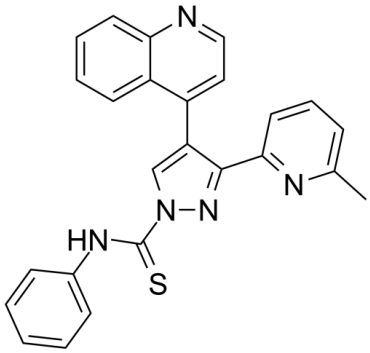
Data Sheet

Product Name:	A 83-01
Cat. No.:	CS-1437
CAS No.:	909910-43-6
Molecular Formula:	C25H19N5S
Molecular Weight:	421.52
Target:	TGF-β Receptor
Pathway:	TGF-beta/Smad
Solubility:	DMSO : 30 mg/mL (71.17 mM; Need ultrasonic); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

A 83-01 is a potent inhibitor of **TGF-β type I receptor ALK5 kinase**, type I nodal receptor **ALK4** and type I nodal receptor **ALK7**, with **IC_{50}**s of 12, 45 and 7.5 nM against the transcription induced by ALK5, ALK4 and ALK7, respectively. IC50 & Target: IC50: 12 nM (ALK5, cell-based), 45 nM (ALK4 cell-based), 7.5 nM (ALK7 cell-based)[1] **In Vitro:** A 83-01 is a potent inhibitor of TGF-β type I receptor ALK5 kinase, ALK4 and ALK7, reduces the level of ALK-5-induced transcription with an IC_{50} of 12 nM in Mv1Lu cells, also blocks the ALK4-TD and ALK7-TD induced transcription with IC_{50}s of 45 nM and 7.5 nM in R4-2 cells, and weakly suppresses that induced by constitutively active ALK-6, ALK-2, ALK-3, and ALK-1. A 83-01 (0.03-10 μM) potently prevents the growth-inhibitory effects of TGF-β, and completely inhibits the effect at 3 μM. A 83-01 (1-10 μM) inhibits TGF-β-induced Smad activation in HaCaT cells[1]. A 83-01 (1 μM) decreases cell motility, adhesion and invasion increased by TGF-β1 in HM-1 cells, but does not change cell proliferation[2]. **In Vivo:** A 83-01 (50, 150 and 500 μg/mouse, i.p.) significantly improves survival of the mice without body weight or neurobehavioral appearances[2]. A 83-01 (0.5 mg/kg, i.p.) shows a significantly strong antitumor effect in mice bearing M109 cells[3].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: A 83-01 is dissolved in DMSO[2].[2]**HM-1 cells** are seeded into a 96-well plate and are incubated for **18 hr**. **A 83-01 (1 μM)** or vehicle are then added for 12 hr followed by the addition of TGF-β1 (1 ng/mL) or vehicle for 60 hr. The number of viable cells in each well is examined using the WST-1 assay[2].

Animal Administration: A 83-01 is formulated in PBS with 0.5% DMSO[2].[2]Mice[2]

Female B6C3F1 mice used for the in vivo studies are maintained under specific pathogen-free conditions. To evaluate the effect of A 83-01 on the survival of mice bearing peritoneal dissemination, **HM-1 cells (1×10^6)** are injected into the abdominal cavity via the left flank of the mouse. Starting the next day, **A 83-01 (150 μg/body)** or vehicles (**PBS with 0.5% DMSO**) are **injected into the abdominal cavity three times per week**. Mice are euthanized before reaching the moribund state[2].

References:

[1]. Tojo M, et al. The ALK-5 inhibitor A-83-01 inhibits Smad signaling and epithelial-to-mesenchymal transition by transforming growth factor-beta. Cancer Sci. 2005 Nov;96(11):791-800.

[2]. Yamamura S, et al. The activated transforming growth factor-beta signaling pathway in peritoneal metastases is a potential therapeutic target in ovarian cancer. Int J Cancer. 2012 Jan 1;130(1):20-8.

[3]. Taniguchi Y, et al. Enhanced antitumor efficacy of folate-linked liposomal Adriamycin with TGF-β type I receptor inhibitor. Cancer Sci. 2010 Oct;101(10):2207-13.

CAIndexNames:

1H-Pyrazole-1-carbothioamide, 3-(6-methyl-2-pyridinyl)-N-phenyl-4-(4-quinolinyl)-

SMILES:

S=C(N1N=C(C2=NC(C)=CC=C2)C(C3=CC=NC4=CC=CC=C34)=C1)NC5=CC=CC=C5

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