Bortezomib

Bortezomib (BAN, INN and USAN; marketed as Velcade by Millennium Pharmaceuticals; Neomib by Getwell and Bortecad by Cadila Healthcare) is an anticancer drug and the first therapeutic proteasome inhibitor to be used in humans.

In some cancers, the proteins that normally kill cancer cells are broken down too quickly. Bortezomib interrupts this process and lets those proteins kill the cancer cells. It is approved in the U.S. and Europe for treating relapsed multiple myeloma and mantle cell lymphoma.

In multiple myeloma, complete clinical responses have been obtained in patients with otherwise refractory or rapidly advancing disease.

Bortezomib for Glioblastoma

see Bortezomib for Glioblastoma.

Beehler et al. studied the effect in denervated skeletal muscle in rats. Rats were given vehicle or Velcade (3 mg/kg po) daily for 7 days beginning immediately after induction of muscle atrophy by crushing the sciatic nerve. At the end of the study, the rats were euthanized and the soleus and extensor digitorum longus (EDL) muscles were harvested. In vehicle-treated rats, denervation caused a 33.5 +/- 2.8% and 16.2 +/- 2.7% decrease in the soleus and EDL muscle wet weights (% atrophy), respectively, compared to muscles from the contralateral (innervated) limb. Velcade significantly reduced denervation-induced atrophy to 17.1 +/- 3.3% in the soleus ($P < 0.01$), a 51.6% reduction in atrophy associated with denervation, with little effect on the EDL (9.8 +/- 3.2% atrophy). Histology showed a preservation of muscle mass and preservation of normal cellular architecture after Velcade treatment. Ubiquitin mRNA levels in denervated soleus muscle at the end of the study were significantly elevated 120 +/- 25% above sham control levels and were reduced to control levels by Velcade. In contrast, testosterone proprionate (3 mg/kg sc) did not alleviate denervation-induced skeletal muscle atrophy but did prevent castration-induced levator ani atrophy, while Velcade was without effect. These results show that proteasome inhibition attenuates denervation-induced muscle atrophy in vivo in soleus muscles. However, this mechanism may not be operative in all types of atrophy [1)].

Proteasome inhibitors reduce vascular thrombotic and inflammatory events and consequently protect vascular function. In a study Qu et al. evaluated the neuroprotective effect of Velcade (bortezomib), a potent and selective inhibitor of proteasomes, which is in clinical use for the treatment of multiple myeloma. When administered within 2 h after TBI onset, Velcade reduced inflammatory responses, lesion volume, and neurological functional deficits, and enhanced neuronal survival. Western blot and ELISA showed that Velcade decreased the expression of NF-κB. These results suggest that in the experimental setting, Velcade is an effective neuroprotective agent for the treatment of TBI [2)].

1)

Beehler BC, Sleph PG, Benmassaoud L, Grover GJ. Reduction of skeletal muscle atrophy by a

proteasome inhibitor in a rat model of denervation. Exp Biol Med (Maywood). 2006 Mar;231(3):335-41. PubMed PMID: 16514182.

2)

Qu C, Mahmood A, Ning R, Xiong Y, Zhang L, Chen J, Jiang H, Chopp M. The treatment of traumatic brain injury with velcade. J Neurotrauma. 2010 Sep;27(9):1625-34. doi: 10.1089/neu.2010.1359. PubMed PMID: 20649468; PubMed Central PMCID: PMC2966855.

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