For Research Use Only

AT7519 Hydrochloride

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Catalog Number: CM03367

产品信息

Catalog Number:
CM03367

CAS号:
902135-91-5

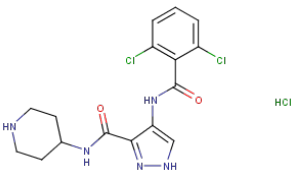
分子式:
$C_{16}H_{18}Cl_3N_5O_2$

主要靶点:
Apoptosis|CDK|GSK-3

主要通路:
干细胞|PI3K/Akt/mTOR 信号通路|凋亡|细胞周期

分子量:
418.71

溶解度:
H2O:1 mg/mL (2.38 mM);Ethanol:28 mg/mL (66.87 mM);DMSO:40 mg/mL (95.53 mM)



靶点活性

CDK4-CyclinD1:100 nM|CDK5-p35:13 nM|CDK2-CyclinA:47 nM|CDK9-CyclinT:<10 nM|GSK-3β:89 nM

体外活性

AT7519是一种与ATP竞争的CDK抑制剂，对CDK1的Ki值为38nM。除了对GSK3β（IC50=89nM）有活性外，AT7519对所有非CDK激酶均无活性。在多种人类肿瘤细胞系中表现出强大的抗增殖活性，IC50值从MCF-7的40nM到SW620的940nM不等，这与CDK1和CDK2的抑制一致。[1] AT7519在48小时内对多发性骨髓瘤（MM）细胞系产生剂量依赖性细胞毒性，IC50值从0.5μM到2μM不等，对MM.1S（0.5μM）和U266（0.5μM）细胞系最为敏感，对MM.1R（>2μM）耐药性较强。它不对周围血单个核细胞（PBMNC）产生细胞毒性。AT7519能部分克服IL6和IGF-1提供的增殖优势以及骨髓基质细胞（BMSCs）的保护作用。AT7519快速促使RNA聚合酶II CTD在丝氨酸2和丝氨酸5位点的去磷酸化，导致转录抑制，部分促成了对MM细胞的AT7519诱导的细胞毒性。通过下调GSK-3β磷酸化促进GSK-3β的激活，也为AT7519诱导的凋亡提供了帮助，这一过程与转录抑制无关。[2]

体内活性

每日两次给予AT7519（9.1 mg/kg）可以导致HCT116和HT29结肠癌异种移植模型中，无论是早期还是晚期的皮下肿瘤退化。[1] AT7519治疗（15 mg/kg）抑制了人类MM异种移植小鼠模型中的肿瘤生长，并通过增加caspase 3激活，延长了小鼠的中位总生存时间。[2]

细胞实验

Cells are incubated with different concentrations of AT7519 for 24 or 48 hours at 37°C. Cell viability is assessed by measuring 3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyl tetrasodium bromide (MTT) dye absorbance. DNA synthesis is measured by tritiated thymidine uptake (3H-TdR). Apoptosis is assessed by using Annexin V/PI staining. The percentage of cells undergoing apoptosis is defined as the sum of early apoptosis (Annexin V-positive cells) and late apoptosis (Annexin V-positive and PI-positive cells(Only for Reference)

储存

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