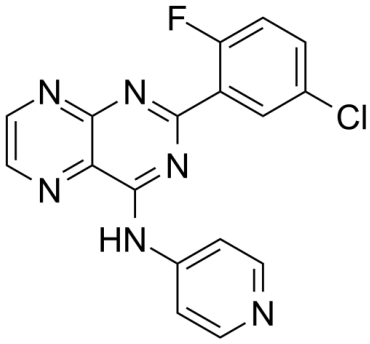
Data Sheet

Product Name:	SD-208
Cat. No.:	CS-0895
CAS No.:	627536-09-8
Molecular Formula:	C17H10ClFN6
Molecular Weight:	352.75
Target:	TGF-β Receptor
Pathway:	TGF-beta/Smad
Solubility:	DMSO : 9.09 mg/mL (25.77 mM; Need ultrasonic); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

SD-208 is a selective **TGF-βRI (ALK5)** inhibitor with **IC_{50}** of 48 nM, and > 100-fold selectivity over TGF-βRII. IC50 & Target: IC50: 48 nM (TGF-βRI) **In Vitro:** SD-208 inhibits the cell growth and constitutive and TGF-beta-evoked migration and invasion, and enhances immunogenicity in murine SMA-560 and human LN-308 glioma cells[1]. SD-208 blocks TGF-beta-induced phosphorylation of the receptor-associated Smads, Smad2 and Smad3, and stimulates epithelial-to-mesenchymal transdifferentiation, migration, and invasiveness into Matrigel in vitro[2]. SD-208 also abolishes the promoting effect of TGF-β on neointimal smooth muscle-like cell (SMLC) proliferation and migration in vitro[3]. **In Vivo:** SD-208 (1 mg/mL, p.o.) significantly prolongs the median survival of SMA-560 glioma-bearing mice[1]. In syngeneic 129S1 mice, SD-208 (60 mg/kg/d, p.o.) inhibits primary R3T tumor growth, and reduces the number and the size of lung metastases[2]. In the murine aortic allograft model, SD-208 effectively reduces the formation of intimal hyperplasia of transplant arteriosclerosis (TA)[3].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [1]Various kinase activities are assayed by measuring the incorporation of radiolabeled ATP into a peptide or protein substrate. The reactions are performed in 96-well plates and included the relevant kinase, substrate, ATP, and appropriate cofactors. The reactions are incubated and then stopped by the addition of phosphoric acid. Substrate is captured onto a phosphocellulose filter, which is washed free of unreacted ATP. The counts incorporated are determined by counting on a microplate scintillation counter. The ability of SD-208 to inhibit the respective kinase is determined by comparing counts incorporated in the presence of compound with those incorporated in the absence of compound. **Cell Assay:** [1]Glioma cells are cultured in the absence or presence of SD-208 (1 μM) for 48 hours. The cells are pulsed for the last 24 hours with [methyl-^{3}H]thymidine (0.5 μCi) and harvested, and incorporated radioactivity is determined in a liquid scintillation counter. **Animal Administration:** [1]VM/Dk mice are purchased from the TSE Resource Center. Mice of 6 to 12 weeks of age are used for the survival experiments. Groups of eight mice are anesthesized before all intracranial procedures and placed in a stereotaxic fixation device. A burr hole is drilled in the skull 2 mm lateral to the bregma. The needle of a Hamilton syringe is introduced to a depth of 3 mm. SMA-560 cells [5×10^3cells] resuspended in a volume of 2 μL of PBS are injected into the right striatum. Three days later, the mice are allowed to drink SD-208 at 1 mg/mL in deionized water. The mice are observed daily and, in the survival experiments, sacrificed on development of neurologic symptoms.

References:

[1]. Uhl M, et al. SD-208, a novel transforming growth factor beta receptor I kinase inhibitor, inhibits growth and invasiveness and enhances immunogenicity of murine and human glioma cells in vitro and in vivo. Cancer Res. 2004 Nov 1;64(21):7954-61.

[2]. Ge R, et al. Inhibition of growth and metastasis of mouse mammary carcinoma by selective inhibitor of transforming growth factor-beta type I receptor kinase in vivo. Clin Cancer Res. 2006 Jul 15;12(14 Pt 1):4315-30.

[3]. Sun Y, et al. Inhibition of intimal hyperplasia in murine aortic allografts by the oral administration of the transforming growth factor-beta receptor I kinase inhibitor SD-208. J Heart Lung Transplant. 2014 Jun;33(6):654-61.

CAIndexNames:

4-Pteridinamine, 2-(5-chloro-2-fluorophenyl)-N-4-pyridinyl-

SMILES:

FC1=CC=C(Cl)C=C1C2=NC3=NC=CN=C3C(NC4=CC=NC=C4)=N2

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