D-I03

Cat. No.: HY-124691

CAS No.: 688342-78-1

Molecular Formula: $C_{23}H_{36}N_6S$

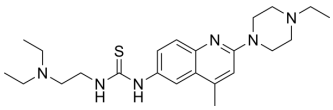
Molecular Weight: 429

Target: DNA/RNA Synthesis

Pathway: Cell Cycle/DNA Damage

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (116.55 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3310 mL	11.6550 mL	23.3100 mL
5 mM	0.4662 mL	2.3310 mL	4.6620 mL
10 mM	0.2331 mL	1.1655 mL	2.3310 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.83 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.83 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.83 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

D-I03 is a selective RAD52 inhibitor with a K_d of 25.8 μM. D-I03 specifically inhibits RAD52-dependent single-strand annealing (SSA) and D-loop formation with IC_{50}s of 5 μM and 8 μM, respectively. D-I03 suppresses growth of BRCA1- and BRCA2-deficient cells and inhibits formation of damage-induced RAD52 foci, but does not effect on RAD51 foci induced by Cisplatin [1][2].

IC_{50} & Target

Ki: 25.8 μM (RAD52)[1][2]

In Vitro

D-I03 (0-10 μM; on days 1 and 3; Capan-1 and UWB1.289 cells) treatment preferentially suppressed the growth of Capan-1 and UWB1.289 cells in a concentration-dependent manner[1].

?D-I03 inhibits RAD52 foci formation induced by cisplatin in BCR-ABL1-positive BRCA1-deficient 32Dcl3 murine hematopoietic cell line that expresses GFP-RAD52. In the presence of D-I03 (2.5 μM), the fraction of cells with RAD52 foci is decreased, from 38.7% to 171%; at the same time, the fraction of Cisplatin-treated cells without foci is increased from 48.4% to 71.9%.? D-I03 does not effect on RAD51 foci induced by Cisplatin. Also, D-I03 alone induce neither RAD51 foci nor RAD52 foci (in BRCA1-deficient cells) indicating low genotoxicity of D-I03[1].

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

Cell Proliferation Assay[1]

Cell Line:	Capan-1 ($BRCA2^-$) and UWB1.289 ($BRCA1^+$) cells
Concentration:	0 μM, 2.5 μM, 5 μM, or 10 μM
Incubation Time:	On days 1 and 3
Result:	Preferentially suppressed the growth of Capan-1 and UWB1.289 cells.

In Vivo

D-I03 (50 mg/kg/day; intraperitoneal injection; daily; for 7 days; nu/nu mice) treatment reduces BRCA1-deficient MDA-MB-436 tumor growth. Talazoparib puls D-I03 does not affect the growth of BRCA1-proficient tumors and does not exert any significant toxicity against normal tissues and organs[3].

?Pharmacokinetic and toxicity studies indicates that maximal tolerated dose of D-I03 is ≥50 mg/kg, and $t_{1/2}$ is 23.4 hours, resulting in >1 μM maximal concentration in peripheral blood[1].

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

Animal Model:	Nu/nu mice injected with BRCA1-deficient MDA-MB-436 cells[3]
Dosage:	50 mg/kg/day
Administration:	Intraperitoneal injection; daily; for 7 days
Result:	Reduced BRCA1-deficient MDA-MB-436 tumor growth.

CUSTOMER VALIDATION

- bioRxiv. 2023 Jun 29.

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REFERENCES

[1]. Huang F, et al. Targeting BRCA1- and BRCA2-deficient cells with RAD52 small molecule inhibitors. Nucleic Acids Res. 2016 May 19;44(9):4189-99.

[2]. Hengel SR, et al. Small-Molecule Inhibitors Targeting DNA Repair and DNA Repair Deficiency in Research and Cancer Therapy. Cell Chem Biol. 2017 Sep 21;24(9):1101-1119.

[3]. Sullivan-Reed K, et al. Simultaneous Targeting of PARP1 and RAD52 Triggers Dual Synthetic Lethality in BRCA-Deficient Tumor Cells. Cell Rep. 2018 Jun 12;23(11):3127-3136.

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

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