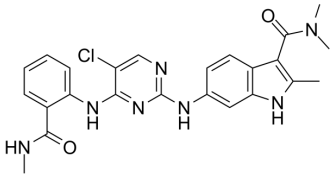
ALK-IN-22

Cat. No.:	HY-147833
CAS No.:	2468219-09-0
Molecular Formula:	$C_{24}H_{24}ClN_7O_2$
Molecular Weight:	477.95
Target:	ALK; Apoptosis
Pathway:	Protein Tyrosine Kinase/RTK; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

ALK-IN-22 (compound I-24) is a potent ALK inhibitor with IC_{50} values of 2.3, 3.7 and 2.9 nM for ALK, ALK^{L1196M} and ALK^{G1202R}, respectively. ALK-IN-22 down-regulated the phosphorylation of ALK and its downstream proteins. ALK-IN-22 induces apoptosis. ALK-IN-22 can be used for tumor research[1].

In Vitro

ALK-IN-22 (compound I-24) (72 hours) has anti-proliferative activities against ALK-positive karpas299, H2228 and H3122 cell lines with IC_{50} values of 11, 37 and 27 nM, respectively[1].

ALK-IN-22 (compound I-24) (0-100 nM; 24 hours; H2228 cells) has inhibitory effect on ALK and downstream signaling AKT and ERK[1].

ALK-IN-22 (compound I-24) (0-100 nM; 48 hours; H2228 cells) can induce apoptosis and achieve cell cycle arrest in G1 phase [1].

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

Western Blot Analysis[1]

Cell Line:	H2228 cells
Concentration:	0, 25, 50 and 100 nM
Incubation Time:	24 hours
Result:	Downregulated the phosphorylation level of ALK and blocked the expressions of ALK downstream key signaling AKT, ERK along with their activated forms in a dose-dependent fashion.

Apoptosis Analysis[1]

Cell Line:	H2228 cells
Concentration:	0, 25, 50 and 100 nM
Incubation Time:	48 hours
Result:	The apoptotic rates were 14.23%, 23.94% and 31.70% at concentrations of 25 nM, 50 nM and 100 nM, respectively.

Cell Cycle Analysis[1]

Cell Line:	H2228 cells
Concentration:	0, 25, 50 and 100 nM
Incubation Time:	48 hours
Result:	The percentage of cells in the G1 phase increased from 49.72% to 58.51% in a dose-dependent fashion.

In Vivo

ALK-IN-22 (compound I-24) (25-50 mg/kg; i.g.; Twice daily, for 14 days) has antitumor efficacy in vivo[1].
ALK-IN-22 (compound I-24) (10 mg/kg; p.o.) shows the C_{max} and $t_{1/2}$ values of 345.7 ng/mL and 4.1 hours, respectively[1].
ALK-IN-22 (compound I-24) (2 mg/kg; i.v.) shows the CL and $t_{1/2}$ values of 36.2 mL/min/kg and 2.5 hours, respectively[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female BALB / c nude mice[1]
Dosage:	25 and 50 mg/kg
Administration:	Intragastric; Twice daily, for 14 days.
Result:	The tumor growth inhibition (TGI) value of 50 mg/kg reached 93.5%.

Animal Model:	SD rats[1]
Dosage:	2 and 10 mg/kg (Pharmacokinetic Analysis)
Administration:	Oral administration and intravenous injection
Result:	

Parameter	F16	VP-16
Dose (i.v.) mg/kg	10	10
C_{max} (ng/mL)	26952	17712
T_{max} (min)	5	5
AUC_{plasma} (min*ng/mL)	2878363	409528
$T_{1/2}$ (min)	151	45
Vd (L/Kg)	0.2341	0.432
CL (L/min/kg)	0.001	0.007

REFERENCES

[1]. Thacker PS, et al. Synthesis and biological evaluation of some coumarin hybrids as selective carbonic anhydrase IX and XII inhibitors. Bioorg Chem. 2020

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