For Research Use Only

Luminespib

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Catalog Number: CM04651

产品信息

Catalog Number:
CM04651

CAS号:
747412-49-3

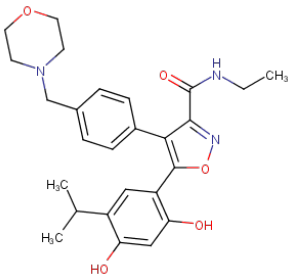
分子式:
$C_{26}H_{31}N_3O_5$

主要靶点:
Apoptosis|Autophagy|HSP

主要通路:
代谢|自噬|凋亡|细胞骨架

分子量:
465.54

溶解度:
Ethanol:29 mg/mL (62.3 mM),DMSO:86 mg/mL (184.7 mM),H2O:<1 mg/mL



靶点活性

HSP90β :21 nM (cell free)|HSP90α :7.8 nM (cell free)

体外活性

Luminespib (NVP-AUY922) potently inhibits HSP90 (Kd = 1.7 nmol/L) and proliferation of human tumor cells with GI50 values of approximately 2 to 40 nmol/L, inducing G(1)-G(2) arrest and apoptosis [1]. In 11 human gastric cancer cell lines, The IC50 values of NVP-AUY922 fell in the nanomolar range of 2–40 nM. The IC50 values for the cell lines NCI-N87 and SNU-216, cells with HER-2 amplification, were 3.23 nM and 11.99 nM, respectively [2]. NVP-AUY922 inhibited the proliferation of oral squamous cell carcinoma cells in vitro. NVP-AUY922 caused degradation of client protein inducing ErbB2, p-Akt, p-S6, HIF1-α and VEGF and up-regulation of HSP70 in HSC-2 oral squamous cell carcinoma [3].

体内活性

Daily dosing of NVP-AUY922 (50 mg/kg i.p. or i.v.) to athymic mice generated peak tumor levels at least 100-fold above cellular GI(50). This produced statistically significant growth inhibition and/or regressions in human tumor xenografts with diverse oncogenic profiles: BT474 breast tumor treated/control, 21%; A2780 ovarian, 11%; U87MG glioblastoma, 7%; PC3 prostate, 37%; and WM266.4 melanoma, 31% [1]. Luminespib was administered at 50 mg/kg daily i.p. to athymic mice bearing HCT116 human colon carcinoma xenografts. The rate of tumor growth was significantly inhibited by Luminespib administration, and treated tumor weights measured at day 12 were 49.8% of the control values [4].

动物实验

In vivo, pharmacokinetic studies in female NCr athymic mice bearing WM266.4 human melanoma xenografts were essentially as described. NVP-AUY922 was dissolved in DMSO and diluted in sterile saline/Tween 20. A single dose of 50 mg/kg NVP-AUY922 was given i.v. or i.p. and groups of three animals were taken at intervals for pharmacokinetic analyses [1].

细胞实验

Cell lines were grown in DMEM/10% FCS, 2 mmol/L glutamine, and nonessential amino acids in a humidified atmosphere of 5% CO2 in air. All lines were free of Mycoplasma. Cell proliferation was determined using the sulforhodamine B (SRB) assay for tumor cells and prostate epithelial cells, the WST-1 assay for MCF10A and HB119, or an alkaline phosphatase assay for HUVEC and HDMEC. GI50 was the compound concentration inhibiting cell proliferation by 50% compared with vehicle controls. Cell cycle analysis was as described. Active caspase-3/7 was measured using a homogenous caspase assay kit [1].

描述

AUY922 (NVP-AUY922) is a new-type inhibitor of HSP90 (IC50s: 7.8/21 nM for HSP90α / β in cell free assay).

储存

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