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624.HODGKIN LYMPHOMAS AND T/NK CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Neurofilaments As Serum Biomarkers of Brentuximabvedotin-Induced Peripheral Neurotoxicity in CD30 + Lymphoma Patients: A Prospective Single-Center Study

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Introduction: Brentuximab vedotin (Bv) is increasingly being used for the treatment of CD30+ lymphomas, being Bv-induced peripheral neurotoxicity (BvPN) one of the greatest concerns for treating physicians. The mechanisms of BvPN are still partially known, and currently, no biomarker to predict this side effect and its severity is available. Neurofilament (NfL) is a neuron specific protein; high levels can be detected in peripheral blood with ongoing neuronal damage. It can be useful to quantify the extend of chemotherapy induced peripheral neurotoxicity due to axonal injury but its role in early detecting and predicting severity of BvPN is unknown. The objective of this study is to determine the association between pNfL and BvPN in lymphoma patients receiving Bv.

Methods: This is anobservational prospective study that includes patients treated with Bv as a single drug (n=12, 30%) or in combination with other chemotherapy agents (n=28, 70%), being neurotoxic chemotherapy drugs in 15 out of 28 (53,5%). Patients were recruited from January 2021 to June 2023. All patients were assessed using the Total Neuropathy Score (TNS), which measures the severity of peripheral nerve damage (higher values equals worse neuropathy) and the Common Toxicity Criteria for Adverse Events toxicity scale at the following timepoints: before, periodically (every 1-2 cycles), and at three, six and twelve months after the end of Bv-based treatment. Nerve conduction studies (NCS) in upper and lower limbs before and after Bv-based treatment were performed. Serial pNfL were collected at the same timepoints and quantified using the SIMOA technique. Changes in pNfL were correlated with clinical data, depending on the degree of BvPN.

Results: Fortypatients are included in the present analysis, with a predominance of males (n=22, 55%) and a median age of 47.5 [21-81] years. The majority of patients had Hodgkin lymphoma (HL, n=25, 62.5%), followed by mycosis fungoides (n=8, 20%) and peripheral T-cell lymphoma (n=7, 17.5%). Of the whole series, 85% of patients developed some degree of BvPN (55% grade 1, 30% grade 2). Baseline pNfL level was normal [15.09 ± 11.90 pg/mL] in most of the patients (n=35, 87.5%). and, as expected, they were correlated with age (r= 0.482, p=0.002) and the amplitude of the left (r= -0.408, p=0.048) and right (r= -0.380, p=0.061) sural (sensory) nerves. pNfL levels early increased with Bv-based therapy and rapidly decreased within the follow-up period (Figure). When completing half of the planned Bv-based therapy, the total increase in pNfL was significantly higher in those receiving combination schedules including other neurotoxic agents (40.07 vs 21.81 pg/mL, p<0.001), without differences according to BvPN development (p=0.7). At the end of treatment, no differences in pNfL were observed with regards to BVPN severity: No BVPN: 52.71±39.77 pg/mL; grade 1: 61.22 ±21.36 pg/mL, and grade 2: 55.46 ± 45.80 pg/mL. In all patients, TNS scores increased during treatment and decreased within the follow-up period (see Figure).

Conclusion: NfL is a sensitive blood biomarker that dynamically responds to Bv-based therapy. Our results suggest that additional mechanisms beyond the axonal damage may be associated with BvPN. The present study provides new insights into the pathophysiology of BvPN.

Disclosures Domingo Domenech: *Takeda:* Consultancy, Honoraria, Speakers Bureau; *BMS:* Speakers Bureau; *BeiGene:* Consultancy. **Gonzalez Barca:** *Janssen, Abbvie, Takeda, EUSAPharma, AstraZeneca, Lilly:* Speakers Bureau; *Janssen, Abbvie, AstraZeneca:* Other: Travel; *Janssen, Abbvie, Kiowa, EUSA Pharma, Beigene, Sobi:* Consultancy. **De Oliveira:** *Janssen:* Other: Travel Expenses; *Janssen, Alexion:* Consultancy. **Sureda Balari:** *MSD:* Research Funding; *Kite:* Consultancy, Speakers Bureau; *Takeda:* Consultancy, Honoraria, Speakers Bureau. **Velasco:** *Takeda:* Honoraria, Speakers Bureau; *Kite:* Honoraria.

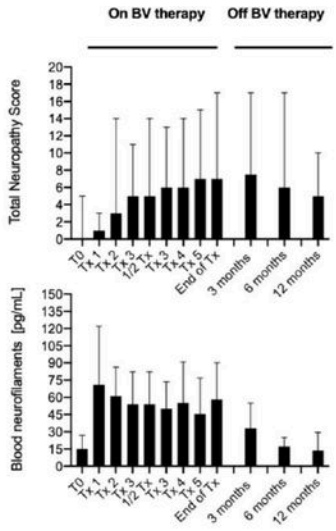

Figure 1

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