For Research Use Only

Linsitinib

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Catalog Number: CM04707

产品信息

Catalog Number:
CM04707

CAS号:
867160-71-2

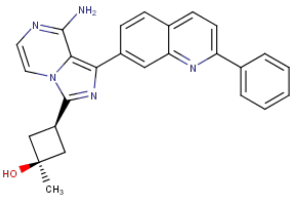
分子式:
$C_{26}H_{23}N_5O$

主要靶点:
IGF-1R

主要通路:
蛋白酪氨酸激酶

分子量:
421.49

溶解度:
Ethanol:< 1 mg/mL (insoluble or slightly soluble);DMSO:45 mg/mL (106.76 mM);H2O:< 1 mg/mL (insoluble or slightly soluble)



靶点活性

IGF-1R:35 nM|IRR:75 nM|Insulin receptor:75 nM

体外活性

Linsitinib通过与C-helix的相互作用使目标蛋白质呈现中间构象，抑制IGF-1R自磷酸化以及下游信号蛋白Akt、ERK1/2和S6激酶的激活，其IC50值为0.028至0.13 μM。Linsitinib在肝微粒体中表现出良好的代谢稳定性，并在1 μM浓度完全抑制IR和IGF-1R的磷酸化。此外，Linsitinib还能抑制包括非小细胞肺癌和结直肠癌（CRC）肿瘤细胞系在内的多种肿瘤细胞系的增殖，EC50值为0.021至0.810 μM。[1]

体内活性

Linsitinib在IGF-1R驱动的异种移植小鼠模型中抑制肿瘤生长，75 mg/kg剂量下实现100%的肿瘤生长抑制(TGI)和55%的肿瘤退缩，25 mg/kg剂量下实现60%的TGI且无肿瘤退缩。Linsitinib在狗、大鼠和小鼠体内展示不同的自身清除半衰期，分别为1.18小时、2.64小时和2.14小时。在雌性Sprague-Dawley大鼠和雌性CD-1小鼠中，Linsitinib不同单一剂量每日一次给药，显示其最大速率(Vmax)与剂量不成比例。12天给药后，25 mg/kg剂量的Linsitinib使血糖水平升高。在IGF-1R驱动的全长人IGF-1R(LISN)异种移植小鼠模型中，75 mg/kg单次剂量的Linsitinib在4至24小时内达到IGF-1R磷酸化的最大抑制（80%），血浆化合物浓度为26.6-4.77 μM。[1] 60 mg/kg剂量的Linsitinib在NCI-H292异种移植小鼠中单次给药后，在体内2、4和24小时抑制葡萄糖摄取，并抑制NCI-H292异种移植小鼠模型中的肿瘤生长。[2]

细胞实验

For assays of cell proliferation, cells are seeded into 96-well plates in appropriate media containing FCS 10% and incubated for 3 days in the presence of OSI-906 at various concentrations. Inhibition of cell growth is determined by luminescent quantitation of intracellular ATP content using CellTiterGlo. Data is presented as a fraction of maximal proliferation, calculated by dividing the cellular density in the presence of varying concentrations of OSI-906 by the cellular density of control cells treated with vehicle (DMSO) only.(Only for Reference)

储存

Powder: -20°C for 3 years | In solvent: -80°C for 1 year | Shipping with blue ice.