For Research Use Only

AZD-7762

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Catalog Number: CM03452

产品信息

Catalog Number:
CM03452

CAS号:
860352-01-8

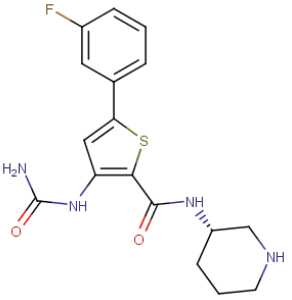
分子式:
$C_{17}H_{19}FN_4O_2S$

主要靶点:
Chk

主要通路:
细胞周期

分子量:
362.42

溶解度:
H2O:< 1 mg/mL (insoluble or slightly soluble);DMSO:47 mg/mL (129.7 mM);Ethanol:< 1 mg/mL (insoluble or slightly soluble)



靶点活性

Chk1:5 nM

体外活性

AZD7762，作为一种选择性更强的Chk1抑制剂，通过可逆地结合到Chk1的ATP结合位点，抑制cdc25C肽的Chk1磷酸化作用，其IC50为5 nM，Ki为3.6 nM。AZD7762以EC50为0.620 μM的浓度引起细胞阻滞，并且通过阻断chk1依赖的Cdc25A降解和Cyclin A激活，显著消除了以EC50为10 nM的浓度的喜树碱诱导的G2阶段阻滞。在300 nM浓度下，AZD7762增强了对SW620细胞的吉西他滨和对MDA-MB-231细胞的拓扑替康的抗肿瘤效果，将GI50值分别从24.1 nM和2.25 μM减少到1.08 nM和0.15 μM。[1]
AZD7762还对携带p53野生型、p53突变、Mdm2扩增或p14缺失的多种神经母细胞瘤细胞系显示出IC50值在82.6-505.9 nM范围内的细胞毒性。[2]

体内活性

AZD7762以25 mg/kg的剂量，在H460-DNp53移植小鼠和SW620移植小鼠中几乎不显示出抗肿瘤活性；但与吉西他滨（60 mg/kg）联合应用时，在两种移植小鼠中表现出显著的抗肿瘤效果，低剂量（12.5 mg）下的细胞杀伤量为0.9或治疗对照组百分比（%T/C）为26。在H460-DNp53移植大鼠中，AZD7762与吉西他滨（10 mg/kg）联合给药能够以剂量依赖性方式抑制肿瘤体积，10和20 mg/kg AZD7762的%T/C值分别为48和32。在与伊立替康（25或50 mg/kg）联合应用时，AZD7762（25 mg/kg）能够使SW620移植小鼠中的肿瘤完全消退，%T/C值显著增加至-66%和-67%。[1]

细胞实验

For the checkpoint abrogation assay, HT29 cells are treated for 2 hours with camptothecin (topoisomerase I inhibitor; 0.07 μg/mL) to induce the G2 checkpoint. Cells are then treated for 20 hours with a 12-point titration of AZD7762 (12.5 μM to 6 nM) plus nocodazole. Cells are fixed with 3.7% formaldehyde for 1 hour, permeabilized with PBS containing 0.05% Triton X, and incubated with anti-phH3 antibody for 1 hour followed by Alexa Fluor 488 anti-rabbit and Hoechst stain for 1 hour. Mitotic index is determined on the ArrayScan and expressed as the percentage of cells undergoing mitosis. For the potentiation assays, SW620 or MDA-MB-231 cells are dosed for 24 hours with a 9-point titration of gemcitabine ranging from 0.01 to 100 nM with a constant dose of AZD7762 (300 nM). After 24 hours, medium is removed and AZD7762 alone is added back to the wells for an additional 24 hours. Cells are then incubated in AZD7762-free medium for an additional 72 hours. The effect on cell proliferation is determined by MTT.(Only for Reference)

储存

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

This product is exclusively available under Proteintech Group brand and is not available to purchase from any other manufacturer.