For Research Use Only

(+)-JQ-1

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Catalog Number: CM00812

产品信息

Catalog Number:
CM00812

CAS号:
1268524-70-4

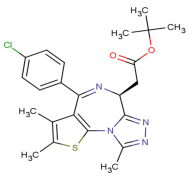
分子式:
$C_{23}H_{25}ClN_4O_2S$

主要靶点:
Epigenetic Reader Domain|Autophagy|Ligands for Target Protein for PROTAC

主要通路:
表观遗传|PROTAC|自噬

分子量:
456.99

溶解度:
DMSO:29.41 mg/mL (64.36 mM),Sonification is recommended.,Ethanol:45.7 mg/mL (100 mM)



靶点活性

BRD4 (1):77 nM(cell free)|BRD4 (2):33 nM(cell free)

体外活性

Binding of a tetra-acetylated Histone H4 peptide to BRD4 was strongly inhibited by (+)-JQ1, with IC50 values of 77 nM and 33 nM for the first and second bromodomain, respectively. Compared to vehicle control, JQ1 (500 nM) markedly accelerated time to half fluorescence recovery in photobleached regions of cells transfected with GFP-BRD4-NUT. Treatment of the patient-derived 797 NMC cell line for 48 hours with JQ1 (500 nM) effaces nuclear foci, producing diffuse nuclear NUT staining by IHC [1]. MM cell proliferation was uniformly inhibited by JQ1, including several MM cell lines selected for resistance to FDA-approved agents (dexamethasone-resistant MM.1R and melaphalan-resistant LR5) [2].

体内活性

A marked reduction in 18F-fluorodeoxyglucose (FDG) uptake was observed with JQ1 treatment (50 mg/kg), whereas vehicle-treated animals demonstrated progressive disease. A reduction in tumor growth with JQ1 treatment [1]. Treatment of mice with JQ1 reduced seminiferous tubule area, testis size, and spermatozoa number and motility without affecting hormone levels. Although JQ1-treated males mate normally, inhibitory effects of JQ1 evident at the spermatocyte and round spermatid stages cause a complete and reversible contraceptive effect [3]. Raji BL tumors grew significantly slower in (+)-JQ1-treated (twice a day at 30 mg/kg or once a day at 50 mg/kg, i.p.) mice compared with vehicle-treated controls. In this model, the average tumor volume was 45% smaller in the compound-treated group at day 14 [4].

动物实验

(Harlan) inoculated s.c. with 3 × 10^6 cells per mouse resuspended in 10% Matrigel. Two weeks later (average tumor volume 150 mm3), mice were assigned into two groups: 15 mice were treated with vehicle control (5:95 DMSO:10% 2-Hydroxypropyl- β -cyclodextrin), and 15 mice were treated with 30 mg/kg (+)-JQ1 by i.p. injection twice a day for 28 d. Body weight and tumor volume were measured daily. Tumor volume was calculated from caliper measurements by using the following formula: W × H × L × 0.52. Mice were killed when tumor volume reached 2,000 mm3, when body weight decreased >20% of initial weight, or when the mice were in poor health as established in the IACUC protocol. Survival was plotted and analyzed in GraphPad Prism software, and statistical significance was calculated by using log-rank (Mantel-Cox) and Gehan–Breslow–Wilcoxon tests. MV4-11 xenografts were established in nude mice injected with 10 × 10^6 cells per mouse. JQ1 was dosed i.p. and formulated as described above. Mice were divided into 4 groups of 10 animals: vehicle control once a day; 50 mg/kg (+)-JQ1 once a day; 30 mg/kg (+)-JQ1 twice a day; and cytarabine 100 mg/kg daily (5 d on, 2 d off). Treatment of mice with cytarabine at 100 mg/kg resulted in significant weight loss at day 8 and, therefore, the dose needed to be decreased to 75 mg/kg [4].

细胞实验

Cells were plated at 5,000 cells per well of 96-well plates containing titrations of the compounds as indicated. After incubation, the cells were washed once with PBS and resuspended in 175 μL of ice-cold 70% ethanol and fixed for a minimum of 16 h at 4 °C. The cells were pelleted and washed 1× with PBS and stained for 30 min at room temperature (RT) with 120 μL of staining solution [propidium iodide (20 μg/mL), RNase A (25 μg/mL), 0.1% Triton X-100 in PBS]. Cell number and cell cycle data were obtained by using a flow cytometer using the Express Pro module. DNA content histograms were analyzed by using ModFit LT 3.2 Software. To calculate the number of viable cells in each well, the concentration of events measured using the Guava was multiplied by the volume of cells in the well, then by the fraction of cells in G1+S+G2/M. GI50 values for each cell line were calculated as the concentration of compound giving a 50% reduction in cell number relative to the DMSO control [4].

描述

(+)-JQ1 is a BET bromodomain inhibitor (IC50: 77 nM/33 nM for BRD4 (1/2)).

储存

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