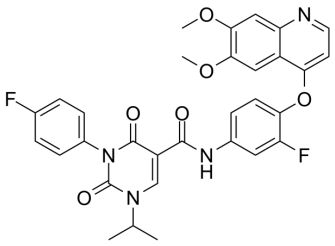
CEP-40783

Cat. No.:	HY-100946
CAS No.:	1437321-24-8
Molecular Formula:	$C_{31}H_{26}F_2N_4O_6$
Molecular Weight:	588.56
Target:	TAM Receptor; c-Met/HGFR
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 3.12 mg/mL (5.30 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6991 mL	8.4953 mL	16.9906 mL
	5 mM	0.3398 mL	1.6991 mL	3.3981 mL
	10 mM	---	---	---

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

BIOLOGICAL ACTIVITY

Description

CEP-40783 is a potent, selective and orally available inhibitor of AXL and c-Met with IC_{50} values of 7 nM and 12 nM, respectively.

IC_{50} & Target

IC50: 7 nM (AXL) and 12 nM (c-Met)[1]

In Vitro

In AXL-transfected 293GT cells, CEP-40783 is 27-fold more active compared to recombinant enzyme with an IC_{50} value of 0.26 nM. CEP-40783 also demonstrates superior activity against c-Met in GTL-16 cells (IC_{50}=6 nM). The increased inhibitory activity of CEP-40783 in cells could be attributed to its extended residence time on both AXL and c-Met, consistent with a Type II mechanism. CEP-40783 shows high kinome selectivity against 298 kinases with an S90 of 0.04 (fraction of kinases showing >90% inhibition at 1 μM)[1].

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

In Vivo

CEP-40783 shows dose- and time-dependent inhibition of AXL phosphorylation using NCI-H1299 NSCL xenografts with 80% target inhibition at 0.3 mg/kg 6 h post dose and complete target inhibition to >90% inhibition at 1 mg/kg between 6-24 h, while a 10 mg/kg po dose resulted in complete AXL inhibition up to 48 h post dosing[1]. In 3/5 (60%) of the tumor models,

CEP-40783 shows in vivo efficacy, including tumor regressions, significantly superior to that achieved with an optimal regimen of paclitaxel. In 4/4 (100%) of the erlotinib-insensitive tumor models, CEP-40783 demonstrates significant efficacy (66 to 118% TGI) compared to the control group at the 30 mg/kg dose. Additionally, CEP-40783 in combination with erlotinib demonstrate superior anti-tumor efficacy compared to CEP-40783 and erlotinib single agents in the one erlotinib-sensitive model evaluated. CEP-40783 as a single agent and in combination with erlotinib are well tolerated[2].

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PROTOCOL

Animal Administration [2]	Mice: Mice bearing established Champions TumorGrafts are treated orally with 10 mg/kg and 30 mg/kg qd of CEP-40783 for 10 to 34 days and anti-tumor efficacy and tolerability are evaluated[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Sheila M, et al. CEP-40783: A potent and selective AXL/c-Met inhibitor for use in breast, non-small cell lung (NSCLC), and pancreatic cancers. [abstract]. In: Proceedings of the AACR-NCI-EORTC International Conference: Molecular Targets and Cancer Therape

[2]. Jay F, et al. Antitumor activity of the dual AXL/c-Met inhibitor CEP-40783 in Champions primary TumorGraft? models of human non-small cell lung cancer (NSCLC). [abstract]. In: Proceedings of the AACR-NCI-EORTC International Conference: Molecular Targets a

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