CHARACTERIZATION OF THE NEUROTOXICITY AND ANTINEOPLASTIC ACTIVITY OF BORTEZOMIB IN A NEW MYELOMA-BEARING MURINE MODEL

Valentina Alda Carozzi*, Cristina Meregalli, Alessia Chiorazzi, Barbara Sala, Norberto Oggioni, Guido Cavaletti
Neuroscience and Biomedical Technologies Dpt, University of Milan-Bicocca, Via Cadore 48, 20900, Monza (MB).
*e-mail: valentina.carozzi1@unimib.it

Bortezomib (BTZ) is an effective antineoplastic drug for the treatment of multiple myeloma. Its clinical use induce the development of a peripheral neuropathy characterized by sensory alterations and neuropathic pain.
Rat models of BTZ-induced peripheral neuropathy had been established. However, since only a few cancer cell lines induce the development of cancer in the rat, these models don't represent the most effective way to study, at the same time, the antineoplastic activity and the neurotoxic effects of BTZ.
Here, immunodeficient SCID mice were s.c injected with RPMI8266 human myeloma cells. Three weeks after tumour injection, mice were i.v treated with BTZ 1 mg/kg once a week for five weeks. The tumour volume was assessed as a measure of BTZ antitumor activity; the mechanical nociceptive threshold and nerve conduction velocities were measured to assess the neuropathic pain and the toxic effect of BTZ on the peripheral nervous system, respectively.
Starting from the first administration, BTZ 1 mg/Kg was able to block tumour-growth but inducing the development of mechanical allodynia and an impairment of nerve functions. Interestingly, myeloma itself seemed to be able to induce mild functional alterations of peripheral nerves.
This mouse model and treatment schedule allowed the study of the antineoplastic activity and of the neurotoxic effects of BTZ at the same time. Moreover, a preliminary evaluation of the effect of myeloma itself on the peripheral nervous system was assessed.
This animal model should be used in the preclinical discovery of new neuroprotective as well as of analgesic compounds.

This work was partially sponsored by
POR della Lombardia OB. 2 FSE 2007-2013, Asse IV - Sviluppo del Capitale Umano