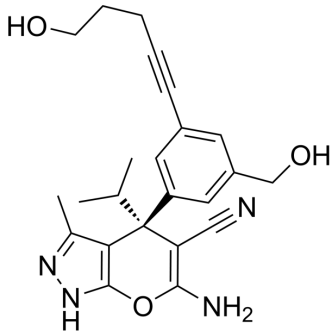
(+)SHIN2

Cat. No.:	HY-134978A
Molecular Formula:	$C_{23}H_{26}N_4O_3$
Molecular Weight:	406.48
Target:	SHMT
Pathway:	Metabolic Enzyme/Protease

Storage:

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



BIOLOGICAL ACTIVITY

Description

(+)SHIN2 is a serine hydroxymethyltransferase (SHMT) inhibitor, whose target can be traced with ^{13}C-serine. (+)SHIN2 increases survival in NOTCH1-driven mouse primary acute lymphoblastic leukemia (T-ALL) in vivo with a synergistic effect with Methotrexate (HY-14519)[1]. (+)SHIN2 is a click chemistry reagent, it contains an Alkyne group and can undergo copper-catalyzed azide-alkyne cycloaddition (CuAAc) with molecules containing Azide groups.

IC_{50} & Target

Serine hydroxymethyltransferase (SHMT)[1]

In Vitro

(+)SHIN2 (0-10 μM; 24 h) blocks proliferation of HCT116 Ras-driven colon cancer cells, in a stereoselective manner with an IC_{50} value of 300 nM[1].

(+)SHIN2 (0-100 μM; 48 h) achieves a nearly complete blockade of SHMT activity as evidenced by the decrease in M+1 and M+2 serine, M+2 glycine, and the incorporation of serine-derived glycine and 1C units into ATP, GTP, and dTTP (M+1-M+4 ATP and GTP and M+1 dTTP), and inhibits human T-ALL cell line Molt4 growth with a IC_{50} value of 89 nM[1].

(+)SHIN2 (2 μM; 24 h) arrests cell cycle at S phase[1].

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

In Vivo

(+)SHIN2 (200 mg/kg; i.p.; single dose) shows therapeutic activity in mouse primary T-ALL in vivo[1].

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Animal Model:	Male C57BL/6 mice (10-14 weeks old) with mouse primary T-ALL[1]
Dosage:	200 mg/kg
Administration:	Intraperitoneal injection; prepared with 30 mM U-^{13}C-Serine (0.1 μL/min/g; infusion by catheter implanted on the right jugular vein); tested at 8 hr after treatment
Result:	Decreased thymus weight and cellularity, which normalized after treatment discontinuation. Showed generally well tolerated activity with modest hematological toxicity.

REFERENCES

[1]. García-Cañaveras JC, et al. SHMT inhibition is effective and synergizes with methotrexate in T-cell acute lymphoblastic leukemia. Leukemia. 2021 Feb;35(2):377-388.

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