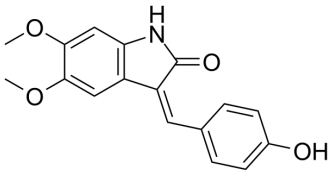
RPI-1

Cat. No.:	HY-101246
CAS No.:	269730-03-2
Molecular Formula:	$C_{17}H_{15}NO_4$
Molecular Weight:	297.31
Target:	RET
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (420.44 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.3635 mL	16.8175 mL	33.6349 mL
5 mM	0.6727 mL	3.3635 mL	6.7270 mL
10 mM	0.3363 mL	1.6817 mL	3.3635 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (7.00 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

RPI-1 is a specific, orally available 2-indolinone Ret tyrosine kinase inhibitor. RPI-1 inhibits proliferation, Ret tyrosine phosphorylation, Ret protein expression, and the activation of PLCgamma, ERKs and AKT in human medullary thyroid carcinoma TT cells. Antitumor activity[1].

In Vitro

TPC-1 cells are sensitive to the growth inhibitory effect of RPI-1 with an IC_{50} of 5.1 μM, following 72 hours of treatment. RPI-1 (7.5-60 μM) inhibits Ret/Ptc1 autophosphorylation in TPC-1 cells. RPI-1 inhibitory effects in the TPC-1 cell culture conditions lead to inhibition of pathways involving JNK2 and AKT[1].

The RPI-1 IC_{50} value for cell proliferation is 3.6 μM in NIH3T3 cells expressing the Ret mutant compared with 16 μM in non-transfected NIH3T3 cells, and that for colony formation in soft agar was 2.4 μM and 26 μM in RET mutant-transfected and H-RAS-transfected NIH3T3 cells, respectively. In NIH3T3 cells expressing the Ret mutant, Ret protein and tyrosine phosphorylation were undetectable after 24 hours of RPI-1 treatment. In TT cells, RPI-1 inhibits proliferation, Ret tyrosine phosphorylation, Ret protein expression, and the activation of PLCgamma, ERKs and AKT[2].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	RPI-1 (50, 100 mg/kg; p.o.; twice a day for 10 days) inhibits the tumor growth of TT xenografts by 81%[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	8- to 11-week-old female athymic nude CD-1 mice (bearing TT cells)[2]
Dosage:	50, 100 mg/kg
Administration:	P.o.; twice a day for 10 days
Result:	A dose-dependent effect on tumor growth was observed, with a dose of 2*50 mg/kg/day resulting in less tumor weight inhibition than the 2*100mg/kg/day dose after 10 days of treatment.

REFERENCES

[1]. Lanzi C, et al. Inactivation of Ret/Ptc1 oncoprotein and inhibition of papillary thyroid carcinoma cell proliferation by indolinone RPI-1. Cell Mol Life Sci. 2003;60(7):1449-1459.

[2]. Cuccuru G, et al. Cellular effects and antitumor activity of RET inhibitor RPI-1 on MEN2A-associated medullary thyroid carcinoma. J Natl Cancer Inst. 2004;96(13):1006-1014.

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