



## The 65th ASH Annual Meeting Abstracts

## POSTER ABSTRACTS

## 705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALY AVAILABLE THERAPIES

**Blood-Brain Barrier and Neuronal Damage during Icans in Patients Treated with Anti-CD19 CAR-T Cells**

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**Background**

Immune effector cell-associated neurotoxicity syndrome (ICANS) is the most frequent neurological toxicity occurring after treatment with chimeric antigen receptor T-cells (CAR-T), with a reported incidence of around 30-50% according to different settings and products. Clinical manifestations may widely range from dizziness to seizures, and tend to achieve response with high-dose steroids. The pathogenesis of ICANS is unclear; despite some data suggest a role for endothelial activation and impairment of the blood-brain barrier (BBB).

Glial fibrillary acidic protein (GFAP) and neurofilament light chain (NFL) are reliable astroglial and axonal neuronal damage biomarkers, respectively. NFL provides structural support to neurons, while GFAP is crucial for astrocyte function and BBB maintenance. Elevated levels of NFL and GFAP in cerebrospinal fluid indicate BBB damage, aiding the diagnosis and monitoring of neurological conditions like multiple sclerosis and traumatic brain injury. Recently, preliminary studies reported that NFL serum levels correlate with the severity of neurotoxicity after CAR T-cell treatment.

**Aim and Methods**

In our study, we measured GFAP and NFL both at baseline and at day 7 in 34 patients with R/R B-cell malignancies treated with CD19 CAR-T cells (15 Axi-cel, 12 Tisa-cel, 7 Brexu-cel), and explored their association with clinically relevant neurological toxicities and markers of endothelial impairment. We have collected peripheral blood samples from patients treated with CD19-directed CAR-T cells at baseline and at every other day up to 14 days after CAR-T infusion. We have measured GFAP and NFL levels and compared them with clinical neurotoxicity and serum markers of endothelial damage or inflammatory activity.

**Results**

Elderly patients tended to have higher values of GFAP at day 0 and to raise those levels after CAR-T infusion.

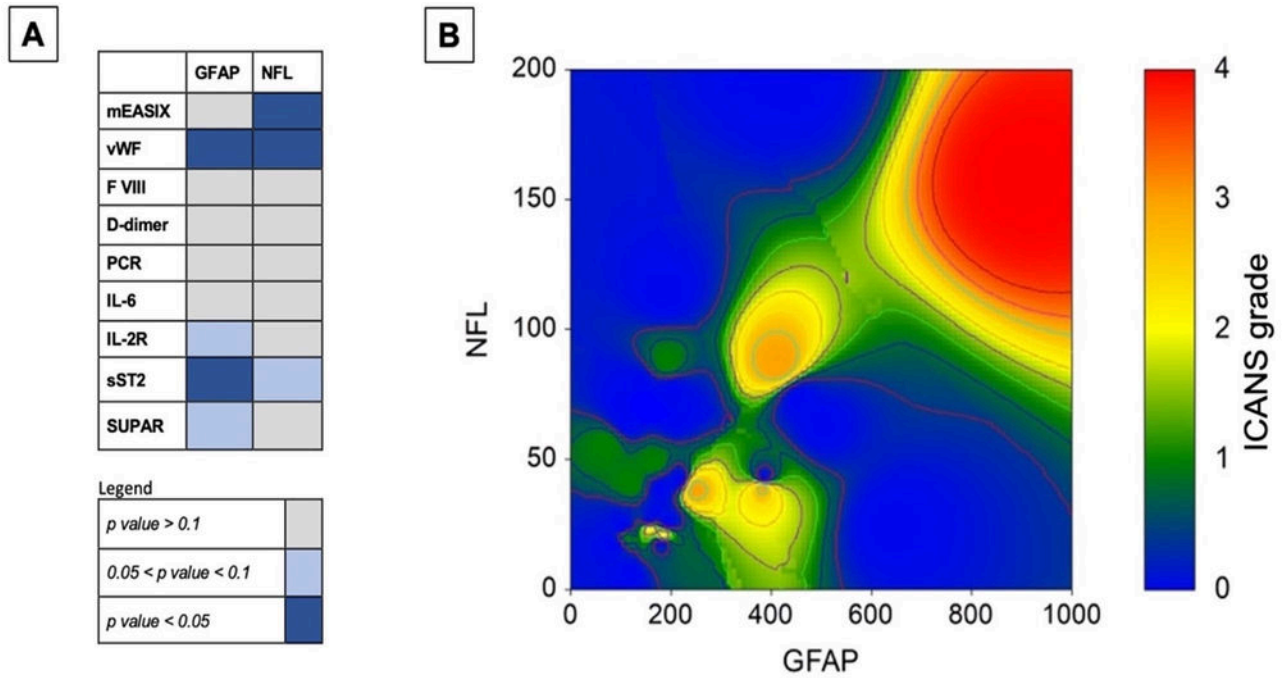
When measured after infusion, GFAP positively correlated with endothelial biomarkers such as von Willebrand factor ( $p=0.041$ ) and sST2 ( $p=0.015$ ) and got some trends with IL-2R ( $p=0.050$ ) and SUPAR ( $p=0.074$ ). NFL positively correlated with the vWF ( $p=0.021$ ) and with the endothelial activation score mEASIX ( $p=0.015$ ) (Figure 1A).

Overall, 11/34 patients (33%) developed ICANS. Baseline GFAP and NFL values did not impact the subsequent development of CRS or ICANS. When compared to the baseline, an increase of NFL was observed in 50% of cases. Patients experiencing an increase in NFL values after CAR-T infusion were more likely to develop ICANS of higher grades ( $p=0.046$ , OR 4.14) and to receive treatment with steroids ( $p=0.023$ ). The median increase of NFL in patients with ICANS was of 25% of baseline levels. When representing values measured after CAR-T infusion in a heatmap, it emerges that a profile with higher GFAP and NFL may describe patients with ICANS of a higher grade (Figure 1B).

**Conclusion**

To sum up, our data confirm a correlation between severe ICANS and elevated NFL and G-FAP serum levels. Interestingly, these data also correlate with markers of endothelial activation, suggesting an active role of BBB impairment - considered in both its components- and concomitant neuronal damage in the pathogenesis of ICANS.

**Disclosures** No relevant conflicts of interest to declare.



**Figure 1**

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