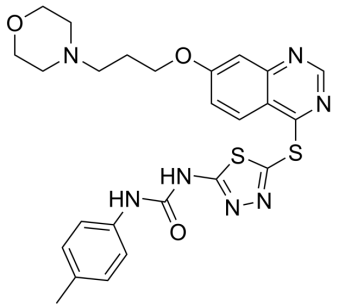
SKLB4771

Cat. No.:	HY-12960
CAS No.:	1370256-78-2
Molecular Formula:	$C_{25}H_{27}N_7O_3S_2$
Molecular Weight:	537.66
Target:	FLT3; c-Kit; Apoptosis
Pathway:	Protein Tyrosine Kinase/RTK; Apoptosis
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 : 33.33 mg/mL (61.99 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8599 mL	9.2996 mL	18.5991 mL
	5 mM	0.3720 mL	1.8599 mL	3.7198 mL
	10 mM	0.1860 mL	0.9300 mL	1.8599 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 (4.65 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (4.65 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.65 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SKLB4771 is a potent and selective Flt3 inhibitor with an IC_{50} value of 10 nM. SKLB4771 downregulates the phosphorylation of FLT3/STAT5/ERK, blocks cell proliferation, and induces apoptosis in tumor tissue[1][2].

IC_{50} & Target

IC50: 10 nM (Flt3); 3.7 μM (Flt4); 1.5 μM (Aurora A); 6.8 μM (c-kit); 2.8 μM (FMS)[1]

In Vitro

SKLB4771 (compound 20c) (72 h) inhibits FLT3-ITD-expressing MV4-11 cells with an IC_{50} value of 6 nM, and inhibits other cancer cells with IC_{50}s of 3.05 μM (Jurkat), 6.25 μM (Ramos), 3.72 μM (PC-9), 6.94 μM (H292), and 8.91 μM (A431), respectively

[1].

SKLB4771 (0-300 nM; 20 h) inhibits FLT3 phosphorylation and also decreases the phosphorylation of the downstream signaling proteins STAT5 and ERK1/2 at concentrations >0.1 μM[1].

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

Western Blot Analysis[1]

Cell Line:	MV4-11 cells
Concentration:	0, 30, 100, 300 nM
Incubation Time:	20 hours
Result:	Resulted inhibition against the human FLT3 kinase in a dose-dependent manner, and decreased the phosphorylation level of STAT5 and ERK1/2 at 100 nM and 300 nM.

In Vivo

SKLB4771 (20-100 mg/kg; i.p.; once daily; 21 d) inhibits tumor growth in vivo without significant weight loss or any other obvious signs of toxicity on mice[1].

Pharmacokinetic Analysis of SKLB4771 in rat (40 mg/kg; i.p.)[1]

C_{max} (μg/mL)	$T_{1/2}$ (h)	AUC_{max} (h·μg/mL)	T_{max} (h)	CL_{obs} (L/h/kg)
5.31	13.9	21.86	1.0	2.21

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

Animal Model:	Female NOD-SCID mouse (6−7 weeks old)[1]
Dosage:	20, 40, 100 mg/kg; dissolved in 25% (v/v) PEG400 plus 5% DMSO, administered at a dose of 5 mL/kg
Administration:	Intraperitoneal injection; once daily; 21 days
Result:	Inhibited tumor growth by 66% and 84% at concentration of 20 mg/kg and 40 mg/kg, respectively. Resulted cell proliferation inhibition and apoptosis induction.

REFERENCES

[1]. Yan HX, et al. Accumulation of FLT3(+) CD11c (+) dendritic cells in psoriatic lesions and the anti-psoriatic effect of a selective FLT3 inhibitor. Immunol Res. 2014 Oct;60(1):112-26.

[2]. Li WW, et al. Discovery of the novel potent and selective FLT3 inhibitor 1-{5-[7-(3- morpholinopropoxy)quinazolin-4-ylthio]-[1,3,4]thiadiazol-2-yl}-3-p-tolylurea and its anti-acute myeloid leukemia (AML) activities in vitro and in vivo. J Med Chem. 2012 Apr 26;55(8):3852-66.

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