CCT196969

Cat. No.: HY-12846

CAS No.: 1163719-56-9

Molecular Formula: $C_{27}H_{24}FN_7O_3$

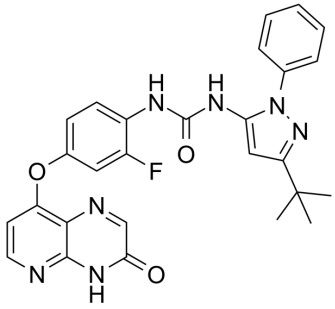
Molecular Weight: 513.52

Target: Raf

Pathway: MAPK/ERK Pathway

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 : ≥ 32 mg/mL (62.31 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9473 mL	9.7367 mL	19.4734 mL
5 mM	0.3895 mL	1.9473 mL	3.8947 mL
10 mM	0.1947 mL	0.9737 mL	1.9473 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: ≥ 2.08 mg/mL (4.05 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.05 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.05 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CCT196969 is a pan-Raf inhibitor, which inhibits B-Raf, $BRaf^{V600E}$ and CRAF with IC_{50}s of 0.1, 0.04, and 0.01 μM, respectively.

IC_{50} & Target

$BRaf^{V600E}$ 0.04 μM (IC_{50})	Braf 0.1 μM (IC_{50})	CRAF 0.01 μM (IC_{50})	LCK 0.02 μM (IC_{50})
SRC 0.03 μM (IC_{50})			

In Vitro	CCT196969 is a pan-Raf inhibitor with anti-SRC activity. CCT196969 is an orally available, well-tolerated B-Raf inhibitor that directly inhibits B-Raf^{V600E} in cells. CCT196969 inhibits B-Raf at 100 nM and B-Raf^{V600E} at 40 nM. It inhibits CRaf at 12 nM, SRC at 26 nM, and LCK at 14 nM. CCT196969 is active against melanoma and colorectal cancer cell lines that are mutant for B-Raf. CCT196969 induces caspase 3 and PARP cleavage, demonstrating that it induces apoptosis[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	CCT196969 is extremely well tolerated and does not produce any significant adverse effects in vivo. It inhibits the growth of NRAS mutant DO4 tumor xenografts in nude mice. CCT196969 inhibits ERK and SRC and induce tumor regression in a PDX from the resistant tumor without causing body weight loss in the mice[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Cultured cells are seeded into 96-well plates (2,000 cells per well). At 24 hr later, serial dilutions of the B-Raf inhibitors PLX4720 and SB590885, the MEK inhibitor PD184352, or compounds CCT241161 and CCT196969 are added. Cells are incubated for a further 72 hr, and viability is measured by CellTiter-Glo assays. Relative survival in the presence of drugs is normalized to the untreated controls after background subtraction[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: Tumors are established in female nude mice. Treatment is by oral gavage daily with vehicle (5% DMSO, 95% water), 90 mg/kg PLX4720, 20 mg/kg CCT196969, or 20 mg/kg CCT241161. All the inhibitors are administered 7 days/week, with no weekend break. Tumor size is determined by caliper measurements of tumor length, width, and depth; volume is calculated as volume = 0.5236×length×width×depth (in millimeters)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Girotti MR, et al. Paradox-breaking RAF inhibitors that also target SRC are effective in drug-resistant BRAF mutant melanoma. Cancer Cell. 2015 Jan 12;27(1):85-96.

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