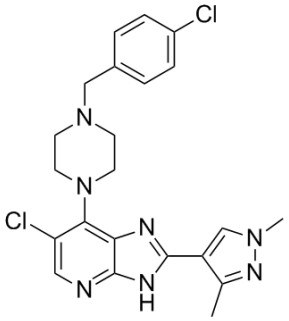
CCT241736

Cat. No.:	HY-18161
CAS No.:	1402709-93-6
Molecular Formula:	$C_{22}H_{23}Cl_2N_7$
Molecular Weight:	456.37
Target:	FLT3; Aurora Kinase
Pathway:	Protein Tyrosine Kinase/RTK; Cell Cycle/DNA Damage; Epigenetics
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 : 75 mg/mL (164.34 mM; Need ultrasonic)
H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1912 mL	10.9560 mL	21.9120 mL
	5 mM	0.4382 mL	2.1912 mL	4.3824 mL
	10 mM	0.2191 mL	1.0956 mL	2.1912 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 (5.48 mM); Suspended solution; Need ultrasonic and warming
2. Add each solvent one by one: **10% DMSO >> 90% (20% SBE-β-CD in saline)**
   Solubility: 2.5 mg/mL (5.48 mM); Suspended solution; Need ultrasonic and warming
3. Add each solvent one by one: **10% DMSO >> 90% corn oil**
   Solubility: ≥ 2.5 mg/mL (5.48 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CCT241736 is a potent and orally bioavailable dual **FLT3** and **Aurora kinase** inhibitor, which inhibits Aurora kinases (Aurora-A **K_d**, 7.5 nM, **IC_{50}**, 38 nM; Aurora-B **K_d**, 48 nM), FLT3 kinase (**K_d**, 6.2 nM), and FLT3 mutants including FLT3-ITD (**K_d**, 38 nM) and FLT3(D835Y) (**K_d**, 14 nM).

IC_{50} & Target

IC50: 38 nM (Aurora-A)[1]

	Kd: 7.5 nM (Aurora-A), 48 nM (Aurora-B), 6.2 nM (FLT3), 38 nM (FLT3-ITD), 14 nM (FLT3(D835Y))[1]
In Vitro	CCT241736 (Compound 27e) is a potent and orally bioavailable dual FLT3 and Aurora kinase inhibitor, which inhibits Aurora kinases (Aurora-A K_d, 7.5 nM, IC_{50}, 38 nM, Aurora-B K_d, 48 nM), FLT3 kinase (K_d, 6.2 nM), and FLT3 mutants including FLT3-ITD (K_d, 38 nM) and FLT3(D835Y) (K_d, 14 nM). CCT241736 exhibits antiproliferative activity in a range of human tumor cell lines, such as HCT116 human colon carcinoma (GI_{50}, 0.300 μM), the human FLT3-ITD positive AML cell lines MOLM-13 (GI_{50}, 0.104 μM) and MV4-11 (GI_{50}, 0.291 μM). CCT241736 also inhibits both the autophosphorylation of Aurora-A at T288 (a biomarker for Aurora-A inhibition: IC_{50}, 0.030 μM) and histone H3 phosphorylation at S10 (a biomarker for Aurora-B inhibition: IC_{50}, 0.148 μM), consistent with potent cellular activity versus both Aurora-A and -B. CCT241736 suppresses Aurora-A in MOLM-13 cells with concomitant inhibition of FLT3 signaling[1].
In Vivo	CCT241736 (50, 100 mg/kg, b.i.d, p.o.) dose-dependently suppresses the growth of MV4-11 human tumor xenografts, and completely abolishes the tumors at 100 mg/kg via p.o. administration twice a day[1].

PROTOCOL

Animal Administration [1]	Mice[1] Female adult **CrTacNCr-Fox1(nu) athymic mice** are implanted subcutaneously with 10^7 FLT3-ITD-positive MV4-11 human leukemia cells. When the tumor xenografts are well-established (10 days after implantation, mean tumor volumes of at least 100 mm^3), animals are treated with either vehicle (**10% DMSO, 20% PEG 400, 5% Tween 80 and 65% water**) or **CCT241736 administered orally** at two doses, **50 and 100 mg/kg** (n = 5 per group). Dosing is **twice daily for 7 days**, and **once daily for a further 4 days**[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Bavetsias V, et al. Optimization of imidazo[4,5-b]pyridine-based kinase inhibitors: identification of a dual FLT3/Aurora kinase inhibitor as an orally bioavailable preclinical development candidate for the treatment of acute myeloid leukemia. J Med Chem. 2012 Oct 25;55(20):8721-34.

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