Dxd

Cat. No.: HY-13631D

CAS No.: 1599440-33-1

Molecular Formula: $C_{26}H_{24}FN_3O_6$

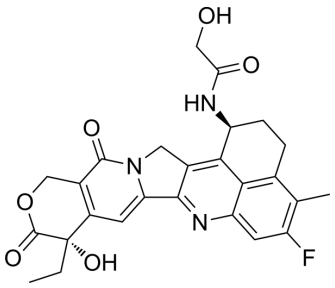
Molecular Weight: 493.48

Target: Topoisomerase; ADC Cytotoxin

Pathway: Cell Cycle/DNA Damage; Antibody-drug Conjugate/ADC Related

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 40 mg/mL (81.06 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0264 mL	10.1321 mL	20.2642 mL
	5 mM	0.4053 mL	2.0264 mL	4.0528 mL
	10 mM	0.2026 mL	1.0132 mL	2.0264 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

Dxd (Exatecan derivative for ADC) is a potent DNA topoisomerase I inhibitor, with an IC_{50} of 0.31 μM, used as a conjugated drug of HER2-targeting ADC (DS-8201a).

IC_{50} & Target

Topoisomerase I
0.31 μM (IC_{50})

Camptothecins

In Vitro

Dxd (Exatecan derivative for ADC) is a potent DNA topoisomerase I inhibitor, with an IC_{50} of 0.31 μM, used as a conjugated drug of HER2-targeting ADC (DS-8201a). Dxd is cytotoxic to human cancer cell lines of KPL-4, NCI-N87, SK-BR-3, and MDA-MB-468 with IC_{50}s of 1.43 nM-4.07 nM, but the control IgG-ADC (Dxd is the payload) shows no inhibition on the four cell lines (with HER2 expression). DS-8201a (Dxd is the payload) displays significant suppression on the HER2-positive KPL-4, NCI-N87, and SK-BR-3 cell lines, with IC_{50} values of 26.8, 25.4, and 6.7 ng/mL, respectively, but with no such inhibition on MDA-MB-468 (IC_{50}, >10,000 ng/mL)[1].

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

In Vivo

DS-8201a (Dxd is the payload, 10 mg/kg, i.v.) shows potent antitumor activity in HER2-positive models with KPL4, JIMT-1,

	and Capan-1 and in HER2 low-expressing ST565 and ST313 models with HER2 IHC 1+/FISH-negative expression[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Cells are seeded to a 96-well plate at 1,000 cells per well. After overnight incubation, Dxd is added. Cell viability is evaluated after 6 days using a CellTiter-Glo Luminescent Cell Viability Assay. For the detection of HER2 expression in each cell line, cells are incubated on ice for 30 minutes with FITC Mouse IgG1, κ Isotype Control, or anti-HER2/neu FITC. After washing, the labeled cells are analyzed by FACSCalibur. Relative mean fluorescence intensity (rMFI) is calculated[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] Briefly, each cell suspension or tumor fragment is inoculated subcutaneously into specific pathogen-free female nude mice. When the tumor has grown to an appropriate volume, the tumor-bearing mice are randomized into treatment and control groups based on the tumor volumes, and dosing is initiated on day 0. Each substance (DS-8201a, 1 or 10 mg/kg, i.v.; Dxd is the payload) is administered intravenously to the mice. Tumor growth inhibition (TGI, %) is calculated[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Rep. 2023 Nov 28;42(12):113503.
- Int J Mol Sci. 2023 Dec 18;24(24):17631.
- Int J Mol Sci. 2023 Nov 7;24(22):16056.
- Am J Cancer Res. 2023 Jan 30;13(1):161-175.
- Pharmaceuticals. 2021, 14(3), 247.

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REFERENCES

[1]. Ogitani Y, et al. DS-8201a, A Novel HER2-Targeting ADC with a Novel DNA Topoisomerase I Inhibitor, Demonstrates a Promising Antitumor Efficacy with Differentiation from T-DM1. Clin Cancer Res. 2016 Oct 15;22(20):5097-5108.

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