PREVENTION OF NEUROTOXICITY WITH DOCOSAHEXAENOIC ACID AND ALPHA LIPOIC ACID IN PATIENTS WITH MULTIPLE MYELOMA: PRELIMINARY DATA

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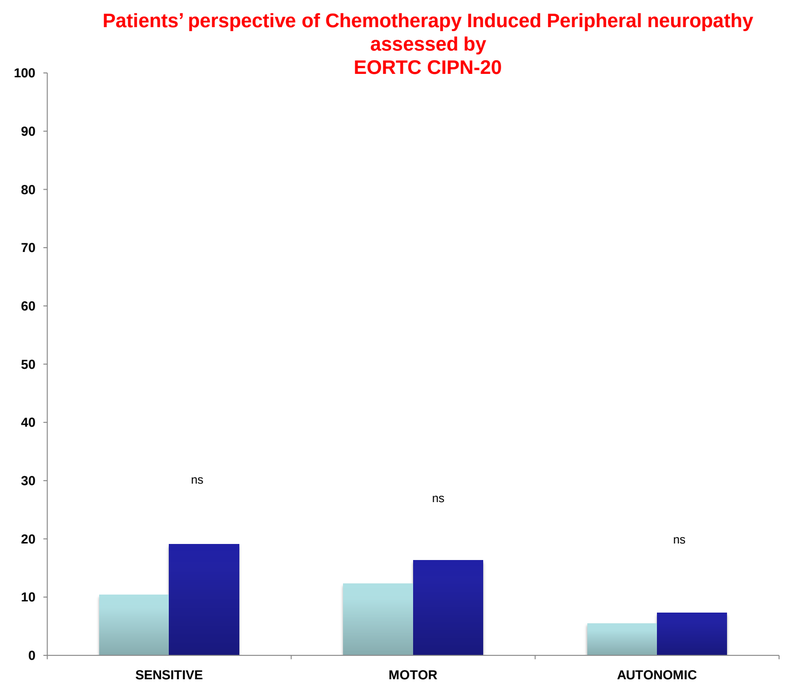
Introduction:
Neurotoxicity is a common complication of chemotherapy (CT) that is usually dose-dependent and can induce marked disability that negatively affect the quality of life in patients with Multiple Myeloma (MM). Among newly diagnosed MM patients, up to 54% are suffering from polyneuropathy (PN).

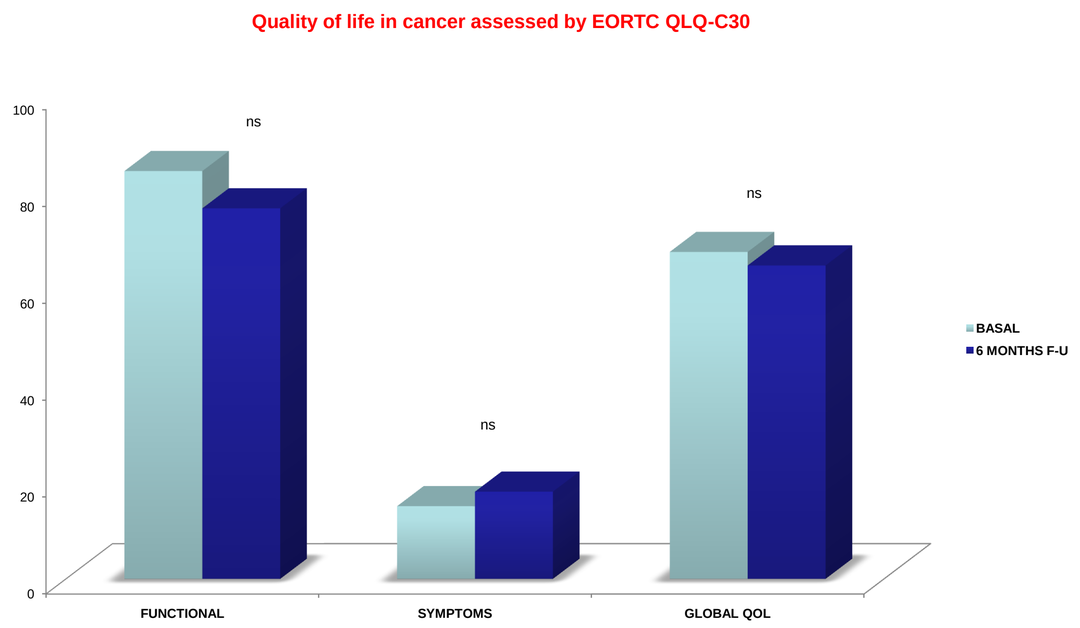
Using Bortezomib, a first line CT for MM, grade 1 and 2 neurotoxicity can occur in 33 % of patients newly diagnosed, while grades 3 and 4 neurotoxicity are present in 18 % of newly diagnosed patients.
Delay or prevention of the onset of toxicity could be very important in these patients.
To date the American Society of Clinical Oncology Clinical practice published on guidelines some therapy to reduce existing CIPN, but no agents were recommended for the prevention.
Literature data indicate that the association of docosahexaenoic acid (DHA) and alpha lipoic acid (ALA) can be useful in reducing inflammation and promoting the formation of new axons and intersynaptic connections thus protecting from or slowing down CT neurotoxicity.

For that reason we conducted a Phase II prospective study to evaluate the effect of new neuroprotective compound (DHA 400 mg, ALA 600 mg, Vit C 60 mg, Vit E 10 mg bid) on 33 patients with MM, for whom Bortezomib has been indicated as a first line CT.
We report preliminary data on 18 patients (out of 33) that completed the current study (6 months).

Methods:
At first visit and at finally follow-up (6 months) neuropathy was evaluated with:
neurological visit, electroneurography (ENG), Common Terminology Criteria for Adverse Event (CTCAE), reduce version of Total Neuropathic Score (TNSr), auto-evaluation of pain (Visual Analog Scale – VAS); Quality of Life and Functional evaluation using: EORTC QLQ-C30 scale for the evaluation of functioning status, symptoms and quality of life of the oncological patient; EORTC QLQ-CIPN20 scale for the evaluation of the chemotherapy induced peripheral neuropathy; scale of Daily Life Activities (ADL/IADL).
At first visit patients assumed a tablet containing DHA 400 mg, ALA 600 mg, Vit C 60 mg, Vit E 10 mg bid for all follow-up period.

Results:
18 patients (F 7, M 11; mean age 69.0). All patients were in CT with BTZ, according hematological treatment schedule of 1.3mg/mq.
At 6 months: no patient interrupted chemotherapy and only 1 patient reduced the 50% dose but for hematologic toxicity and no patients reported side effects due to DHA 400 mg, ALA 600 mg, Vit C 60 mg, Vit E 10 mg
55.5% of patients (10/18) achieved CTCAE scores for mild sensory peripheral neuropathy, but no patient reached grade II, indicative of moderate PN.
All TNSr scores remained stable within the range of mild neurotoxicity, and no patient reached at least 10 at TNSr, indicative of moderate neurotoxicity.
One patient showed the appearance of a painful symptomatology but did not require specific therapy; even VAS scores confirm the absence of pain remaining stable (median 0.4).
Scores on ADL, IADL and QoL scales (EORTC-QLQC30) remain firmly indicative of a preserved and complete functional autonomy and the persistence of a good QoL (Mean ADL / IADL score: 6/6 and 8/8; Mean Global QoL score: 64.7).
The evaluation of CIPN using EORTC QLQ-CIPN20 show mild neurological symptoms associated with stable neuropathy with respect to baseline.





Discussion:
Our preliminary data suggests that early introduction of a neuroprotective agent consisting of DHA 400 mg, ALA 600 mg, Vit C 60 mg, Vit E 10 mg bid in patients with MM in therapy with BTZ has allowed to have no neuropathic pain during treatment, not to worsen mild neuropathy, not to suspend therapy with Bortezomib, and to mantain a good functional autonomy to allow normal daily activities to be conducted.
We believe that a combined and daily approach of patients being assessed by both a haematologist and neurologist could provide a safer and accurate follow-up evaluation reducing risk to develop CIPN.
Further studies on larger cohorts and longer follow-up will be needed to confirm these results.

References:

SB Park, Goldstein D, Krishnan AV, Lin CSY, Friedlander ML, Cassidy J, Koltzenburg M, Kirernan MC. Chemotherapy-InducedPeripheralNeurotoxicity: A Critical Analysis. Ca Cancer J clinic 2013;63:419-437

Bilinska M, Usnarska-Zubkiewicz L, Pokryszko-Dragan A. Bortezomib-inducedpainfulneuropathy in patients with multiple myeloma. ContempOncol 2013; 17 (5):421-426

Rossini G, Stankov BM. Alpha-lipoic acid and docosahaenoic acid.A positive interaction on the carrageenaninfiammatoryresponse in rats.Nutrafoods2010; 9(3): 21-25

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