IMPACT OF PRE-EXISTING ANXIETY AND DEPRESSION 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 therapy for diffuse large B-cell lymphoma (DLBCL). Cytokine release syndrome (CRS) and immune effector cell associated neurotoxicity syndrome (ICANS) remain concerning adverse events for patients with psychiatric conditions.

AIM

This study evaluates the impact of anxiety and depression 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. Routine pre-CAR-T psychological testing included the evaluation of anxiety measured by Generalized Anxiety Disorder 7-item scale (GAD7) and depression measured by Patient Health Questionnaire-9 (PHQ9) and scores ≥10 were defined as clinically significant. Multivariate analyses (MVA) were adjusted for covariates: age, sex, and EASIX scores (disease burden surrogate = LDH x creatinine / platelets). The cumulative incidence and severity of CRS and ICANS were calculated for patients with and without clinically significant GAD7 and PHQ9. Severe CRS (sCRS) and ICANS were defined as grade ≥3. Log-rank Kaplan-Meier (LRKM) analyses assessed PFS and OS.

CONCLUSIONS

Pre-CART psychological testing is an important method of risk stratification. Depression was associated with increased risk of severe CRS and both anxiety and depression were associated with decreased OS and PFS. Psychiatric conditions may warrant early management to prevent toxicities.

RESULTS

Category	Axicel (n=320)
Median age, years (SD)	62.27 (12.62)
Male sex, n (%)	201 (62.8%)
Anxiety, n (%)	25 (8%)
Depression, n (%)	50 (16%)

Table 1. Baseline Patient Demographics.

Variable	GAD-7 ≥10 (n=25)	GAD-7 <10 (n=245)	P value
CRS	24 (96.0%)	221 (90.2%)	0.341
Severe CRS	4 (16.0%)	12 (4.9%)	**0.025**
ICANS	17 (68.0%)	147 (60.0%)	0.862
Severe ICANS	10 (40.0%)	63 (25.7%)	0.126
Length ICANS, days	7.71 (9.31)	5.26 (138.31)	0.833

Table 2. CRS and ICANS Outcomes by Anxiety Status (GAD-7). Frequency of CRS, severe CRS, ICANS, and severe ICANS, and mean duration of ICANS, compared between patients with and without clinically significant anxiety (GAD-7 ≥10) prior to axi-cel infusion. Categorical variables were compared using chi-square testing and continuous variables using independent samples t-test. Anxiety was significantly associated with severe CRS.

Variable	PHQ-9 ≥10 (n=50)	PHQ-9 <10 (n=220)	P value
CRS	48 (96.0%)	197 (89.5%)	0.155
Severe CRS	8 (16.0%)	8 (3.6%)	**<0.001**
ICANS	37 (74.0%)	127 (57.7%)	0.193
Severe ICANS	19 (38.0%)	54 (24.5%)	0.053
Length ICANS, days	11.59 (14.65)	3.76 (148.59)	0.558

Table 3. CRS and ICANS Outcomes by Depression Status (PHQ-9). Frequency of CRS, severe CRS, ICANS, and severe ICANS, and mean duration of ICANS, compared between patients with and without clinically significant depression (PHQ-9 ≥10) prior to axi-cel infusion. Categorical variables were compared using chi-square testing and continuous variables using independent samples t-test. Depression was significantly associated with severe CRS.

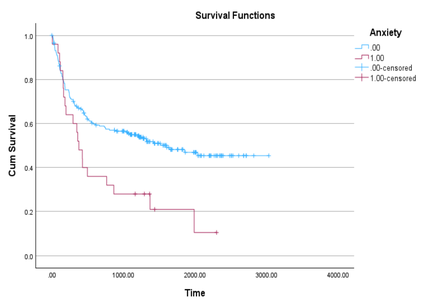

Figure 1. Kaplan-Meier Curves for Overall Survival by Anxiety Status (GAD-7). Kaplan-Meier analysis comparing groups with and without anxiety shows that the group with anxiety has a lower estimated mean overall survival (768.44 days) than the group without anxiety (1650.18 days). The log-rank test showed that the difference was statistically significant (Chi-square 7.727, df 1, P=0.005).

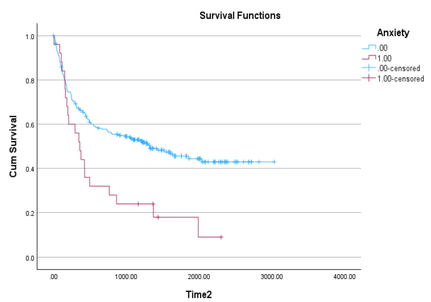

Figure 2. Kaplan-Meier Curves for Progression-Free Survival by Anxiety Status (GAD-7). Kaplan-Meier analysis comparing groups with and without anxiety shows that the group with anxiety has a lower estimated mean progression-free survival (698.67 days) than the group without anxiety (1591.22 days). The log-rank test showed that the difference was statistically significant (Chi-square 9.011, df 1, P=0.003).

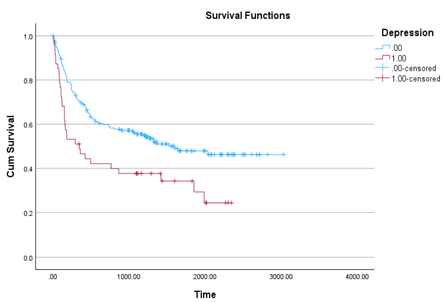

Figure 3. Kaplan-Meier Curves for Overall Survival by Depression Status (PHQ-9). Kaplan-Meier analysis comparing groups with and without depression shows that the group without depression has a higher estimated mean overall survival (1679.02 days) than the group with depression (937.87 days). The log-rank test showed that the difference was statistically significant (Chi-square 8.971, df 1, P=0.003).

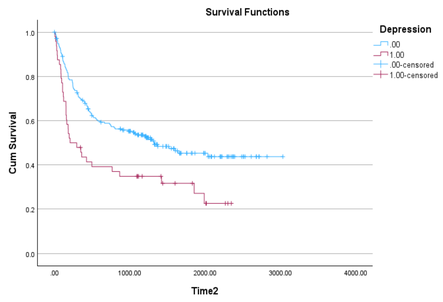

Figure 4. Kaplan-Meier Curves for Progression-Free Survival by Depression Status (PHQ-9). Kaplan-Meier analysis comparing groups with and without depression shows that the group without depression has a higher estimated mean progression-free survival (1620.10 days) than the group with depression (881.49 days). The log-rank test showed that the difference was statistically significant (Chi-square 9.916, df 1, P=0.002).

CONTACT INFORMATION

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