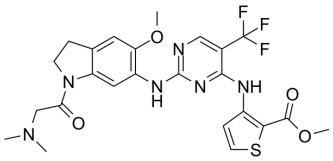
PLK1-IN-4

Cat. No.:	HY-146792
CAS No.:	2622273-55-4
Molecular Formula:	$C_{24}H_{25}F_3N_6O_4S$
Molecular Weight:	550.55
Target:	Polo-like Kinase (PLK)
Pathway:	Cell Cycle/DNA Damage
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	PLK1-IN-4 is a potent and selective PLK1 inhibitor with IC_{50} < 0.508 nM. PLK1-IN-4 has broad antiproliferative activity against a variety of cancer cell lines. PLK1-IN-4 induces mitotic arrest at the G2/M phase checkpoint, leading to cancer cell apoptosis . PLK1-IN-4 can be used for researching hepatocellular carcinoma[1].
IC_{50} & Target	IC_{50}:< 0.508 nM (PLK1) [1]

In Vitro

PLK1-IN-4 (compound 31) (0-5 μM; 48 hours) exhibits excellent antiproliferative activities against HCC cells[1].
PLK1-IN-4 (60 and 100 nM; 24 hours) induces abnormal spindle formation in HepG2 and HT-29 cells[1].
PLK1-IN-4 (10-300 nM; 0-48 hours) induces apoptosis in cancer cells through G2/M arrest[1].
PLK1-IN-4 (0-120 nM; 24 hours) increases phosphorylation of PLK1, histone H3 and NPM and decreases phosphorylation of Cdc2 in a dose-dependent manner[1].

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

Cell Proliferation Assay

Cell Line:	MDA-MB-231, HeLa, HCT 116, HT-29, HepG2, SMMC7721, A549 ,JeKo-1,K562, Karpas299, A375, DU-145 and L02[1]
Concentration:	0-5 μM
Incubation Time:	48 hours
Result:	Exhibited excellent antiproliferative activities against HCC cells, with IC_{50}s of 11.1 nM and 70.9 nM in HepG2 and SMMC7721 cells.

Cell Cycle Analysis

Cell Line:	HepG2[1]
Concentration:	10, 30, 60, 100 and 300 nM
Incubation Time:	0, 12, 24, 36 and 48 hours
Result:	Induced apoptosis in cancer cells through G2/M arrest.

Western Blot Analysis

Cell Line:	HepG2[1]
Concentration:	0, 10, 30, 60, 90 and 120 nM
Incubation Time:	24 hours
Result:	Increased phosphorylation of PLK1, histone H3 and NPM and decreased phosphorylation of Cdc2 in a dose-dependent manner.

In Vivo

PLK1-IN-4 exhibits low metabolic stability in species of human, mouse, dog and monkey, with CL^{hep} of 74.3, 330.9, 61.5 and 196.5 mL/min/kg, respectively[1].

PLK1-IN-4 (30 mg/kg; tail vein injection; once or twice daily, for 12 days) suppresses tumor growth in a dose dependent manner[1].

Pharmacokinetic Parameters of PLK1-IN-4 in male ICR mouse[1].

	IV (5 mg/kg)
C_0 (ng/mL)	1790
$T_{1/2}$ (h)	1.47
MRT_{0-inf} (h)	0.808
MRT_{0-t} (h)	0.704
AUC_{0-t} (ng·h/mL)	767
AUC_{0-inf} (ng·h/mL)	776
CL (mL/min/kg)	107
Vd_{SS} (L/kg)	107

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Animal Model:	Male nu/nu BALB/c mice (4-6 weeks; injected with HepG2 cells)[1]
Dosage:	30 mg/kg
Administration:	Tail vein injection; once or twice daily, for 12 days
Result:	Suppressed tumor growth in a dose dependent manner, and the tumor growth inhibition (TGI) values were 120.0% and 135.2% at doses of 30 mg/kg once daily and 30 mg/kg twice daily, respectively.

Animal Model:	ICR mouse[1]
Dosage:	5 mg/kg
Administration:	IV; single (Pharmacokinetics Analysis)

Result:	Exhibited a short half-life ($T_{1/2}$) of 1.47 h, moderate exposure with an area under the curve (AUC_{0-inf}) of 776 ng·h/mL and volume of distribution at steady state (Vd_{ss}) of 5.21 L/kg.

REFERENCES

[1]. Deng Z, et al. Discovery of methyl 3-((2-((1-(dimethylglycyl)-5-methoxyindolin-6-yl)amino)-5-(trifluoro-methyl) pyrimidin-4-yl)amino)thiophene-2-carboxylate as a potent and selective polo-like kinase 1 (PLK1) inhibitor for combating hepatocellular carcinoma. Eur J Med Chem. 2020;206:112697.

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