

Product Data Sheet

Product Name: CCT196969

Cat. No.: GC19091

Chemical Properties

Cas. No. 1163719-56-9

SMILES O=C1NC2=NC=CC(OC3=CC=C(NC(NC4=CC(C(C)(C)C)=NN4C5=CC=CC=C5)=O)C(F)=C3)=C2N=C1

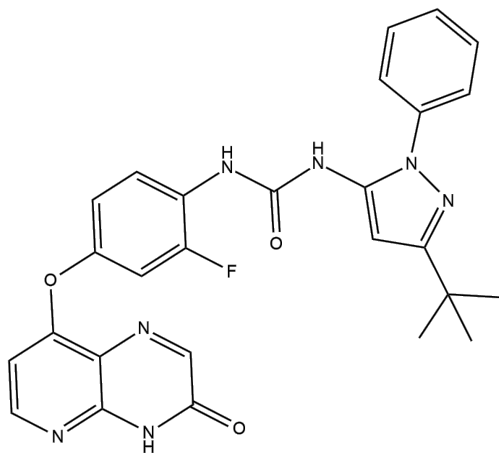
Formula $C_{27}H_{24}FN_7O_3$ M.Wt 513.52

Solubility DMSO : ≥ 32 mg/mL (62.32 mM) Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

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

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Cell experiment: 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].

Animal experiment: 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 = $0.5236 \times \text{length} \times \text{width} \times \text{depth}$ (in millimeters)[1].

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.

Background

CCT196969, a pan-Raf inhibitor, inhibits B-Raf with an IC₅₀ of 0.1 μ M.

CCT196969 is a pan-Raf inhibitor with anti-SRC activity. CCT196969 is an orally available, well-tolerated B-Raf inhibitor that directly inhibits B-RafV600E in cells. CCT196969 inhibits B-Raf at 100 nM and B-RafV600E 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].

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].

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