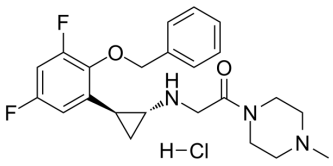
S2157

Cat. No.:	HY-136523
CAS No.:	2262488-39-9
Molecular Formula:	$C_{23}H_{28}ClF_2N_3O_2$
Molecular Weight:	451.94
Target:	Histone Demethylase; Apoptosis
Pathway:	Epigenetics; Apoptosis
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



Relative stereochemistry

SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (221.27 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2127 mL	11.0634 mL	22.1268 mL
	5 mM	0.4425 mL	2.2127 mL	4.4254 mL
	10 mM	0.2213 mL	1.1063 mL	2.2127 mL

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

BIOLOGICAL ACTIVITY

Description

S2157, a N-alkylated tranylcypromine (TCP) derivative, is a potent lysine-specific demethylase 1 (LSD1) inhibitor. S2157 increases H3K9 methylation and reciprocal H3K27 deacetylation at super-enhancer regions. S2157 induces apoptosis in TCP-resistant T-cell acute lymphoblastic leukemia (T-ALL) cells by repressing transcription of the NOTCH3 and TAL1 genes. S2157 efficiently pass through the blood-brain barrier and can almost completely eradicate CNS leukemia in mice transplanted with T-ALL cells[1].

IC_{50} & Target

LSD1[1]

In Vitro

S2157 is particularly effective for T-ALL cell lines with the IC_{50} values between 1.1 μM for human T-ALL cell lines CEM and 6.8 μM for MOLT4[1].

S2157 (4-20 μM; 72 hours) modestly inhibits mitogen-activated normal T-lymphocytes[1].

S2157 (4-8 μM; 24 hours) induces apoptosis and down-regulates the expression of NOTCH3 and TAL1 proteins in T-cell acute lymphoblastic leukemia (T-ALL) cells[1].

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

Cell Viability Assay[1]

Cell Line:	Normal T-lymphocytes
Concentration:	4, 8, 12, 16, 20 μM
Incubation Time:	For 72 hours
Result:	Modestly inhibited mitogen-activated normal T-lymphocytes.

Apoptosis Analysis[1]

Cell Line:	T-cell acute lymphoblastic leukemia (T-ALL) cells
Concentration:	4, 6, 8 μM
Incubation Time:	For 24 hours
Result:	Induced apoptosis, as evidenced by increased annexin-V reactivity on flow cytometry in T-ALL cells in a dose- and time-dependent manner without affecting cell cycle distribution.

Western Blot Analysis[1]

Cell Line:	T-ALL cells
Concentration:	4, 6, 8 μM
Incubation Time:	For 24 hours
Result:	Down-regulated the expression of NOTCH3 and TAL1 proteins in T-ALL cells.

In Vivo

S2157 (50 mg/kg; IP; 3 times a week; for 28 days) causes the size of subcutaneous tumors reduced to less than 20% of that in the untreated control[1].
S2157 (50 mg/kg; IP) has a $T_{1/2}$ of 0.88 hours, a C_{max} of 4.33 μM and an AUC of 5.75 μM•h[1].
S2157 (30 mg/kg or 50 mg/kg; twice a week for 3 weeks) almost completely suppressed the growth of MOLT4 cells in most but not all NOD/SCID mice with MOLT4 cells. S2157 eradicates CNS leukemia in murine xenotransplanted models[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Nonobese diabetic/severe combined immunodeficiency (NOD/SCID) mice with MOLT4 cells[1]
Dosage:	50 mg/kg
Administration:	IP; 3 times a week; for 28 days
Result:	The size of subcutaneous tumors reduced to less than 20% of that in the untreated control.

Animal Model:	8-week-old ICR mice[1]
Dosage:	50 mg/kg (Pharmacokinetic Analysis)
Administration:	IP
Result:	Had a $T_{1/2}$ of 0.88 hours, a C_{max} of 4.33 μM and an AUC of 5.75 μM•h.

REFERENCES

[1]. Shiori Saito, et al. Eradication of Central Nervous System Leukemia of T-Cell Origin With a Brain-Permeable LSD1 Inhibitor. Clin Cancer Res. 2019 Mar 1;25(5):1601-1611.

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