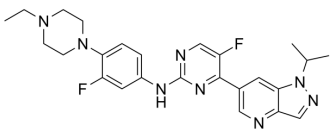
FLT3/CDK4-IN-1

Cat. No.:	HY-115904
CAS No.:	2762296-44-4
Molecular Formula:	$C_{25}H_{28}F_2N_8$
Molecular Weight:	478.54
Target:	CDK; FLT3
Pathway:	Cell Cycle/DNA Damage; Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	FLT3/CDK4-IN-1 is a potent, high selective and orally active FLT3/CDK4 dual inhibitor (IC_{50}=11 and 7 nM for FLT3 and CDK4, respectively). FLT3/CDK4-IN-1 has antiproliferative activities against certain cancer cells. FLT3/CDK4-IN-1 has good antitumor effect in vivo[1].
IC_{50} & Target	CDK4 7 nM (IC_{50})

In Vitro

FLT3/CDK4-IN-1 (compound 23k) (various concentrations; 72 hours) has better cell antiproliferative activities against MV4-11and HCT-116 cells, with IC_{50} of 70 and 100 nM respectively[1].

FLT3/CDK4-IN-1 (12.5-200 nM; 24 hours) arrests the cell cycle in G1 phase in a concentration-dependent manner[1].

FLT3/CDK4-IN-1 (200-3200 nM; 48 hours) induces apoptosis in both MV4-11 and HCT-116 cells with concentration dependent manner, and is more capable in MV4-11 than HCT-116[1].

FLT3/CDK4-IN-1 (0-100 nM; 2hours) inhibits the phosphorylation of FLT3 at Tyr589/591 in a dose-dependent manner[1].

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

Cell Proliferation Assay

Cell Line:	MV4-11, HCT-116, MDA-MB-436[1]
Concentration:	Various concentrations
Incubation Time:	72 hours
Result:	FLT3/CDK4-IN-1 had better cell antiproliferative activities against MV4-11and HCT-116 cells, with IC_{50} of 70 and 100 nM respectively.

Cell Cycle Analysis

Cell Line:	MV4-11, HCT-116[1]
Concentration:	12.5, 25, 50, 100 and 200 nM
Incubation Time:	24 hours
Result:	Arrested the cell cycle in G1 phase in a concentration-dependent manner.

Apoptosis Analysis

Cell Line:	MV4-11, HCT-116[1]
Concentration:	200, 400, 800, 1600 and 3200 nM
Incubation Time:	48 hours
Result:	Induced apoptosis in both MV4-11 and HCT-116 cells with concentration dependent manner, and was more capable in MV4-11 than HCT-116.

Western Blot Analysis

Cell Line:	MV4-11[1]
Concentration:	0, 5, 10, 20, 40, 100 nM
Incubation Time:	2 hours
Result:	Inhibited the phosphorylation of FLT3 at Tyr589/591 in a dose-dependent manner.

In Vivo

FLT3/CDK4-IN-1 (100 and 200 mg/kg; p.o.; 14 days, once daily) significantly inhibits the tumor growth at the dose of 200 mg/kg[1].

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

Animal Model:	Female nu/nu mice (MV4-11-injected)[1]
Dosage:	100 and 200 mg/kg
Administration:	p.o.; 14 days, once daily
Result:	Significantly inhibited the tumor growth at the dose of 200 mg/kg while no significant antitumor effect at 100 mg/kg.

REFERENCES

[1]. Li X, et al. Synthesis and biological evaluation of 6-(pyrimidin-4-yl)-1H-pyrazolo[4,3-b]pyridine derivatives as novel dual FLT3/CDK4 inhibitors. Bioorg Chem. 2022;121:105669.

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