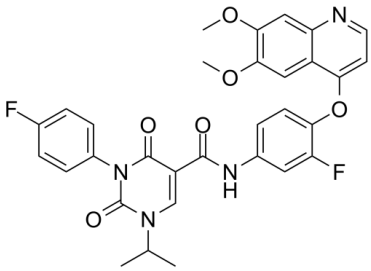
Data Sheet

Product Name:	CEP-40783
Cat. No.:	CS-6371
CAS No.:	1437321-24-8
Molecular Formula:	C31H26F2N4O6
Molecular Weight:	588.56
Target:	c-Met/HGFR; TAM Receptor
Pathway:	Protein Tyrosine Kinase/RTK
Solubility:	DMSO : 7.6 mg/mL (12.91 mM; Need ultrasonic and warming)



BIOLOGICAL ACTIVITY:

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. IC50 & 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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

Animal Administration: [2]Mouse: 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].

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 Therapeutics; 2013 Oct 19-23; Boston, MA. Philadelphia (PA): AACR; Mol Cancer Ther 2013;12(11 Suppl):Abstract nr C275.

[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 and Cancer Therapeutics; 2013 Oct 19-23; Boston, MA. Philadelphia (PA): AACR; Mol Cancer Ther 2013;12(11 Suppl):Abstract nr C272.

CAIndexNames:

5-Pyrimidinecarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]-3-fluorophenyl]-3-(4-fluorophenyl)-1,2,3,4-tetrahydro-1-(1-methylethyl)-2,4-dioxo-

SMILES:

O=C(C1=CN(C(C)C)C(N(C2=CC=C(F)C=C2)C1=O)=O)NC3=CC=C(OC4=CC=NC5=CC(OC)=C(OC)C=C45)C(F)=C3

Caution: Product has not been fully validated for medical applications. For research use only.

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