Product Name: CEP-40783
Catalog Number: T4426
CAS Number: 1437321-24-8
Molecular Formula: C31H26F2N4O6
Molecular Weight: 588.56

Description: CEP-40783 is an effective, specific and orally active AXL/c-Met inhibitor (IC50: 7/12 nM). It also inhibits MER and TYRO3 (IC50: 29/19 nM).

Storage: 2 years -80°C in solvent; 3 years -20°C powder;

Solubility
(< 1 mg/ml refers to the product slightly soluble or insoluble)

Receptor (IC50)
AXL
Mer
Tyro3

In vitro Activity
In AXL-transfected 293GT cells, CEP-40783 is 27-fold more active compared to the recombinant enzyme (IC50: 0.26 nM). In GTL-16 cells, CEP-40783 also has superior activity against c-Met (IC50: 6 nM). The enhanced inhibitory activity of CEP-40783 in cells is attributed to its extended residence time on both c-Met and AXL, similar 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 Activity
CEP-40783 showed 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. In AXL/NH3T3 xenografts, 0.3 mg/kg po resulted in complete tumor regressions. CEP-40783 was also efficacious in reducing spontaneous lymph node and pulmonary metastatic tumor burden in the MDA-MB-231-luc and 4T1-luc orthotopic breast cancer models, respectively, at 10 and 30 mg/kg po. PK/PD evaluation of the c-Met activity of CEP-40783 (10, 30, 55 mg/kg po qdX5d) showed significant to complete inhibition of c-Met phosphorylation in GTL-16 gastric carcinoma xenografts. Efficacy studies in GTL-16 xenografts demonstrated significant anti-tumor efficacy (tumor stasis and regressions) at 10 and 30 mg/kg po. In EBC-1 NSCL xenografts, administration of CEP-40783 (3, 10 and 30 mg/kg, po qd) resulted in dose-related efficacy, with tumor stasis at 3 mg/kg, tumor regressions and >96% TGI at 10 mg/kg.

Reference

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