EVALUATION OF THE NEUROPROTECTIVE EFFECT OF ACETYL-L-CARNITINE IN MYELOMA-BEARING MICE TREATED WITH BORTEZOMIB.

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Bortezomib (BTZ) is a highly effective and widely used antineoplastic drug for the treatment of multiple myeloma. Despite its effectiveness, the use of this proteasome inhibitor is limited by its toxicity and in particular peripheral neurotoxicity is a major and clinically-relevant problem and an unsolved issue.
The administration of Acetyl-L-Carnitine (ALC) in rat models of different peripheral neuropathies induced by other antineoplastic drugs has evidenced a neuroprotective effect of ALC.
To investigate the neuroprotective role of ALC, we used a multiple myeloma-bearing animal model in which *scid* mice were iv treated with BTZ 1 mg/kg (q7dx5) or ALC 200 mg/kg/daily (qdx5/wx5w) alone or in co-treatment. Mice were s.c. injected into the right flank with $10x10^6$ cell/0.1 mL/mouse of RPMI-8226 multiple myeloma. Treatments started three days after tumor injection. Aim of our study was to evaluate if the co-administration of ALC was able to prevent the peripheral neurotoxicity induced by BTZ chronic treatments.
The results of this study evidenced that the administration of BTZ was able to induce significant neurophysiological changes vs. vehicle-treated animals in conduction velocity in the caudal and digital nerves and in potential amplitude in the digital nerve. The same results were observed in nerve conduction velocities in the BTZ+ALC treated mice, while the potential amplitude in the digital nerve was not significantly different from vehicle-treated animals in BTZ+ALC mice.
Moreover, the administration of BTZ induced evident pathological changes vs. vehicle-treated animals in the caudal sciatic nerve or dorsal root ganglia (DRG). The same changes were observed in the BTZ+ALC treated mice, although in the caudal nerve an evident trend toward a less severe effect of BTZ administration was present in the animals co-treated with ALC.
In conclusion, although not all the parameters investigated in this study evidenced a positive effect, a neuroprotective activity of ALC could be evidenced in the caudal nerve investigated at the pathological level and in the amplitude of the potential measured in the digital nerve.