

Catalog Number: CM06624

产品信息

Catalog Number:
CM06624

CAS号:
1062368-24-4

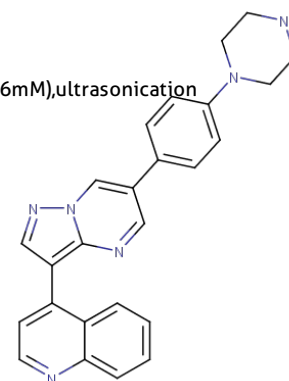
分子式:
C₂₅H₂₂N₆

主要靶点:
ALK|TGF-beta/Smad

主要通路:
蛋白酪氨酸激酶|血管生成|干细胞

分子量:
406.48

溶解度:
H₂O: Insoluble, DMSO: 1.45mg/ml (3.56mM), ultrasonication and adjustment of pH to 2 with HCL, 0.01M
HCL: 1.67mg/ml (4.1mM)



靶点活性

ALK2: 5 nM (C2C12 cells) | ALK3: 30 nM (C2C12 cells)

体外活性

LDN-193189 inhibited BMP4-mediated Smad1, Smad5 and Smad8 activation (IC₅₀: 5 nM). LDN-193189 efficiently inhibited the transcriptional activity of the BMP type I receptors ALK2 and ALK3 (IC₅₀s: 5/30 nM), with substantially weaker effects on activin and the TGF-β type I receptors ALK4, ALK5 and ALK7 (IC₅₀ ≥ 500 nM). LDN-193189 inhibited the induction of alkaline phosphatase activity in C2C12 cells by BMP4 even when administered 12 h after BMP stimulation [1]. Treatment of human aortic endothelial cells with LDN-193189 abrogated the production of reactive oxygen species induced by oxidized LDL. Treatment of mice with LDN-193189 lowered LDL serum cholesterol by 35% and markedly decreased hepatosteatosis without inhibiting HMG-CoA reductase activity. Treatment with BMP2 increased, whereas LDN-193189 inhibited apolipoprotein B100 secretion in HepG2 cells [2].

体内活性

Treatment of Ad.Cre-injected, caALK2-expressing mice with LDN-193189 (3 mg/kg i.p. every 12 h) prevented radiographic lesions at P15 in all mice examined. At P30, LDN-193189 prevented ectopic bone in approximately two-thirds of mice and attenuated lesions in the remainder, whereas at P60 LDN-193189 prevented ectopic bone in one-third of mice and attenuated lesions in the remainder. In contrast to vehicle-treated mice, LDN-193189-treated mice appeared to preserve knee and ankle joints at P30 and P60 [1]. Prolonged treatment of LDLR^{-/-} mice with LDN-193189 was well-tolerated and potentially inhibited development of atheroma, as well as associated vascular inflammation, osteogenic activity, and calcification [2]. Treatment of SCID mice bearing MDA-PCa-118b tumors with LDN-193189 significantly reduced tumor growth [3].

动物实验

In the first experiment, SCID mice were implanted with MDA-PCa-118b tumors. After 7 days when tumors reached measurable sizes, mice were injected with LDN-193189 (3 mg/kg) or with vehicle intraperitoneally twice a day. Tumor sizes and body weights were measured weekly. Mice were injected with calcein at three days and one day prior to sacrifice. Blood was collected and tumors were weighed. A portion of the tumors were fixed in formaldehyde for micro-computed tomography, using EVS CT, or further decalcified for bone histomorphometric analysis, using the OsteoMeasure Analysis System, or flash frozen for RNA preparation. Osteocalcin in the mouse serum was determined by ELISA. In the second experiment, PCa-118b tumors were first digested with Accumax, and the isolated cells were plated overnight, digested by Accutase, resuspended in Matrigel in 1:1 ratio, and injected into SCID mice (1 × 10⁶ cells/mouse) subcutaneously. Mice were treated with LDN-193189 five days post-injection [3].

细胞实验

C2C12 cells were seeded into 96-well plates at 2,000 cells per well in DMEM supplemented with 2% FBS. We treated the wells in quadruplicate with BMP ligands and LDN-193189 or vehicle. We collected the cells after 6 d in culture in 50 μl Tris-buffered saline and 1% Triton X-100. We added the lysates to p-nitrophenylphosphate reagent in 96-well plates for 1 h and then evaluated alkaline phosphatase activity (absorbance at 405 nm). We measured cell viability and quantity by Cell Titer Aqueous One (absorbance at 490 nm), using replicate wells treated identically to those used for alkaline phosphatase measurements [1].

描述

LDN193189 (DM 3189) is a selective BMP signaling inhibitor, inhibiting the transcriptional activity of ALK2 and ALK3 (IC₅₀s: 0.8/0.8/5.3/16.7 nM for ALK1/2/3/6).

储存

Powder: -20°C for 3 years | In solvent: -80°C for 2 years