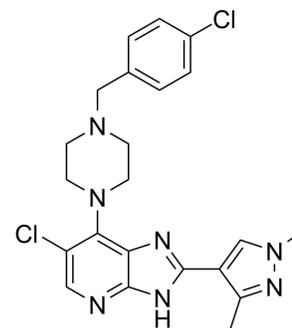


CCT241736

Cat. No.:	HY-18161		
CAS No.:	1402709-93-6		
Molecular Formula:	C ₂₂ H ₂₃ Cl ₂ N 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	2 years
		-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro	DMSO : 12.5 mg/mL (27.39 mM; ultrasonic and warming and heat to 60°C)				
		Solvent Concentration	Mass 1 mg	5 mg	10 mg
	Preparing Stock Solutions	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	<ol style="list-style-type: none"> 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 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 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).
IC₅₀ & Target	IC ₅₀ : 38 nM (Aurora-A) ^[1] K _d : 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 μ M), the human FLT3-ITD positive AML cell lines MOLM-13 (GI_{50} , 0.104 μ M) and MV4-11 (GI_{50} , 0.291 μ M). CCT241736 also inhibits both the autophosphorylation of Aurora-A at T288 (a biomarker for Aurora-A inhibition: IC_{50} , 0.030 μ M) and histone H3 phosphorylation at S10 (a biomarker for Aurora-B inhibition: IC_{50} , 0.148 μ M), 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].

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

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].

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

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 mm³), 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.

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

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