AXL-IN-13

Cat. No.: HY-151904

CAS No.: 2376928-82-2

Molecular Formula: $C_{34}H_{41}FN_6O_5$

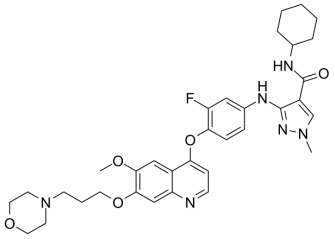
Molecular Weight: 632.72

Target: TAM Receptor; FLT3; PDGFR

Pathway: Protein Tyrosine Kinase/RTK

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (158.05 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.5805 mL	7.9024 mL	15.8048 mL
	5 mM	0.3161 mL	1.5805 mL	3.1610 mL
	10 mM	0.1580 mL	0.7902 mL	1.5805 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.5 mg/mL (3.95 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (3.95 mM); Clear solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (3.95 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

AXL-IN-13 is a potent and orally active AXL inhibitor (IC_{50}: 1.6 nM, K_d: 0.26 nM). AXL-IN-13 reverses TGF-β1-induced epithelial-mesenchymal transition (EMT), and inhibits cancer cell migration and invasion[1].

IC_{50} & Target

PDGFRβ
2.3 nM (Kd)

In Vitro

AXL-IN-13 (compound 6li) inhibits Ba/F_3-TEL-AXL cell proliferation with an IC_{50} of 4.7 nM (determined by ELISA)[1].

AXL-IN-13 also shopws binding affinities against CSF1R, FLT1/3/4, KLT, PDGFRB, TIE2[1].
AXL-IN-13 (0-500 nM, 6 h) inhibits the phosphorylation of AXL in MDA-MB-231 and 4T1 cells[1].
AXL-IN-13 (0-3 μM, 3 days) blocks EMT induced by TGF-β1 (10 ng/mL) in MDA-MB-231 cells[1].
AXL-IN-13 (0-3 μM, 24 h) suppresses MDA-MB-231 cell migration and invasion induced by TGF-β1 (10 ng/mL)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	MDA-MB-231 cells
Concentration:	0, 0.11, 0.33, 1, 3 μM.
Incubation Time:	3 days
Result:	Restored the protein levels of E-cadherin and N-cadherin to control levels.

Cell Migration Assay [1]

Cell Line:	MDA-MB-231 cell
Concentration:	0, 0.11, 0.33, 1, 3 μM.
Incubation Time:	24 h
Result:	Inhibited cell migration at 1 and 3 μM. Inhibited the invasion of MDA-MB-231 cells by 22.6, 34.8, 56.5, and 70.4% at the concentrations of 0.11, 0.33, 1.0, and 3.0 μM, respectively.

In Vivo

AXL-IN-13 (compound 6li) (50 or 100 mg/kg, p.o, 14 days) inhibits 4T1 tumor growth and metastasis[1].
AXL-IN-13 (25 mg/kg, p.o.) displays reasonable PK profiles with an AUC of 8410.21 ng/mL•h, a $T_{1/2}$ value of 4.22 h, and an oral bioavailability (F) of 14.4%[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Xenograft model derived from highly metastatic 4T1 cells.[1]
Dosage:	50 or 100 mg/kg
Administration:	Oral administration (p.o.)
Result:	Suppressed 4T1 tumor growth with a tumor growth inhibition (TGI) of 78.0 and 95.9% at 50 and 100 mg/kg, respectively. Inhibited the phosphorylation of AXL. Showed that liver is one of the most common sites of breast cancer metastasis.

Animal Model:	Rats[1]
Dosage:	5 mg/kg (i.v.), 25 mg/kg (p.o.)
Administration:	Intravenous injection (i.v.), oral administration (p.o.)
Result:	Pharmacokinetic parameters of AXL-IN-13 (Compound 6li).

parameters	$T_{1/2}$ (h)	C_{max} (ng/mL)	AUC_{last}	F (%)

5 mg/kg (i.v.)	3.31	12280.44	11684.24	
25 mg/kg (p.o.)	4.22	887.75	8410.21	14.4

REFERENCES

[1]. Chan S, et al. Discovery of 3-Aminopyrazole Derivatives as New Potent and Orally Bioavailable AXL Inhibitors. J Med Chem. 2022 Nov 24;65(22):15374-15390.

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