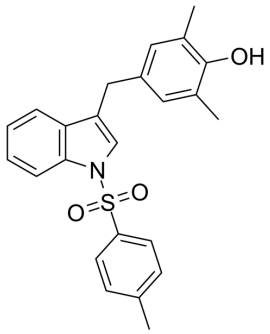
ALK-IN-26

Cat. No.:	HY-156432
CAS No.:	2447607-85-2
Molecular Formula:	$C_{24}H_{23}NO_3S$
Molecular Weight:	405.51
Target:	Anaplastic lymphoma kinase (ALK); mTOR; PARP; Caspase
Pathway:	Protein Tyrosine Kinase/RTK; PI3K/Akt/mTOR; Cell Cycle/DNA Damage; Epigenetics; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

ALK-IN-26 is an ALK inhibitor with IC_{50} value of 7.0 μM for ALK tyrosine kinase. ALK-IN-26 has good pharmacokinetic properties and blood-brain barrier (BBB) permeability. ALK-IN-26 can induce apoptosis, autophagy and necrosis. ALK-IN-26 can be used in glioblastoma studies[1].

In Vitro

ALK-IN-26 (0.5-2 μM, 24 h) can inhibit the activity of ALK in GL216 cells[1].
ALK-IN-26 (0.5-2 μM, 24 h) can reduce the expression of mTOR protein in GL216 cells [1].
[1].
ALK-IN-26 (0.5-2 μM, 24 h) significantly decreases p-ERK1/2 protein level and enhances p-JNK protein level in GL261 and U87MG cells, while has little effect on p-AKT and p-STAT3 protein levels[1].
ALK-IN-26 (0.5μM-2.0 μM, 24h) can induce autophagy in GL261 cells[1].
ALK-IN-26 (0.5 μM-0.5 μM, 24-72 h) increases the protein levels of cleaved-PARP (c-PARP) and cleaved-caspase-3 (c-caspase 3) in GL261 cells[1].
ALK-IN-26 (0.5 μM-2μM, 24-72 h) induces apoptosis in GL261 cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Apoptosis Analysis[1]

Cell Line:	GL261
Concentration:	0.5 μM, 1.0 μM, 2.0 μM
Incubation Time:	24 h, 48 h, 72 h
Result:	Induced apoptosis of glioblastoma in a concentration- and time-dependent manner, and caused the cells (24.5%) entered the S phase but barely proceeded to the G2/M phase when treated with 1 μM for 72 h.

Cell Viability Assay[1]

Cell Line:	GL216, U87MG, Hela
Concentration:	0.5 μM, 1.0 μM, 2.0 μM, 5 μM, 10 μM for GL216 and U87MG cells5 μM, 10 μM, 20 μM, 40 μM, 80 μM, 160 μM for Hela cells
Incubation Time:	24 h, 48h, 72h

Result:	Inhibited the activity of GL216 cells with the inhibition rate of cells at 80% when incubated with 2 μM for 72 h and inhibited U87MG cells viability with a dose- and time-dependent manner, while showed limited inhibition on Hela cells, even at 160 μM, the inhibition rate is less than 50%. Can inhibit the activity of ALK tyrosine kinase with a dose-dependent manner.

Cell Autophagy Assay[1]

Cell Line:	GL261
Concentration:	0.5 μM, 1.0 μM, 2.0 μM
Incubation Time:	24 h
Result:	Induced autophagy death in glioblastoma cells.

In Vivo

ALK-IN-26 (5 mg/kg, i.v., single dose) has pharmacokinetic properties in male C57BL6/J mice[1].
ALK-IN-26 is (20 mg/kg, i.p., single dose) able to penetrate the blood-brain barrier in male C57BL6/J mice[1].

Pharmacokinetic parameters of C57BL6/J in male rats (n = 3) [1]

Pharmacokinetic property	$T_{1/2}$(h)	T_{max}(h)	C_{max} (ng/mL)	$AUC_{(0-8)}$ (h*ng/mL)	$AUC_{(0-\infty)}$ (h*ng/mL)	$MRT_{(0-8)}$ (h)	$MRT_{(0-\infty)}$ (h)	V_{∞} (L/kg)	V_2 (L/kg)	bioavailablity F (%)
i.v.(5mg/kg)	1.13	0.08	1978.21	884.88	924.56	0.63	0.84	4.59	8.89	38.40
i.p.(5mg/kg)	3.55	0.58	117.57	339.79	420.50	2.25	4.60	/	/	/

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Animal Model:	Male C57BL/6J mice[1]
Dosage:	5 mg/kg
Administration:	Intravenous injection (i.v.), Single dose
Result:	Could be rapidly absorbed (Tmax = 0.58 h) with an acceptable half-life (T1/2 = 3.55 h) and bioavailability (F = 38.4%).

Animal Model:	Male C57BL/6J mice[1]
Dosage:	20mg/kg
Administration:	Intraperitoneal injection (i.p.), Single dose
Result:	Could enter the body at concentrations up to 2.7μmol/kg (after 2 h administration at 20 mg/kg) and penetrate the blood-brain barrier.

REFERENCES

[1]. Feng L, et al. Synthesis and Bioevaluation of 3-(Arylmethylene) indole Derivatives: Discovery of a Novel ALK Modulator with Antiglioblastoma Activities[J]. Journal of

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