For Research Use Only

Bortezomib

www.ptgcn.com

Catalog Number: CM00034

产品信息

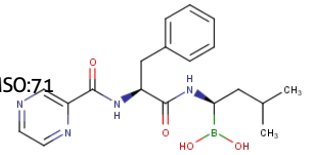
Catalog Number:
CM00034

CAS号:
179324-69-7

分子式:
$C_{19}H_{25}BN_4O_4$

分子量:
384.24

溶解度:
Ethanol:Insoluble,H2O:Insoluble,DMSO:71 mg/mL (184.8 mM)



主要靶点:
Proteasome|Autophagy|Apoptosis|NF-κB

主要通路:
蛋白酶体|NF-κB信号通路|自噬|凋亡|泛素化

靶点活性

20S proteasome:0.6 nM (cell free)

体外活性

The average growth inhibition of 50% (GI50) value for Bortezomib across the entire NCI cell panel was 7 nM. Bortezomib was shown to penetrate into cells and inhibit proteasome-mediated intracellular proteolysis of long-lived proteins (IC50: ~0.1 μM) [1]. Exposure to bortezomib has been shown to stabilize p21, p27, and p53, as well as the proapoptotic Bid and Bax proteins, caveolin-1. Bortezomib also promoted the activation of the proapoptotic c-Jun-NH2 terminal kinase, as well as the endoplasmic reticulum stress response [2]. Bortezomib (0.01-10 μM) treatment caused cell accumulation at the G2-M phase and induced cell apoptotic death in a concentration-dependent manner. The slower mobility of the Bcl-2 band corresponded to the phosphorylation of the Bcl-2 protein and could be seen in the cells exposed to 0.01–0.05 μM Bortezomib for 24 h. Another slower band could be discerned, which corresponded to a superphosphorylated form of Bcl-2, and was detected when cells were exposed to higher concentrations of Bortezomib (0.1–10 μM) for 24 h [3].

体内活性

On 4 consecutive days, Bortezomib (1.0 mg/kg) was administered (in 10 μl) into established PC-3 tumors, and results showed a dramatic decrease in tumor burden. In addition to the large decrease in tumor volume (70%), two of five mice (40%) had no detectable tumors at the end of the study [1]. The mice were injected s.c. with 3 x 10(7) RPMI-8226 myeloma cells. When tumors became measurable, mice were assigned to treatment groups receiving Bortezomib 0.05 mg/kg, 0.1 mg/kg, 0.5 mg/kg, or 1.0 mg/kg twice weekly via the tail vein, or to control groups receiving the vehicle only. Significant inhibition of tumor growth, even with some complete tumor regression, was observed in Bortezomib-treated mice. The median overall survival was also significantly prolonged compared with controls [4].

动物实验

Mice were inoculated s.c. into the right flank with 3 × 10^7 MM cells in 100 μl of RPMI 1640, together with 100 μl of Matrigel basement membrane matrix. When tumor was measurable, mice were assigned into four treatment groups receiving PS-341 or into a control group. Treatment with PS-341 was given i.v. twice weekly via tail vein at 0.05, 0.1, 0.5, and 1.0 mg/kg for 4 weeks. Subsequently, it was administered once weekly. The control group received the vehicle alone (0.9% sodium chloride) at the same schedule. Caliper measurements of the longest perpendicular tumor diameters were performed every alternate day to estimate the tumor volume, using the following formula: 4π/3 × (width/2)^2 × (length/2), representing the three-dimensional volume of an ellipse. Animals were sacrificed when their tumors reached 2 cm or when the mice became moribund. Survival was evaluated from the first day of treatment until death [4].

细胞实验

PC-3 cells were treated with different doses of PS-341 for different periods of time. The cells were washed with PBS, harvested, and fixed in suspension with 3.7% formaldehyde in the neutral buffer for 10 min at room temperature. The cells were centrifuged, and the cell pellet was resuspended in 0.5 ml of 80% ethanol. The cell suspension (25–50 μl) was then placed onto a microscope slide precoated with poly-l-lysine and air-dried. The slides were washed four times with 0.1% Triton X-100 in PBS. The slide was incubated with the DNA stain Hoechst 33342 (Molecular Probes; 1.0 μg/ml in PBS with 0.1% Triton-X-100) for 1.0 min. The slides were rinsed in PBS and mounted with 70% glycerol containing 25 mg/ml 1,4-diazabicyclo[2.2.2]octane. Nuclear staining was visualized using a fluorescent microscope [1].

描述

Bortezomib (PS-341) is a potent 20S proteasome inhibitor (Ki: 0.6 nM, in a cell-free assay).

储存

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