IMPACT OF PRE-EXISTING COGNITIVE IMPAIRMENTS ON TOXICITY AND OUTCOMES AFTER AXICABTAGENE CILOLEUCEL FOR PATIENTS WITH DIFFUSE LARGE B-CELL LYMPHOMA

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INTRODUCTION

Axicabtagene Ciloleucel (axi-cel) is a CD-19 directed chimeric antigen receptor T-cell (CART) therapy for diffuse large B cell lymphoma (DLBCL). Adverse events such as cytokine release syndrome (CRS) and immune effector cell associated neurotoxicity syndrome (ICANS) are concerning for patients with neurocognitive impairment (NCI).

AIM

Evaluate the effects of NCI on CRS, ICANS, progression free-survival (PFS) and overall survival (OS).

METHOD

A retrospective cohort study of DLBCL patients treated with axi-cel at Moffitt Cancer Center from 2018-2023 was conducted. Baseline pre-CAR-T neuropsychological testing - Color Trails Test (Parts 1 & 2), Repeatable Battery for the Assessment of Neuropsychological Status, Conners CPT-3, and Stroop Test- quantified attention, executive function, verbal ability, immediate verbal memory, visuospatial ability, and delayed memory and averaged them into a total neuropsychological performance (TNP) score. Clinically significant NCI was pre-defined as ≥2 SDs below the mean in ≥1 domain. The cumulative incidence of CRS and ICANS were calculated for patients with vs without NCI. Severe CRS and ICANS were defined as grade ≥3. Multivariate analyses (MVA) were adjusted for covariates - gender, age, and disease burden via EASIX score (LDH x creatinine / platelets). Log-rank Kaplan-Meier analyses assessed PFS and OS.

CONCLUSIONS

Pre-CART neurocognitive testing is an important method of risk stratification. Higher TNP scores were associated with reduced severe CRS risk. Clinically significant NCI may be associated with limited reserve and vulnerability to CAR-T related toxicities. Given no impact on OS or PFS, NCI should not preclude patients from receiving CD19-CAR-T cell therapy. Future research on the prognostic value of neurocognitive measures on CRS and ICANS is warranted.

RESULTS

Category	Axi-cel (n=320)
Median Age	62.27 (12.62)
Male (%)	201 (62.8%)
Female (%)	119 (37.2%)
Patients with NCI (≥1 domain impaired)	38 (11.9%)
Patients with abnormal TNP score	11 (3.4%)

Table 1. Demographics.

Association of Total Neuropsychological Performance Score with Severe CRS (n=320)				
Variable	Univariable		Multivariable	
	n	OR (95% CI)	n	OR (95% CI)
Total Neuropsychological Performance Score	267	**0.874 (0.794, 0.963)**	266	**0.872 (0.791, 0.963)**
Sex (Female)	320	**1.937 (0.827, 4.540)**	266	**2.224 (0.739, 6.688)**
Age	320	**0.984 (0.954, 1.015)**	266	**0.986 (0.945, 1.029)**
Easix Score	317	**1.034 (0.988, 1.083)**	266	**1.026 (0.972, 1.082)**

Table 2. Association of Total Neuropsychological Performance Score With Severe CRS (n=320). This table compares univariable and multivariable associations of Total Neuropsychological Performance (TNP) score, sex, age, and EASIX score with risk of severe CRS. In multivariable analysis, a higher TNP was associated with decreased risk of severe CRS (OR, 0.872; 95% CI, 0.791–0.963), adjusting for sex, age, and disease burden via EASIX score.

Variable	≥1 Impairment (n=34)	0 Impairments (n=241)	p-value
CRS	35 (92.1%)	254 (90.4%)	0.734
Severe CRS	5 (13.2%)	18 (6.4%)	0.129
ICANS	24 (63.2%)	168 (59.8%)	0.941
Severe ICANS	13 (34.2%)	69 (24.5%)	0.197

Table 3. Neurocognitive Impairment Analysis. This table compares CRS and ICANS outcomes between patients with and without neurocognitive impairment (NCI). Thirty-eight patients (11.9%) had NCI in ≥1 domain, and 11 patients (3.4%) had an abnormal composite TNP score. There was no statistically significant difference between patients with and without NCI in the incidence of CRS, severe CRS, ICANS, or severe ICANS.

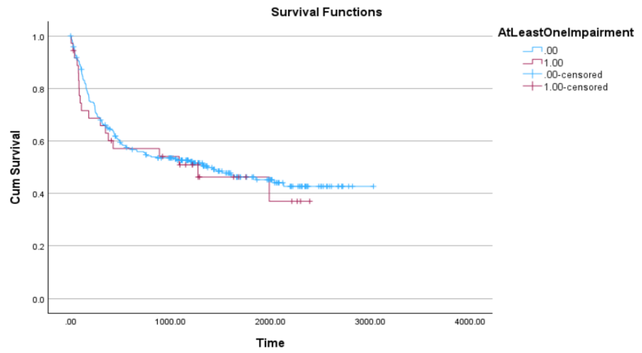

Figure 1. Kaplan-Meier Curve for Overall Survival by Neurocognitive Impairment Status. Estimated mean OS was 1583.31 days for patients without NCI versus 1257.11 days for patients with NCI. Log-rank Kaplan-Meier analysis showed no statistically significant difference in OS between groups ($\chi^2 = 0.232$, df = 1, p = 0.630), indicating NCI should not preclude patients from receiving CD19 CAR T-cell therapy.

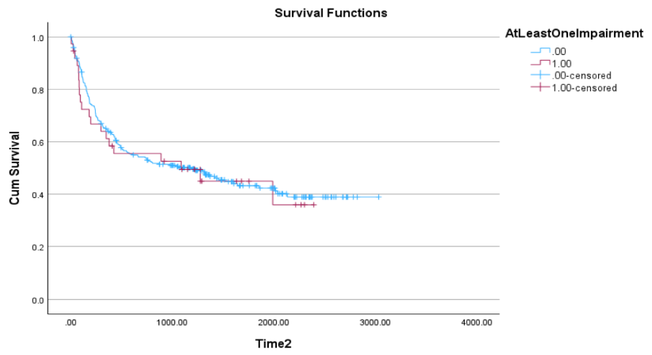

Figure 2. Kaplan-Meier Curve for Progression-Free Survival by Neurocognitive Impairment Status. Estimated mean PFS was 1502.21 days for patients without NCI versus 1227.53 days for patients with NCI. Log-rank Kaplan-Meier analysis showed no statistically significant difference in PFS between groups ($\chi^2 = 0.113$, df = 1, p = 0.737).

CONTACT INFORMATION

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