Product Data Sheet

Product Name: c-Met-IN-2
Cat. No.: GC33203

Chemical Properties

Cas. No.	1635406-73-3		
SMILES	OCCN1N=CC(C2=CN=C3C(N(C(C4=C(F)C=C(N=CC(C5=CN(C)N=C5)=C6)C6=C4)C)N=N3)=N2)=C1		
Formula	$C_{24}H_{21}FN_{10}O$	M.Wt	484.49
Solubility	Soluble in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	c-Met-IN-2		

Protocol

Cell experiment:

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. IC50 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].

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Animal experiment:

Mice[1]The SNU-5 at a density of 6 × 106 tumor cells in 200 µL or NCI-H1993 at a density of 7 × 106 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 mm3 for SNU-5 and 150-250 mm3 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 × B2)/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].

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.

Background

c-Met-IN-2 is a potent, selective and orally available c-Met inhibitor, with an IC50 of 0.6 nM, with antitumor

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activity.

c-Met-IN-2 (Compound 14) is a potent and selective c-Met inhibitor, with an IC50 of 0.6 nM. c-Met-IN-2 also shows weak activity on other kinases, with IC50s of 1075 nM (Axl), 731 nM (RON), 18364 nM (VEGFR2), 5396 nM (c-Kit), 2357 nM (PDGFRa), 17056 nM (c-Src).

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].

[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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