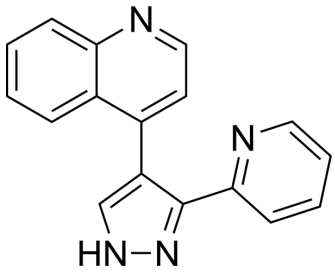
LY-364947

Cat. No.:	HY-13462
CAS No.:	396129-53-6
Molecular Formula:	$C_{17}H_{12}N_4$
Molecular Weight:	272.3
Target:	TGF-β Receptor
Pathway:	TGF-beta/Smad
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 : 15.62 mg/mL (57.36 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.6724 mL	18.3621 mL	36.7242 mL
	5 mM	0.7345 mL	3.6724 mL	7.3448 mL
	10 mM	0.3672 mL	1.8362 mL	3.6724 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: ≥ 1.25 mg/mL (4.59 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (4.59 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

LY-364947 (HTS466284) is a potent ATP-competitive inhibitor of TGFβR-I with IC_{50} of 59 nM, and exhibits 7-fold selectivity over TGFβR-II[1].

IC_{50} & Target

IC50: 59 nM (TGFβR-I)

In Vitro

LY-364947 is an ATP competitive and tight-binding inhibitor, inhibiting phosphorylation of P-Smad3 by TGFβR-I Kinase with K_i of 28 nM. LY-364947 inhibits in vivo Smad2 phosphorylation within the NMuMg cells with IC_{50} of 135 nM. LY-364947 reverses TGF-β-mediated growth inhibition in NMuMg cells with IC_{50} of 0.218 μM. LY-364947 potentiates the xVent2-lux BMP4 response in NMuMg cells by 30% at concentrations as low as 0.25 μM. LY-364947 (2 μM) prevents TGF-β-induced epithelial?mesenchymal transition in NMuMg cells[1]. LY-364947 (3 μM) induces expression of Prox1 and LYVE-1 in almost all

	HDLECs after 24 hours[2]. LY-364947 promotes nuclear export of Foxo3a, with low Smad2/3 and high Akt phosphorylation levels in leukaemia-initiating cells. LY-364947 (< 20 μM) suppresses leukaemia-initiating cells colony-forming ability after co-culture with OP-9 stromal cells[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	LY-364947 (1 mg/kg, i.p.) accelerates lymphangiogenesis, as evidence by significantly increasing the LYVE-1-positive areas in a mouse model of chronic peritonitis. LY-364947 (1 mg/kg, i.p.) significantly increases the LYVE-1-positive areas in tumor tissues in tumor xenograft models using BxPC3 pancreatic adenocarcinoma cells[2]. LY-364947 (25 mg/kg) increases p-Akt and decreases nuclear Foxo3a in leukaemia-initiating cells in CML-affected mice[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	BALB/c nude mice 5 to 6 weeks of age are used in the assay. Parental, or VEGF-C- or TGF-β1-expressing tumor cells (5×10^6) in 100 μL PBS are implanted subcutaneously into male nude mice and allowed to grow for 2 to 3 weeks to reach proliferative phase, before initiation of TβR-I inhibitor administration. TβR-I inhibitor LY-364947, dissolved in 5 mg/mL in DMSO and diluted with 100 μL PBS, or the vehicle control, is injected intraperitoneally at 1 mg/kg, 3 times a week for 3 weeks. Excised samples are directly frozen in dry-iced acetone for immunohistochemistry. Frozen samples are further sectioned at 10-μm thickness in a cryostat and subsequently incubated with primary and secondary antibodies. Samples are observed using a confocal microscope. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Discov. 2022 Sep 20;8(1):94.
- Haematologica. 2020 Mar;105(3):674-686.
- Pharmacol Res. 2021 Aug 2;105797.
- Oncogene. 2019 Jun;38(23):4637-4654.
- Cell Biosci. 2019 Jun 14;9:48.

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REFERENCES

[1]. Peng SB, et al. Kinetic characterization of novel pyrazole TGF-beta receptor I kinase inhibitors and their blockade of the epithelial-mesenchymal transition. Biochemistry, 2005, 44(7), 2293-2304.

[2]. Oka M, et al. Inhibition of endogenous TGF-beta signaling enhances lymphangiogenesis. Blood, 2008, 111(9), 4571-4579.

[3]. Naka K, et al. TGF-beta-FOXO signalling maintains leukaemia-initiating cells in chronic myeloid leukaemia. Nature, 2010, 463(7281), 676-680.

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