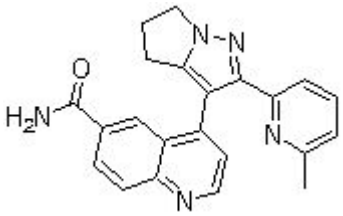
Product Introduction

LY2157299

LY2157299 is a potent **TGFβ receptor I (TβRI)** inhibitor with **IC50** of 56 nM. Phase 2.

Technical Data:

Molecular Weight (MW):	369.42	
Formula:	C22H19N5O	
Solubility (25°C) *** <1 mg/ml means slightly soluble or insoluble:**	DMSO 74 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	700874-72-2	

Biological Activity

LY2157299 potently inhibits the TGFβ receptor signaling. LY2157299 abolishes the TGFβ induced Smad2 phosphorylation in HUVEC cells. LY2157299 also shows dose dependent potentiation of VEGF or bFGF induced cell proliferation in HUVEC. LY2157299 also promotes VEGF induced HUVEC cell migration. LY2157299 potentiates angiogenesis in the in vitro VEGF-stimulated cord formation assay. [2] LY2157299 inhibits TGF-β-mediated SMAD2 activation and hematopoietic suppression in primary hematopoietic stem cells in a dose-dependent manner. LY2157199 treatment stimulates hematopoiesis from primary MDS bone marrow specimens. [3] In human glioblastoma (GBM) cells, LY2157299 treatment blocks signaling

through the heteromeric TGFβ receptor complex to reduce levels of active, phosphorylated SMAD. [4]

Although anti-tumor activity has been observed in several pre-clinical models, LY2157299 fails to show significant in vivo angiogenic effects in the 4T1, Colo205, or A549 xenograft models. [2] Administration of LY2157299 ameliorates anemia in a TGF-β overexpressing transgenic mouse model of bone marrow failure. [3] Oral administration of LY2157299 at 75 mg/kg/day displays significant antitumor activity against both Calu6 and MX1 xenografts in mice. [5] In vivo, LY2157299 induces angiogenesis and enhances VEGF and basic-fibroblast-growth-factor-induced angiogenesis in a Matrigel-plug assay, whereas adding an alpha5-integrin-neutralizing antibody to the Matrigel selectively inhibits this enhanced response. [6]

References

[1] Mundla SR, Patent, 2006, US7872020.
[2] Yingling JM, et al. Proc Am Assoc Cancer Res. 2006, 47, abstract 250.
[3] Zhou L, et al. Cancer Res, 2011, 71(3), 955-963.
[4] Parsons S, et al. Mol Cancer Ther, 2011, 10(11), Suppl 1, Abst C201.
[5] Bueno L, et al. Eur J Cancer, 2008, 44(1), 142-150.
[6] Liu Z, et al. J Cell Sci, 2009, 122(18), 3294-3302.

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