P1169 ELEVATED CRP AT INFUSION OF AXICABTAGENE CILOLEUCEL PREDICTS HIGH-GRADE CAR-T TOXICITY AND OUTPERFORMS MORE COMPLEX SCORES

Topic: 19. Aggressive Non-Hodgkin lymphoma - Clinical

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Background: Predicting CRS and ICANS prior to CAR-T infusion is desirable as it may help to plan management. Two groups1,2 have recently shown that a modification of the Endothelial Activation and Stress Index (EASIX) score, developed to predict toxicity in bone marrow transplant recipients3, can predict CRS and ICANS severity in CAR-T patients, however these have not been externally validated or are difficult to apply in practice.

Aims: We aimed to determine whether the EASIX or related scores could predict CAR-T toxicity in our patients and if not, then to identify other potential predictors from the available clinical information.

Methods:

We reviewed the medical records of adult patients who received axicabtagene ciloleucel (axi-cel) as standard of care at our centre over a 2yr period, collecting data on timing and severity of CRS and ICANS as well as baseline demographic and biochemical factors. We calculated an EASIX score for all patients and an ‘EASIX-F’ score based on the values provided by Greenbaum et al (EASIX-F1) and our own interquartile values (EASIX-F2). We then performed a linear regression of each of: the EASIX score; EASIX-F1; EASIX-F2; and other variables of interest with maximum grade of CRS, with a plan to perform a multivariate analysis with any significant variables (p<0.05).

Results:

67 patients were eligible for analysis. Baseline demographics were similar to those described on the licensing trial4. On univariate analysis (UVA), neither EASIX score (p=0.10), nor either iteration of the EASIX-F score (p=0.08 and 0.15 respectively), was associated with severity of CRS for our patients. Pre-infusion C-Reactive Protein (D0 CRP) however appeared strongly associated with CRS severity, both on UVA (p=0.001) and by multiple linear regression, where it was the only variable identified that showed any association with CRS severity (p=0.003). Given the strength of the D0 CRP and CRS association, we evaluated the association of D0 CRP with ICANS severity which was significant (p=0.012) and D0 CRP with a combined outcome of ‘high grade CAR-T toxicity’ (HGT), defined as development of either grade 3+ CRS or grade 3+ ICANS, where it was again strongly associated (p<0.001). We then dichotomised D0 CRP to determine whether we could identify a practically useful cut-off to predict HGT. We looked at D0 CRP values of ≥50, ≥100 and ≥150 individually and all cut-offs performed well with increasing likelihood of HGT with higher CRP values. With D0 CRP ≥50, probability of developing HGT was 42% vs 13% (OR 5.09, p=0.007); with CRP ≥100 it was 55% vs 14% (OR 7.2, p=0.006); and with CRP ≥150 it was 100% vs 13% (OR undefined, p<0.001).

Finally, given these unexpected findings we performed a prospective review of the 19 axi-cel patients treated from our initial data-cut off to 1 Feb 2022 and found that for these patients, a D0 CRP ≥100 or ≥150 predicted HGT well. HGT incidence was 75% vs 7% (OR 42, Fisher’s p=0.016) for both cut-offs because 3 of the 4 patients with HGT had a CRP of >150 (Table 1). The single patient with HGT and D0 CRP <100 interestingly was a non-responder. For the full 86-patient cohort, D0 CRP ≥150 was the best cut-off, predicting a 90% incidence of HGT vs 12% if CRP <150 (OR 42, p<0.001).

Image:
Table 1: Day 0 CRP association with high grade CAR-T toxicity

![Bar chart showing probability of high-grade CAR-T toxicity associated with different CRP levels.]

Summary/Conclusion:

On retrospective analysis of 67 axi-cel patients, D0 CRP was more strongly associated with CRS severity than more complex prognostic scores. D0 CRP level, especially if ≥150, showed strong association with high grade CAR-T toxicity and remained predictive in a 19-patient validation cohort. This has potential implications for management of axi-cel patients.