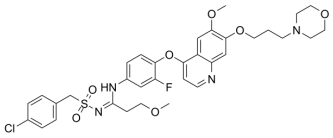
c-Met-IN-14

Cat. No.:	HY-150582
CAS No.:	2443380-34-3
Molecular Formula:	$C_{34}H_{38}ClFN_4O_7S$
Molecular Weight:	701.2
Target:	c-Met/HGFR; c-Kit; FLT3; Apoptosis
Pathway:	Protein Tyrosine Kinase/RTK; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

c-Met-IN-14 (compound 26af) is a selective inhibitor of c-Met kinase from N-sulfonylamidine-based derivatives, with an IC_{50} value of 2.89 nM. c-Met-IN-14 shows anticancer activity by blocking phosphorylation of c-Met, and arrests cell cycle at G2/M phase. c-Met-IN-14 induces apoptosis of A549 cells in a dose-dependent manner[1].

IC_{50} & Target

c-Met
2.89 nM (IC_{50})

In Vitro

c-Met-IN-14 (compound 26af) is a relatively selective inhibitor of c-Met kinase (IC_{50}=2.89 nM), because of high inhibitory effects against c-Kit (IC_{50}=4.26 nM) and Flt-3 (IC_{50}=7.28 nM)[1].
c-Met-IN-14 (0.28-0.72 μM; 24 h) exhibits the remarkable anti-proliferative activities against cancer cell lines (A549, HT-29, MKN-45 and MDA-MB-231), with IC_{50}s of 0.28-0.72 μM[1].
c-Met-IN-14 (0.25, 0.5, and 1.0 μM; 12 h) induces the late apoptotic and early apoptotic and (0.25, 0.5, and 1.0 μM; 24 h) shows anti-proliferative of A549 cells by arresting cell cycle at G2/M phase and apoptosis induction[1].
c-Met-IN-14 (1.35, or 6.12 μM, respectively; 24 h) has moderate selectivity towards cancer cells over normal cells, with the selectivity index of 4.2 and 19.1 to HUVEC (IC_{50}=1.35 μM) and FHC cells (IC_{50}=6.12 μM), respectively[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	A549
Concentration:	0, 2, 4, 8 μM
Incubation Time:	6 hours
Result:	Showed excellent inhibition against c-Met phosphorylation in a concentration-dependent manner.

In Vivo

c-Met-IN-14 (compound 26af) (p.o.; 8 mg/kg) exhibits safety profile and favorable pharmacokinetic properties in BALB/c mouse, with rapid absorption (T_{max}=2.5 h), high maximum concentration (C_{max}=1228.4 ng/mL), high plasma exposure ($AUC_{0-\infty}$=6.8 μg.h.mL^{-1}), accepted elimination half-life ($T_{1/2}$=3.5 h), and well clearance (1.18 L.h$_{-1}$.kg$_{-1}$), has a moderate oral bioavailability (74%) in mouse[1].
c-Met-IN-14 (i.p.; below 200 mg/kg) doesn't cause abnormalities, anaphylactic responses, allergic reactions on mice[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	8-week-old male BALB/c mice [1]
Dosage:	0 (vehicle), 100, 200, 300, or 400 mg/kg
Administration:	Intraperitoneal injection; treatment on day 0 and assessment every 3 days for 15 days
Result:	Showed no obvious toxicity in acute toxicity tests.

Animal Model:	Pharmacokinetic profiles of compound 26af in BALB/c mouse[1]
Dosage:	
Administration:	
Result:	

Route	Dose (mg/kg)	$T_{1/2}$ (h)	C_{max} ($ng.mL^{-1}$)	T_{max} (h)	$AUC_{0-\infty}$ ($\mu g.h.mL^{-1}$)	***CL*** ($L.h^{-1}.kg^{-1}$)	***CL*** (%)
i.v.	2	1.8	675.6	-	2.3	-	
p.o.	8	3.5	1228.4	2.5	6.8	1.18	74

REFERENCES

[1]. Nan X, et al. Design, synthesis and biological evaluation of novel N-sulfonylamidine-based derivatives as c-Met inhibitors via Cu-catalyzed three-component reaction. Eur J Med Chem. 2020 Aug 15. 200:112470.

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