

Catalog Number: CM00837

产品信息

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CM00837

CAS号:
955365-80-7

分子式:
C₂₇H₃₂N₈O₂

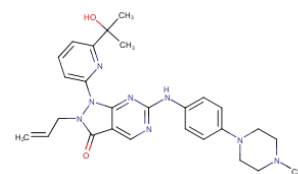
主要靶点:
Wee1

主要通路:
细胞周期

分子量:
500.6

溶解度:

H₂O:< 1 mg/mL (insoluble or slightly soluble); DMSO:50 mg/mL (99.88 mM); Ethanol:< 1 mg/mL (insoluble or slightly soluble)



靶点活性

Wee1:5.2 nM (cell free)

体外活性

方法: 人结肠癌细胞 WiDr 和人肺癌细胞 H1299 用 gemcitabine (0-100 nM) 处理 24 h, 随后用 Adavosertib (30-300 nM) 处理 24 h, 使用 WST-8 assay 检测细胞活力。结果: 在 WiDr 细胞中, 单独 gemcitabine 在细胞活力测定中的 IC₅₀ 值大于 100.0 nmol/L。Adavosertib 联合治疗显著增强了 gemcitabine 的抗生长作用。与 30 和 100 nmol/L 的 Adavosertib 共同处理将 IC₅₀ 分别降低到 21.5 和 7.1 nmol/L。在另一种 p53 缺乏型癌细胞系 H1299 中观察到 gemcitabine 的类似增强作用。[1] **方法:** 人肺癌细胞 H1299 和 A549 用 Adavosertib (200 nmol/L) 处理 1 h, 随后后 7.5 Gy 照射 4-24 h, 使用 flow cytometry 检测细胞周期。结果: 在用 Adavosertib + 辐射处理的 H1299 细胞中, 细胞继续进行 G₂/M, 没有实质性积累。与单独辐射相比, Adavosertib 基本上没有改变照射的 A549 细胞在 G₂/M 中的积累。[2]

体内活性

方法: 为测试体内抗肿瘤活性, 用 Adavosertib (60 mg/kg, 灌胃给药) 和 1 Gy 辐照处理携带人肺癌肿瘤 Calu-6 的 Ncr Nu/Nu 小鼠, 每天两次, 持续五天。结果: 药物/辐射组合显著增强了肿瘤生长延迟。当肿瘤每天两次以 1Gy 照射 5 天, 并且在照射的同一天每天两次给予 60mg/kg Adavosertib 时, 观察到最大的反应。[2]

动物实验

Subcutaneous xenograft tumors were formed by injection of the human cancer cell lines in the hind flank of immunodeficient nude rats (F344/NJcl-rnu). To facilitate tumor formation, cells were injected in medium containing Matrigel, a solubilized basement membrane preparation extracted from the Engelbreth-Holm-Swarm mouse sarcoma. Gemcitabine, carboplatin, and cisplatin were dissolved or diluted in saline and were dosed i.v. MK-1775 was prepared in a vehicle of 0.5% methylcellulose solution and was dosed p.o. 24 h after dosing DNA-damaging agents. For efficacy studies, tumor volumes were measured with a caliper every 3 d and body weights were determined each weekday. Statistical analysis was done using repeated-measure ANOVA followed by Dunnett's test for relative tumor volume. T/C (%) was calculated as $(\Delta T / \Delta C) \times 100$ if $\Delta T > 0$ or $(\Delta T / T_i) \times 100$ if $\Delta T < 0$. ΔT was the change in mean tumor volume to the initial tumor volume for the treatment group, and ΔC was the change in mean tumor volume to the initial tumor volume for the vehicle control group. T_i was the initial tumor volume of the treatment group [1].

细胞实验

Tumor cells were cultured in 96-well plates and incubated with DNA-damaging agents for 24 h, then with MK-1775 and nocodazole for additional 8 h. For p-CDC2Y15 assay, cells were lysed and subjected in a colorimetric ELISA to determine the amounts of p-CDC2Y15 (1:100) and total CDC2 (1:200). For phospho-histone H3 (pHH3), cells were fixed with methanol, stained with anti-pHH3 specific antibody and bound antibody was stained with Alexa Fluor 488 goat anti-rabbit antibody. Images were acquired with an INCell Analyzer 1000 [1].

储存

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