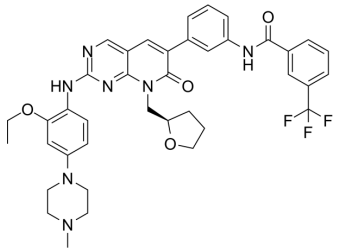
Ack1 inhibitor 1

Cat. No.:	HY-149989
CAS No.:	2924415-92-7
Molecular Formula:	$C_{39}H_{40}F_3N_7O_4$
Molecular Weight:	727.77
Target:	Akt; Ack1
Pathway:	PI3K/Akt/mTOR; Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Ack1 inhibitor 1 is a potent, selective, and orally active inhibitor of ACK1 kinase with an IC_{50} value of 2.1 nM. Ack1 inhibitor 1 inhibits the phosphorylation of ACK1 and activation of downstream AKT. Ack1 inhibitor 1 has anti-tumor activity[1].

In Vitro

Ack1 inhibitor 1 inhibits of cell growth with IC_{50}s of 3.71 μM and 4.18 μM in 67R and H1975 cells[1].
Ack1 inhibitor 1 (0 nM-5000 nM, 72 h) alone or in combination with ASK120067 enhances antitumor effects in 67R[1].
Ack1 inhibitor 1 (1 μM and 5 μM, 6 h) inhibits the phosphorylation of ACK1 and AKT in 67R cells in a dose-dependent manner [1].

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

Cell Viability Assay[1]

Cell Line:	67R cells (ASK120067-resistant cells obtained from parental H1975 cells by a dose escalation method).
Concentration:	0-5000 nM (combined with ASK120067)
Incubation Time:	72 h
Result:	Caused strong synergistic anti-growth effects on 67R cells with high synergy scores of 10.83, respectively

Western Blot Analysis[1]

Cell Line:	67R cells
Concentration:	1 μM and 5 μM
Incubation Time:	6 h (stimulated with or without EGF for 30 min)
Result:	Caused moderate down-regulation of p-ACK1 and p-AKT at 1 μM. Exhibited better potency against p-AKT, while it was unable to completely inhibit p-ACK1 at 5 μM.

In Vivo

Ack1 inhibitor 1 (Compound 10zi) (10 mg/kg; PO; single dose) improves AUC value of 1920.56 h•ng/mL, C_{max} of 119.52 μg/L, and an oral bioavailability of 19.80% in a single oral dose of 10 mg/kg in SD rats[1].
.Hyzetimibe Pharmacokinetic Analysis in SD Rats [1]

SD[1]

Route	Dose (mg/kg)	$AUC_{0-\infty}$ (ng•h/mL)	$t_{1/2}$ (h)	T_{max} (h)	C_{max} (μg/mL)	Cl (mL/h/kg)	F (%)
i.v.	2	1707.13	5.09	0.08	1429.26	19.85	/
p.o.	10	1920.56	7.71	6	119.52	/	19.8

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REFERENCES

[1]. Li Q, et al. Design, Synthesis, and Evaluation of (R)-8-((Tetrahydrofuran-2-yl)methyl)pyrido[2,3-d]pyrimidin-7-ones as Novel Selective ACK1 Inhibitors to Combat Acquired Resistance to the Third-Generation EGFR Inhibitor. J Med Chem. 2023 May 25;66(10):6905-6921.

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