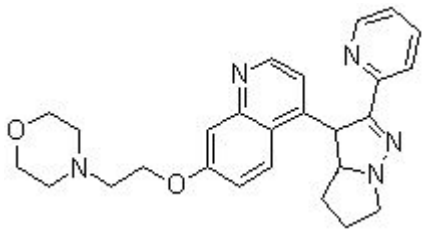
Product Introduction

LY2109761

LY2109761 is a novel selective **TGF-β receptor type I/II (TβRI/II)** dual inhibitor with K_I of 38 nM and 300 nM, respectively; shown to negatively affect the phosphorylation of Smad2.

Technical Data:

Molecular Weight (MW):	441.52	
Formula:	$C_{26}H_{27}N_5O_2$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 2 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	700874-71-1	

Biological Activity

LY2109761 treatment induces a dose-dependent low-anchorage growth inhibition of L3.6pl/GLT cells, leading to ~33% or 73% inhibition at 2 μM and 20 μM, respectively, which can be strongly enhanced when combined with gemcitabine in combination index value of 0.36581. Blocking TβRI/II kinase activity with LY2109761 (5 μM) completely suppresses both the basal and TGF-β1-stimulated migration and invasion of L3.6pl/GLT cells, significantly enhances the detachment-induced apoptosis by 26% at 8 hours treatment, and completely suppresses TGF-β–induced Smad2 phosphorylation. [1] LY2109761 treatment

at 1 nM is sufficient to significantly block the migration and invasion but not adhesion of hepatocellular carcinoma cells by increasing E-cadherin expression. [2] LY2109761 pretreatment enhances radiosensitivity of glioblastoma cells via TGF-β signaling blockage. LY2109761 (10 μM) reduces the self-renewal and proliferation of GBM-derived cancer stem–like cells (CSLC), which can be significantly enhanced when combined with radiation. [3]

Administration of LY2109761 (50 mg/kg) alone or in combination with gemcitabine (25 mg/kg) significantly reduces the tumor volume by ~70% and ~90%, respectively, prolongs the survival with the median survival duration of 45.0 days and 77.5 days, respectively, and reduces spontaneous abdominal metastases in the L3.6pl/GLT Xenograft mice model. [1] In consistent with the in vitro effect, administration of LY2109761 alone or in combination with radiation, markedly inhibits tumor growth in the orthotopical CSLC glioblastoma model by 43.4% and 76.3%, respectively, decreases tumor invasion and tumor microvessel density, and significantly enhances radiation-induced tumor growth delay in the U87MG xenograft mice model. [3]

References

[1] Melisi D, et al. Mol Cancer Ther, 2008, 7(4), 829-840.

[2] Fransvea E, et al. Hepatology, 2008, 47(5), 1557-1566.

[3] Zhang M, et al. Cancer Res, 2011, 71(23), 7155-7167.

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