CEP-37440

Cat. No.: HY-15841

CAS No.: 1391712-60-9

Molecular Formula: $C_{30}H_{38}ClN_7O_3$

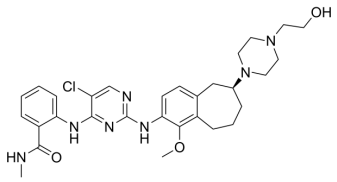
Molecular Weight: 580.12

Target: Anaplastic lymphoma kinase (ALK); FAK

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 : 100 mg/mL (172.38 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7238 mL	8.6189 mL	17.2378 mL
	5 mM	0.3448 mL	1.7238 mL	3.4476 mL
	10 mM	0.1724 mL	0.8619 mL	1.7238 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 (4.31 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.31 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.31 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CEP-37440 is a potent, orally active dual FAK/ALK inhibitor with IC_{50} values of 2.3 nM and 3.5 nM for FAK and ALK, respectively. CEP-37440 decreases proliferation by blocking the autophosphorylation kinase activity of FAK1 (Tyr 397)[1][2].

IC_{50} & Target

IC_{50}:2.3 nM (FAK) and 3.5 nM (ALK)[2]

In Vitro

CEP-37440 (0-3000 nM; 0-192 h) decreases the proliferation of inflammatory breast cancer (IBC) cells in a dose-dependent manner[1].
CEP-37440 (1000 nM; 0-120 h) decreases phospho-FAK1 (Tyr 397) and maintains its low level over time in FC-IBC02, SUM 190, and KPL4[1].

CEP-37440 (0-3000 nM; Sup-M2 and Karpas-299 cells) induces proapoptotic caspases in a dose-dependent manner[2].

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

Cell Viability Assay[1]

Cell Line:	FC-IBC02, KPL4, SUM190, MDA-IBC03 and SUM149 cells
Concentration:	0, 300, 1000, 2000 and 3000 nM
Incubation Time:	0, 24, 48, 72, 96, 120, 144, 168, and 192 hours
Result:	Reduced the proliferation of three out of five IBC cell lines at low concentration. Inhibited the proliferation almo completely at 3000 nM concentration.

Western Blot Analysis[1]

Cell Line:	FC-IBC02, SUM 190, and KPL4 cells
Concentration:	1000 nM
Incubation Time:	0, 48, 72, 96 and 120 hours
Result:	Decreased phospho-FAK1 by half in FC-IBC02, SUM190, and KPL4 cells after 48 hours.

In Vivo

CEP-37440 (3-55 mg/kg; p.o.; b.i.d and q.d., for 12 d) inhibits breast tumor growth in Sup-M2 xenograftin SCID mice[2].

CEP-37440 (30 mg/kg; p.o; once, for 24 h) inhibits tyrosine phosphorylation in Sup-M2 xenografts mice[2].

CEP-37440 (55 mg/kg; p.o; once, for 24 h) inhibits FAK phosphorylation in CWR22 xenografts in Nude mice[2].

CEP-37440 (1-10 mg/kg; p.o and i.v.; CD-1 mouse, Sprague-Dawley (SD) rats) has good pharmacokinetic parameters[2].

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

Animal Model:	SCID/Beige with Sup-M2 xenografts[2]
Dosage:	3 mg/kg (b.i.d), 10 mg/kg (b.i.d), 30 mg/kg (b.i.d and q.d.), and 55 mg/kg (q.d.)
Administration:	Oral administration; b.i.d and q.d., for 12 days
Result:	Inhibited tumor growth in a dose-dependent manner.

Animal Model:	SCID/Beige with Sup-M2 xenografts and Nu/Nu mice female with Sup-M2 xenografts[2]
Dosage:	30 mg/kg
Administration:	Oral administration; once, for 24 hours
Result:	Decreased NPM-ALK phosphorylation (>85%).

Animal Model:	Nu/Nu mice female with CWR22 xenografts[2]
Dosage:	55 mg/kg
Administration:	Oral administration; once, for 24 hours
Result:	Inhibited FAK phosphorylation in a time-dependent manner.

Animal Model:	CD-1 mouse, Sprague-Dawley (SD) rats[2]

Dosage:	1, 5, and 10 mg/kg
Administration:	Oral administration (5, and 10 mg/kg), intravenous injection (1 mg/kg); once
Result:	

	PK parameter	CD-1 mouse	SD rat
iv	dose (mg/kg)	1	1
iv	$t_{1/2}$ (h)	3.0	2
iv	$AUC_{0-\infty}$ (ng*h/mL)	1612	4005
iv	Vd (L/kg)	2.7	0.8
iv	CL (mL/min/kg)	10	4
po	dose (mg/kg)	10	5
po	C_{max} (ng/mL)	1533	1340
po			

REFERENCES

[1]. Salem I, et, al. The effects of CEP-37440, an inhibitor of focal adhesion kinase, in vitro and in vivo on inflammatory breast cancer cells. Breast Cancer Res. 2016 24;18(1):37.

[2]. Ott GR, et, al. Discovery of Clinical Candidate CEP-37440, a Selective Inhibitor of Focal Adhesion Kinase (FAK) and Anaplastic Lymphoma Kinase (ALK). J Med Cl 2016 Aug 25;59(16):7478-96.

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