Zn-DPA-maytansinoid conjugate 1

Cat. No.: HY-151559

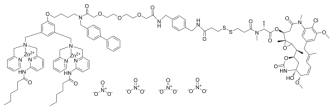
Molecular Formula: $C_{115}H_{145}ClN_{18}O_{31}S_2Zn_2$

Molecular Weight: 2505.83

Target: Checkpoint Kinase (Chk); STAT; CXCR; CCR

Pathway: Cell Cycle/DNA Damage; JAK/STAT Signaling; Stem Cell/Wnt; GPCR/G Protein; Immunology/Inflammation

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



BIOLOGICAL ACTIVITY

Description

Zn-DPA-maytansinoid conjugate 1 is a small molecule-based maytansinoid conjugate targeting immune checkpoint. Zn-DPA-maytansinoid conjugate 1 induces lasting regression of tumor growth and rejuvenates tumor microenvironment (TME) to an “inflamed hot tumor”[1].

In Vitro

Zn-DPA-maytansinoid conjugate 1 (compound 40a) (0-20 mM; 72 h) inhibits the growth of human pancreatic cancer MIA PaCa2 cells and triple-negative breast cancer HCC1806 cells and displays no effect on normal fibroblast (Detroit 551)[1].
Zn-DPA-maytansinoid conjugate 1 increases $CD8^+$ T cell infiltration significantly in the tumor mass that sensitized tumors from the intrinsic immune-suppressive TME[1].
Zn-DPA-maytansinoid conjugate 1 induces tumor inflammation-related mRNA expression such as STAT1, CXCL10, CCL5, and CCL2[1].
Zn-DPA-maytansinoid conjugate 1 leads to rejuvenation of TME with enhancement in T cell, macrophage, NK cell, chemokine, and cytokine functions[1].

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

Cell Viability Assay[1]

Cell Line:	Detroit 551, human pancreatic cancer MIA PaCa2 cells and triple-negative breast cancer HCC1806 cells
Concentration:	0-20 mM
Incubation Time:	72 hours
Result:	Inhibited cancer cells with IC_{50}s of 676 nM (MIA PaCa2) and 39 nM (HCC1806), respectively. Showed low cytotoxicity against Detroit 551 cells (IC_{50}>20 mM).

In Vivo

Zn-DPA-maytansinoid conjugate 1 (compound 40a) (1-2.5 mg/kg; i.v.; twice a week for 2 weeks) effectively shrank the growth of many solid tumors, exerts antipancreatic cancer, anti-triple-negative breast cancer and anti-sorafenib-resistant HCC tumor activities[1].

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

Animal Model:	Nude mice bearing MIA PaCa-2, HCC1806 or sorafenib-resistant HCC xenograft tumors, respectively[1]

Dosage:	1 mg/kg, 2 mg/kg, 2.5 mg/kg
Administration:	Intravenous injection; twice (day 1 and day 4) a week for 2 weeks; measured tumor twice weekly
Result:	Resulted a lasting regression of tumor growth.

Animal Model:	Male SD rats (8-week-old)[1]
Dosage:	1 mg/kg
Administration:	Intravenous injection; once a week for 4 weeks (days 1, 8, 15, and 22); measured body weights daily
Result:	Showed no effect on rats body weight.

Animal Model:	Pharmacokinetic study in ICR mice (6-week-old) bearing HCC1806 tumors[1]
Dosage:	5 mg/kg (in 10% DMA/20% Cremophor EL/70% (5% dextrose))
Administration:	Intravenous injection; single dose; collected blood samples at 0.003, 0.083, 0.25, 0.5, 1, 2, 4, 6, 8, and 24 h and collected tumor samples at 0.5, 2, 6, 24, 72, and 168 h
Result:	CL (mL/min/kg)=0.9; V_{ss} (L/kg)=0.12; AUC (0-24 h) (ng/mL·h)=105599.

REFERENCES

[1]. Lo CF, et al. Targeting the Phosphatidylserine-Immune Checkpoint with a Small-Molecule Maytansinoid Conjugate. J Med Chem. 2022 Oct 13;65(19):12802-12824.

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