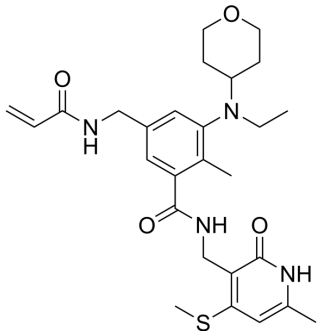
BBDDL2059

Cat. No.:	HY-154854
CAS No.:	2691174-27-1
Molecular Formula:	$C_{27}H_{36}N_4O_4S$
Molecular Weight:	512.66
Target:	Histone Methyltransferase
Pathway:	Epigenetics
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

BBDDL2059 is a selective covalent inhibitor of histone methyltransferase EZH2 with an IC_{50} of 1.5 nM for EZH2-Y641F. BBDDL2059 inhibits lymphoma cell growth at nanomolar concentrations and can be used for anticancer research[1].

IC_{50} & Target

EZH2 Y641F mutant type
1.5 nM (IC_{50})

In Vitro

BBDDL2059 (Compound 16) (0-65 nM; 6 days) inhibits cell growth in KARPAS-422 and Pfeiffer cells[1].
BBDDL2059 (0-1 μM; 48-96 hours) inhibits EZH2 enzymatic activity and maintains long-lasting inhibition of EZH2 after washing out[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	KARPAS-422 cells and Pfeiffer cells
Concentration:	0-65 nM
Incubation Time:	6 day
Result:	Inhibited cell growth with IC_{50}s of 64 nM and 22 nM for KARPAS-422 and Pfeiffer cells, respectively.

Western Blot Analysis[1]

Cell Line:	KARPAS-422 cells and Pfeiffer cells
Concentration:	0.05,0.1,0.5,1 μM
Incubation Time:	48-96 hours
Result:	Effective reduces H3K27me3 in Pfeiffer cells in a concentration- and time-dependent manner. Significantly inhibited the levels ofH3K27me3 in cells after treated within 96h after being washed out, and the levels of H3K27me3 were still lower than negative control after 120 h.

In Vivo

BBDDL2059 (Compound 16) (3 mg/kg for i.v., 10 mg/kg for p.o.) shows a $T_{1/2}$ of 0.28 h (i.v.), and oral bioavailability (F%) of

0.05% in rats[1].

Pharmacokinetic parameters for BBDDL2059 (Compound 16) in rats[1]

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Route	Dose (mg/kg)	$T_{1/2}$ (h)	C_{max} (ng/mL)	$AUC_{0\text{-last}}$ (h•ng/mL)	CL (mL•min^{-1}/kg^{-1})	V_{ss} (L/kg)	F (%)
iv	3	0.28	/	4886	11.1	161	/
po	10	/	29.5	8.16	/	/	0.05

Animal Model:	Rats(Pharmacokinetic assay)[1]
Dosage:	3 or 10 mg/kg
Administration:	Oral gavage (p.o.), Intravenous injection (i.v.)
Result:	Showed a $T_{1/2}$ of 0.28h (i.v.) and oral bioavailability (F%) of 0.05%.

REFERENCES

[1]. Zhang Y, et.al. Discovery of a New-Generation S-Adenosylmethionine-Noncompetitive Covalent Inhibitor Targeting the Lysine Methyltransferase Enhancer of Zeste Homologue 2. J Med Chem. 2023 Jun 8;66(11):7629-7644.

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