(PB4125) INFLAMMATORY MARKER KINETICS AND THEIR ASSOCIATION WITH CRS AND ICANS IN A REAL-WORLD CAR-T COHORT

Topic: 26. Gene therapy, cellular immunotherapy and vaccination - Clinical

Maryam Hajiabbasi*[1, 1], Steven C. Tsai[1]

[1]David Geffen School of Medicine, University of California, Department of Hematology/Oncology, Los Angeles, United States of America;

Background

Chimeric antigen receptor T-cell (CAR-T) therapy is an established treatment for relapsed or refractory hematologic malignancies with improved clinical outcomes. Cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS) remain common toxicities. We evaluated real-world inflammatory markers and their association with these toxicities.

Aims

To evaluate the incidence and timing of CRS, ICANS, and delayed neurotoxicity and their associations with baseline and dynamic inflammatory markers in a real-world CAR-T cohort.

Methods

In this retrospective single-center cohort of 93 patients treated with CAR-T, CRS and ICANS were graded per ASTCT criteria; delayed neurotoxicity was defined as events >14 days post-infusion. Inflammatory markers (CRP, ferritin, LDH) were collected at baseline, peak, and day 14. Logistic regression (log2-transformed markers) evaluated associations with toxicity, adjusting for product. Correlation between marker peak timing and CRS onset was analyzed.

Results

Ninety-three patients received CAR-T (Carvykti n=48; Yescarta n=17; Breyanzi n=16; Aucatzyl n=5; Tecartus n=4; others n=3). CRS occurred in 64 (68.8%) and ICANS in 22 (23.7%). CRS was highest with Yescarta (94%; median onset 2 days), followed by Carvykti (66.7%; 7 days) and Breyanzi (62.5%; 5 days). ICANS was most frequent with Yescarta (64.7%; 5 days), then Breyanzi (25%; 5 days) and Carvykti (10.4%; 6 days). Delayed non-ICANS neurotoxicity occurred in 8 patients (8.6%), most commonly with Carvykti (4/48).

Baseline CRP was not associated with CRS (OR 0.86, 95% CI 0.34–2.19, p=0.76), nor was baseline ferritin (OR 1.47, 95% CI 0.56–3.85, p=0.43). However, higher baseline ferritin was associated with CRS grade ≥2 (OR 1.41 per doubling, 95% CI 1.00–1.99, p=0.050); median ferritin was higher in grade ≥2 vs 0–1 CRS (930 vs 345, p=0.027). Baseline LD showed a borderline association (OR 2.46, 95% CI 0.88–6.88, p=0.087).

Higher baseline ferritin was associated with ICANS (OR 1.56 per doubling, 95% CI 1.15–2.12, p=0.004), remaining significant after adjustment for therapy (adjusted OR 1.54, 95% CI 1.06–2.22, p=0.023). Baseline CRP was not associated with ICANS.

CRP peak day was strongly correlated with CRS onset (Spearman ρ=0.74, p<0.001), peaking 1 day after onset (IQR 0–1). Ferritin peak day also correlated with onset and peaked 3 days after CRS. The lag between CRP and ferritin peaks was significant (median difference 3 days, p<0.001).

Early CRS (≤3 days) was associated with ICANS in unadjusted analysis (OR 8.36, 95% CI 2.53–27.64, p=0.001) but not after adjustment for therapy (OR 2.91, p=0.17).

CAR-T product type was the strongest predictor of delayed neurotoxicity, with higher odds observed for Carvykti. Peak ferritin (OR 1.43, p=0.044) and day 14 ferritin (OR 1.52, p=0.024) were associated in univariable analysis but not after adjustment. CRP and ALC were not associated. Findings should be interpreted with caution given the small number of events.

Summary/Conclusion

In this real-world cohort, CRS and ICANS incidence varied by CAR-T product. Baseline ferritin was independently associated with ICANS and with severe CRS. CRP closely tracked the timing of CRS onset, peaking one day after onset, whereas ferritin peaked later. Delayed non-ICANS neurotoxicity was uncommon and was most strongly associated with CAR-T product type; Sustained ferritin elevation was associated with delayed non-ICANS neurotoxicity in univariable analysis.