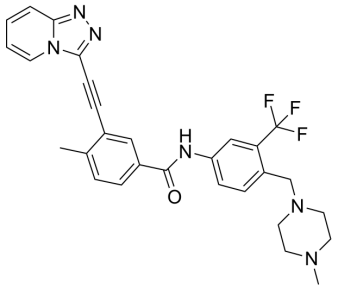
Vamotinib

Cat. No.:	HY-147414
CAS No.:	1416241-23-0
Molecular Formula:	$C_{29}H_{27}F_3N_6O$
Molecular Weight:	532.56
Target:	Bcr-Abl
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	4°C, sealed storage, away from moisture and light * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (93.89 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8777 mL	9.3886 mL	18.7772 mL
	5 mM	0.3755 mL	1.8777 mL	3.7554 mL
	10 mM	0.1878 mL	0.9389 mL	1.8777 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 (4.69 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.69 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Vamotinib (PF-114) is a potent, selective and orally active tyrosine kinase inhibitor. Vamotinib inhibits the autophosphorylation of BCR/ABL and BCR/ABL-T315I. Vamotinib induces apoptosis. Vamotinib shows anti-proliferative and anti-tumor activity. Vamotinib has the potential for the research of resistant philadelphia chromosome-positive (Ph+) leukemia. Vamotinib inhibits ABL series kinases with IC_{50}s of 0.49 nM (ABL), 0.78 nM (ABL^{T315I}), 9.5 nM (ABL^{E255K}), 2.0 nM (ABL^{F317I}), 7.4 nM (ABL^{G250E}), 1.0 nM (ABL^{H396P}), 2.8 nM (ABL^{M351T}), 12 nM (ABL^{Q252H}), and 4.1 nM (ABL^{Y253F}), respectively[1] [2]. Vamotinib is a click chemistry reagent, it contains an Alkyne group and can undergo copper-catalyzed azide-alkyne cycloaddition (CuAAc) with molecules containing Azide groups.

IC_{50} & Target

IC50: 0.49 nM (ABL), 0.78 nM (ABL^{T315I}), 9.5 nM (ABL^{E255K}), 2.0 nM (ABL^{F317I}), 7.4 nM (ABL^{G250E}), 1.0 nM (ABL^{H396P}), 2.8 nM (ABL^{M351T}), 12 nM (ABL^{Q252H}), and 4.1 nM (ABL^{Y253F})[2]

In Vitro

Vamotinib (0-1 μM) inhibits ABL kinase and its mutants with IC_{50}s of 0.49, 0.78, 1.0 μM for ABL, ABL(T315I), ABL(H396P), respectively[1].
Vamotinib (0-1000 nM) inhibits the autophosphorylation of BCR/ABL and BCR/ABL-T315I in a dose-dependent manner[1].
Vamotinib (0-2000 nM) shows anti-proliferative activity in Ba/F3 cells expressing native BCR/ABL[1].
Vamotinib (0-100 nM) induces apoptosis in Ba/F3 cells expressing BCR/ABL and BCR/ABL-T315I[1].
Vamotinib (0-1000 nM) inhibits the growth of Ph+ patient-derived cell lines in k562, kcl-22, SupB15, Tom-1, BV-173 cells[1].
Vamotinib (0-1000 nM) suppresses growth of Ph+ PD-LTC with nonmutational resistance as well as T315I mutation[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	Ba/F3 cells
Concentration:	0, 10, 25, 50, 100, 500, 1000 nM
Incubation Time:	
Result:	Inhibited the autophosphorylation of BCR/ABL and BCR/ABL-T315I in a dose-dependent manner and inhibited substrate phosphorylation as shown by the reduced Crkl-phosphorylation and downstream activation of Stat5 by BCR/ABL, as well as by BCR/ABL-T315I.

Cell Proliferation Assay[1]

Cell Line:	Ba/F3 cells
Concentration:	0, 50, 500, 2000 nM
Incubation Time:	
Result:	Potently inhibited proliferation of Ba/F3 cells expressing native BCR/ABL in a dose-dependent manner and shows no effects on empty vector-transduced Ba/F3 cells in the presence of IL-3 (10 ng/ml).

Apoptosis Analysis[1]

Cell Line:	Ba/F3 cells
Concentration:	0-100 nM
Incubation Time:	
Result:	Induced apoptosis in Ba/F3 cells expressing BCR/ABL and BCR/ABL-T315I in a dose dependent manner.

In Vivo

Vamotinib (25, 40 mg/kg; i.g.; daily for 14 consecutive days) shows anti-tumor activity[1].
Vamotinib (50 mg/kg; p.o.; once daily for 20 days) prolongs the survival of mice with both BCR/ABL- and BCR/ABL-T315I-driven CML-like disease[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female BALB/cAnNRj-Foxn1nu mice (K562 nude mouse xenograft model)[1]
Dosage:	25, 40 mg/kg
Administration:	Oral gavage; daily for 14 consecutive days
Result:	Caused a 100% reduction of the mean tumor volume within 4 weeks.

Animal Model:	8-12 weeks, C57BL/6N mice (CML-like disease mouse model)[1]
Dosage:	50 mg/kg
Administration:	P.o.; once daily for 20 days
Result:	Extended median survival significantly from 28 days to 39.

REFERENCES

[1]. Mian AA,et al. PF-114, a potent and selective inhibitor of native and mutated BCR/ABL is active against Philadelphia chromosome-positive (Ph+) leukemias harboring the T315I mutation. Leukemia. 2015 May;29(5):1104-14.

[2]. Ivanova ES, et al. PF□114, a novel selective inhibitor of BCR□ABL tyrosine kinase, is a potent inducer of apoptosis in chronic myelogenous leukemia cells. Int J Oncol. 2019 Jul;55(1):289-297.

[3]. Mian AA, et al. PF-114, a potent and selective inhibitor of native and mutated BCR/ABL is active against Philadelphia chromosome-positive (Ph+) leukemias harboring the T315I mutation. Leukemia. 2015 May;29(5):1104-14.

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