Evaluating Outcomes for Autologous Hematopoietic Cell Transplantation for Diffuse Large B-Cell Lymphoma in the CAR-T Era: A follow-up analysis

Tony Z Zhuang, MD*, Pranav R Santapuram, MD*, *Manali Rupji, MS, Michael Graiser, PhD, Edmund K. Waller, PhD, MD, Kristie A. Blum, MD, Amelia Langston, MD* and Jonathon B. Cohen, MD, MS**

***denotes equal contribution**

Introduction: Autologous hematopoietic stem cell transplant (ASCT) is a standard of care in patients with chemo-sensitive relapsed diffuse large B-cell lymphoma. However, patients with early relapse, incomplete response to salvage therapy, or relapse after ASCT have historically had a poor prognosis. Chimeric antigen receptor (CAR) -T cells are now commonly employed for patients with relapsed/refractory DLBCL, perhaps providing a favorable treatment option for patients with high risk relapsed disease. As a result, we conducted an analysis comparing survival for patients with DLBCL completing ASCT in the pre-CART vs. post-CART era at our site.

Methods: We included patients initially diagnosed with DLBCL since 2012 who subsequently relapsed and received ASCT. Patients who completed ASCT without a documented relapse or who received CART therapy prior to ASCT were excluded as were patients without adequate follow-up data. Based on preliminary findings suggesting a difference in outcome for patients completing ASCT before or after January 1, 2019, this date was utilized to divide treatment eras (Era 1 vs Era 2). We compared demographics as well as disease and treatment-related variables of interest between the pre- and post-CART groups using Fisher's Exact or chi-square tests as appropriate for categorical and ANOVA or Kruskal Wallis test, as appropriate for numeric variables. In addition, we determined progression-free (PFS) and overall survival (OS) from the date of ASCT using the Kaplan-Meier method with log rank test to compare the groups. Median follow up was determined by the reverse Kaplan Meier estimator. Predictors of post-ASCT PFS and OS were determined using the multivariable Cox Proportional Hazards model with backward elimination at alpha of 0.2.

Results: Of 129 included patients, 72 were in Era 1 and 57 were in Era 2. Median age at diagnosis for all patients was 56 years (range 20-73) [Table 1]. Eighty-one (62.8%) were male, and 95 (79.8%) had stage 3 or 4 disease. While there were no differences in demographics based on treatment group, the ECOG performance status for patients in Era 2 was improved compared to those pre-CART (Table 1, $p<0.001$). There was not a significant difference in time from diagnosis to ASCT between the two groups ($p=0.365$). With a median follow-up post ASCT of 2.04 years for Era 1 and 1.08 years for Era 2, the median OS was 4.7 years (95% CI: 3.4 – Not Reached) for the entire cohort, 4.7 years (95% CI: 3.4 – Not Reached) for Era 1 and not reached (95% CI: NR-NR) for Era 2. The median PFS was not reached in either cohort. There were no differences in PFS between pre and post CART groups ($p=0.826$) [Figure 1]. Univariate analysis did not show any covariates as being significant predictors of post-ASCT PFS. However, univariate analysis for post- ASCT OS showed that white race predicted worse outcomes however this was not seen in the multivariable analysis. Neither the ASCT era, conditioning regimen, nor first salvage regimen impacted PFS nor did it impact OS.

Conclusion: In comparison to patients completing ASCT prior to the broad adoption of CAR T cell, those receiving ASCT more recently had improved performance status but no change in

PFS or OS. Our findings suggest that early risk-stratification is critical in identifying patients with a higher probability of early post-ASCT relapse and that the availability of CAR-T has not impacted post-ASCT outcomes. Additional follow-up will be needed to determine if newer currently approved therapies for post-ASCT relapse can improve OS in relapsed/refractory DLBCL who relapse after ASCT.

Overall Survival Curves by Group DLBCL

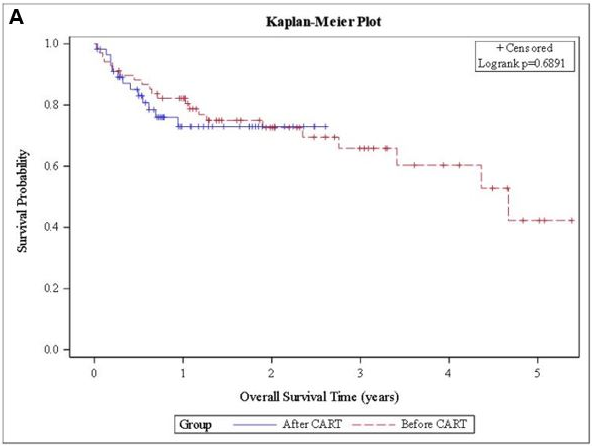
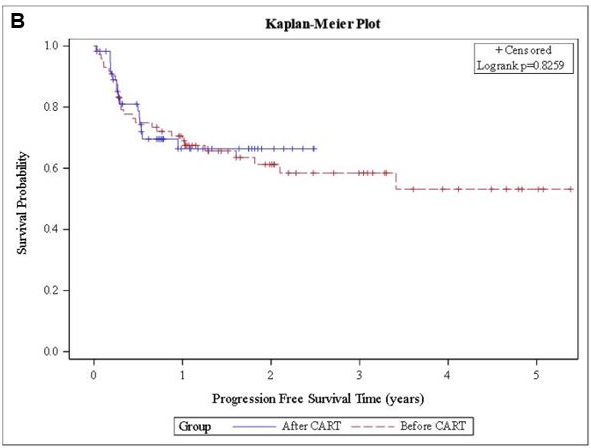


Figure 1. Kaplan-Meier Plots between Pre-CART cell and post-CART cell groups

A: OS (p=0.6891)

B. PFS (p=0.8259)

Progression Free Survival Curves by Group DLBCL



Variable name	All Patients N (%) = 129	Before CART N (%) = 72 (55.8)	After CART N (%) = 57 (44.2)	p-value
Gender	Male 81 (62.8) Female 48 (37.2)	Male 42 (58.33) Female 30 (41.67)	Male 39 (68.42) Female 18 (31.58)	0.239
Race	White 89 (69.0) Other 40 (31.0)	White 47 (65.28) Other 25 (34.72)	White 42 (73.68) Other 15 (26.32)	0.305
Median Age at Diagnosis (yrs)	56 (20-73)	55 (22-73)	56.5 (20-73)	0.447
Stage	I-II 24 (20.2) III-IV 95 (79.8)	I-II 19 (27.54) III-IV 50 (72.46)	I-II 5 (10) III-IV 45 (90)	**0.019**
Initial Chemotherapy	R-CHOP 106 (82.2) Others 23 (17.8)	R-CHOP 56 (77.78) Others 16 (22.22)	R-CHOP 50 (87.72) Others 7 (12.28)	0.143
Response to Initial Therapy	CR 98 (76.0) Non-CR 31 (24.0)	CR 57 (79.17) Non-CR 15 (20.83)	CR 41 (71.93) Non-CR 16 (28.07)	0.339
Response at Time of Transplant	CR1/CR2 80 (72.7) Non-CRs 30 (27.3)	CR1/CR2 42 (61.76) Non-CRs 26 (38.23)	CR1/CR2 38 (90.48) Non-CRs 4 (9.52)	**0.003**
Median Time from Diagnosis to ASCT (yrs)	2.16 (0-18.16)	2.17 (0.38-15.9)	1.99 (0-18.16)	0.365
Performance Status Prior to Transplant	0-1 85 (65.9) 2+ 44 (34.1)	0-1 37 (51.39) 2+ 35 (48.61)	0-1 48 (84.21) 2+ 9 (15.79)	**<0.001**
Conditioning Regimen	BEAM 80 (65.0) Bu/cy/vp 43 (35.0)	BEAM 41 (60.29) Bu/cy/vp 27 (39.71)	BEAM 39 (70.91) Bu/cy/vp 16 (29.09)	0.220

Table 1. Patient characteristics. The parametric p-value is calculated by ANOVA or Kruskal-Wallis as appropriate for numeric covariates and chi-square test for categorical variables.