle/DNA Damage; Epigenetics

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



BIOLOGICAL ACTIVITY

Description

Polθ/PARP-IN-1 (compound 25d) is a potent dual DNA polymerase theta (Polθ) and PARP inhibitor with IC_{50} values of 45.6, 5.4 nM, respectively. Polθ/PARP-IN-1 shows antiproliferative activity. Polθ/PARP-IN-1 induces apoptosis and cell cycle arrest at G2/M phase, causes DNA damage. Polθ/PARP-IN-1 shows anti-tumor activity[1].

In Vitro

Polθ/PARP-IN-1 (compound 25d) (0-80 μM; 3 days) shows antiproliferative activity with IC_{50}s of 20.9, 2.7, 8.9, 2.9, 18.9, >80 μM for HCC1937, MDA-MB-436, HCT116, SW48, SKOV-3, MCF-10A cells, respectively[1].

Polθ/PARP-IN-1 (compound 25d) (2 μM; 3 days) induces apoptosis and cell cycle arrest at G2/M phase, causes DNA damage[1].

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

Cell Proliferation Assay[1]

Cell Line:	HCC1937, MDA-MB-436, HCT116, SW48, SKOV-3, MCF-10A cells
Concentration:	0-80 μM
Incubation Time:	5 days
Result:	Showed antiproliferative activity with IC_{50}s of 20.9, 2.7, 8.9, 2.9, 18.9, >80 μM for HCC1937, MDA-MB-436, HCT116, SW48, SKOV-3, MCF-10A cells, respectively.

Apoptosis Analysis[1]

Cell Line:	MDA-MB-436 cells
Concentration:	2 μM
Incubation Time:	3 days
Result:	Induced apoptosis with a higher apoptosis rate (26.7%) and arrested cell cycle progression at the G2/M phase.

In Vivo

Polθ/PARP-IN-1 (20, 40 mg/kg; i.p.; daily for 21 consecutive days) inhibits tumor growth in MDA-MB-436 xenograft model[1].

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

Animal Model:	18-20 g, Six-week-old female BALB/C nude mice (MDA-MB-436 xenograft model)[1]
Dosage:	20, 40 mg/kg
Administration:	I.p.; daily for 21 consecutive days
Result:	Significantly inhibited the growth of MDA-MB-436 xenografts in a dose-dependent manner, exerted an optimal inhibitory potency with a tumor growth inhibition (TGI) rate of 54.4%, 74.7% at 20, 40 mg/kg, respectively.

REFERENCES

[1]. Ma L, et al. Discovery and Proof of Concept of Potent Dual Polθ/PARP Inhibitors for Efficient Treatment of Homologous Recombination-Deficient Tumors. J Med Chem. 2024 Feb 20.

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