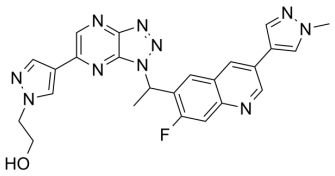
c-Met-IN-2

Cat. No.:	HY-101773
CAS No.:	1635406-73-3
Molecular Formula:	$C_{24}H_{21}FN_{10}O$
Molecular Weight:	484.49
Target:	c-Met/HGFR
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	c-Met-IN-2 is a potent, selective and orally available c-Met inhibitor, with an IC_{50} of 0.6 nM, with antitumor activity.
IC_{50} & Target	IC50: 0.6 nM (c-Met)[1]
In Vitro	c-Met-IN-2 (Compound 14) is a potent and selective c-Met inhibitor, with an IC_{50} of 0.6 nM. c-Met-IN-2 also shows weak activity on other kinases, with IC_{50}s of 1075 nM (Axl), 731 nM (RON), 18364 nM (VEGFR2), 5396 nM (c-Kit), 2357 nM (PDGFRa), 17056 nM (c-Src). MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	c-Met-IN-2 (0.1, 1, 10 mg/kg, p.o., once daily) significantly reduces the volume of tumor in mice bearing H1993 tumors, and has similar effect in SNU-5 xenograft model via oral administration at 0.3, 1 and 3 mg/kg[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	NCI-H1993 cell line and SNU-5 cell line are maintained in RPMI 1640 media and supplemented with 10% fetal bovine serum. NCI-H1993 cells are seeded at 5000 cells/well in 96-well plates and incubated overnight. On the next day, the cells are exposed to various concentrations of c-Met-IN-2 and further cultured for 72 h. After chromogenic reaction with CCK-8, the OD450 (with reference of OD650) is measured using a Flexstation 3 reader. IC_{50} values are calculated using the GraphPad Prism Software. Each experiment is carried out thrice, each time in duplicate. The SNU-5 cell line assay is operated in a similar procedure as NCI-H1993 assay[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] The SNU-5 at a density of 6×10^6 tumor cells in 200 μL or NCI-H1993 at a density of 7×10^6 tumor cells in 140 μL are injected s. c. into the right flank of nude mice. Tumor-bearing animals are sorted into groups with similar mean tumor volumes prior to treatment (usually 100-200 mm^3 for SNU-5 and 150-250 mm^3 for NCI-H1993). The mice are randomly assigned into control and treatment groups (n = 7 (NCI-H1993 model) or n = 6 (SNU-5 model) per group). Control groups are given vehicle alone, and treatment groups receive c-Met-IN-2 as indicated doses via oral administration once daily for 2 weeks in SNU-5 model and oral administration once daily for 3 weeks in NCI-H1993 model, respectively. The sizes of the tumors are measured twice per week using a caliper, and the tumor volume is calculated in cubic millimeter using the formula: V = (A ×

	B^2)/2, where A and B is the long and short diameters of the tumor, respectively. Body weights are monitored throughout the study as a gross measure of toxicity/morbidity. Tumor growth inhibition (TGI), expressed in percent (%), is calculated using the formula: 100% × (1-((treatedfinal day-treatedday 0)/(controlfinal day-controlday 0))). Percent tumor regression (PTR), expressed in percent (%), is calculated using the formula: 100% × (treatedday 0-treatedfinal day)/treatedday 0[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Zhao F, et al. Identification of 3-substituted-6-(1-(1H-[1,2,3]triazolo[4,5-b]pyrazin-1-yl)ethyl)quinoline derivatives as highly potent and selective mesenchymal-epithelial transition factor (c-Met) inhibitors via metabolite profiling-based structural optimization. Eur J Med Chem. 2017 Jul 7;134:147-158.

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