LC-1-40

Cat. No.: HY-158062

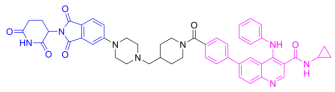
Molecular Formula: $C_{49}H_{48}N_8O_6$

Molecular Weight: 844.96

Target: DNA/RNA Synthesis; Apoptosis; PROTACs

Pathway: Cell Cycle/DNA Damage; Apoptosis; PROTAC

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

LC-1-40 is a PROTAC that selectively degrades NUDT1 (DC_{50}=0.97 nM). LC-1-40 selectively inhibits MYCN-induced tumor growth in mouse models. LC-1-40 also induces nucleotide damage and apoptosis in MYCN-associated tumors. LC-1-40 can be used in cancer research[1]. (Red: NUDT1 binder; Blue: CRBN ligand; Black: Linker).

IC_{50} & Target

DC_{50}: 0.97 nM (NUDT1)[1].

In Vitro

LC-1-40 (0.1, 1, 10, 50, 100 μM; 0.5, 1, 2, 4, 6 h) induces a dose- and time-dependent NUDT1 degradation in SHEP MYCN-ER cells[1].

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

Western Blot Analysis[1]

Cell Line:	SHEP MYCN-ER cells
Concentration:	0.1, 1, 10, 50, 100 μM
Incubation Time:	0.5, 1, 2, 4, 6 h
Result:	Induced NUDT1 degradation in a dose- and time-dependent manner.

In Vivo

LC-1-40 (30 mg/kg; i.p.; once daily for 15 days) selectively impeds the growth of MYCN-amplified T409 tumors in mice[1].

Pharmacokinetic Parameters of LC-1-40 in male C57BL/6 mice[1].

	IV (5 mg/kg)	IP (30 mg/kg)	PO (30 mg/kg)
$T_{1/2}$ (h)	6.34	42.7	7.13
T_{max} (h)	0.08	3.33	3.33
C_{max} (ng/mL)	4373	3080	1923
AUC_{Inf} (h*ng/mL)	32571	59799	25063

CL (mL/min/kg)	2.57	-	-
V_{ss} (mL/kg)	1.2	-	-
F (%)	-	32.7	14.2

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

Animal Model:	T409 xenografts model[1].
Dosage:	30 mg/kg
Administration:	Intraperitoneal injection; once daily for 15 days
Result:	Inhibited the growth of NUDT1-related tumor.

Animal Model:	Male C57BL/6 mice[1].
Dosage:	50 mg/kg, 30 mg/kg
Administration:	Intravenous/Intraperitoneal/Oral; single dose
Result:	Exhibited an oral bioavailability of 14.2%, nominating it as a promising lead for further optimization

REFERENCES

[1]. Ye M, et al. Therapeutic targeting nudix hydrolase 1 creates a MYC-driven metabolic vulnerability. Nat Commun. 2024 Mar 16;15(1):2377.

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