For Research Use Only

Dinaciclib

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Catalog Number: CM01201

产品信息

Catalog Number:
CM01201

CAS号:
779353-01-4

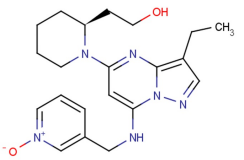
分子式:
$C_{21}H_{28}N_6O_2$

主要靶点:
Apoptosis|CDK

主要通路:
细胞周期|凋亡

分子量:
396.49

溶解度:
DMSO:25 mg/mL (63.1 mM),Ethanol:8 mg/mL (20.17 mM),warmed



靶点活性

CDK2:1 nM (cell free)|CDK1:3 nM (cell free)|CDK5:1 nM (cell free)|CDK9:4 nM (cell free)

体外活性

Dinaciclib (SCH 727965) inhibits CDK2, CDK5, CDK1, and CDK9 activity in vitro with IC50 values of 1, 1, 3, and 4 nmol/L, respectively. In cell-based assays, SCH 727965 completely suppressed retinoblastoma phosphorylation, which correlated with apoptosis onset and total inhibition of bromodeoxyuridine incorporation in >100 tumor cell lines of diverse origin and background [1]. SCH 727965 (SCH) induces the apoptosis of several osteosarcoma cell lines including those resistant to doxorubicin and dasatinib. Apoptosis occurred at low nanomolar concentrations of SCH, as did CDK inhibition, and was p53-independent [2]. Treatment with SCH727965 significantly reduced in vitro cell growth, motility and colony formation in soft agar of MIAPaCa-2 and Pa20C cells [3].

体内活性

SCH 727965 induced regression of established solid tumors in a range of mouse models following intermittent scheduling of doses below the maximally tolerated level [1]. Single-agent therapy with SCH727965 (40 mg/kg i.p. twice weekly) for 4 weeks significantly reduced subcutaneous tumor growth in 10/10 (100%) of tested low-passage human pancreatic cancer xenografts. Treatment of low passage pancreatic cancer xenografts with a combination of SCH727965 and gemcitabine was significantly more effective than either agent alone [3].

动物实验

For tumor implantation, specific cell lines were grown in vitro, washed once with PBS, and resuspended in 50% Matrigel in PBS to a final concentration of 4 × 10^7 to 5 × 10^7 cells per milliliter. Nude mice were injected with 0.1 mL of this suspension s.c. in the flank region. Tumor length (L), width (W), and height (H) were measured by a caliper twice weekly on each mouse and then used to calculate tumor volume using the formula (L × W × H)/2. When the tumor volume reached ~100 mm^3, the animals were randomized to treatment groups (10 mice/group) and treated i.p. with either SCH 727965 or individual chemotherapeutic agents according to the dosing schedule indicated in table and figure legends. Tumor volumes and body weights were measured during and after the treatment periods. Data were expressed as means ± SEM. Animals were euthanized according to the Institutional Animal Care and Use Committee guidelines [1].

细胞实验

A2780 cells were plated into six-well tissue culture dishes and allowed to adhere. Cells were then exposed to differing concentrations of SCH 727965 or a DMSO control vehicle for 24 hours, followed by a brief (30 min) pulsed exposure to bromodeoxyuridine (BrdUrd). Cells were then harvested, immunostained using FITC-conjugated antibodies specific for BrdUrd, counter-stained with propidium iodide/RNase A solution, and analyzed using flow cytometry. Fluorescence-activated cell sorting analyses were done on a FACSCalibur instrument. FITC-positive BrdUrd staining and propidium iodide signal allowed assessment of ongoing DNA replication and the cell cycle stage. Percentages of the cell population in each cell cycle stage were plotted for each test article concentration [1].

描述

Dinaciclib is a new-type and effective CDK inhibitor for CDK2/5/1/9 (IC50: 1 nM/1 nM/3 nM/4 nM) with potential antineoplastic activity.

储存

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