Prognostic Factors for High-grade B cell Lymphoma Patients Treated with Commercial CD19-Targeted CAR T-Cell Therapy

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Background

-CD19-targeted CAR T-cell therapy has transformed survival rates for patients with relapsed/refractory disease, with overall response rates ranging from 52% to 83 % and complete metabolic response rates of 40-65%, leading to a 2-year overall survival rate of up to 61 %.

-Tumor metabolic biomarkers and patients' characteristics pre-CART have been proven to be promising tools in predicting outcomes post-CAR T; however, it is only limited to a few case series published to date.

Objective

-The purpose of our study is to identify the prognostic factors and clinicopathologic characteristics that may predict survival outcomes and response rates among patients with relapsed/refractory HGBCL undergoing CAR T-cell therapy.

Materials & Methods

-A retrospective study was conducted for consecutive HGBCL patients who received either tisagenlecleucel (tisa-cel) or axicabtagene ciloleucel (axi-cel) CAR T-cell therapy between 2017 and 2021 at a single institution.

-Post-CAR T best overall response was defined as the lowest disease burden measured at any time between post-CAR T-cell therapy and additional salvage therapies.

-Progression-free survival (PFS) was defined as the time of CAR T-cell therapy infusion until the time of progression, relapse, or death from any cause.

-Overall survival (OS) was defined as the time between the date of CAR T-cell therapy infusion and death from any cause.

-Predictors with a p-value less than or equal to 0.1 in the univariate analysis were included in the multivariable analyses.

-Multivariate survival analyses were performed using Cox proportional hazards models with a stepwise selection procedure.

Results

-A total of 101 HGBCL patients were identified.

-The median follow-up was 8.3 months (range, 0.13-49.5 months) from the date of CAR T infusion.

-The median OS and PFS for the entire cohort were 15 months (95% CI: 8.6 months-not reached) and 4.4 months (95% CI: 3.03 months-7.23 months), respectively.

-The best overall response (complete response-CR and partial response) and CR rates post-CAR T were 75% (n=71) and 48% (n=46), respectively.

Table 1- Univariate analysis for the influence of disease-related factors on achieving complete response post-CAR T

Factor			Univariate analysis			
			Odds ratio	95% CI		P-value
		N (%)		Lower	Upper	
Gender	Male Female	64 (63%) 37 (37%)	0.73	0.32	1.66	0.46
Age at time apheresis	≥60 <60	69 (68%) 32 (32%)	1.4	0.6	3.3	0.42
Adjuvant RT pre-CAR T	Yes No	6 (6%) 95 (94%)	0.55	0.07	2.9	0.5
Salvage RT pre-CAR T	Yes No	15 (15%) 86 (85%)	0.24	0.05	0.8	**0.03**
Pre-CART transplant	Yes No	27 (27%) 74 (73%)	3.1	1.25	8.1	**0.01**
Double/Triple Hit at time of apheresis	Yes No	18 (18%) 59 (58%)	0.70	0.23	2.04	0.5
Bulky disease at time apheresis (≥5 cm)*	Yes No	31 (41%) 42 (55%)	0.45	0.17	1.17	0.1
Bridging Therapy	Yes No	50 (50%) 51 (50%)	0.5	0.22	1.1	0.09
ECOG PS pre-CAR T infusion	0 1 2 3	41 (41%) 49 (48%) 9 (9%) 2 (2%)	0.5	0.26	0.90	**0.02**
Elevated LDH at time of apheresis	Yes No	65 (64%) 36 (36%)	0.18	0.07	0.44	**<0.001**
Stage at time of apheresis	III+IV I+II	60 (59%) 41 (41%)	0.31	0.13	0.7	**0.005**
IPI score at time of apheresis	>=3 <3	46 (46%) 55 (54%)	0.29	0.12	0.66	**0.003**
CNS disease	Yes No	25 (25%) 76 (75%)	0.15	0.04	0.43	**0.001**
CAR T Product	Axi-cel Tisa-cel	37 (37%) 64 (63%)	2.7	1.2	6.4	**0.01**

RT, Radiation therapy; ECOG, Eastern Cooperative Oncology Group; PS, performance status; LDH, lactate dehydrogenase; IPI, international prognostic index

*Patients with CNS lymphoma were excluded

-Sixteen patients (22%) had bulky disease (≥5 cm) as per PET/CT post-CAR T, 81% (n=13) of which were bulky pre-CAR T-bulky data was missing for 4 patients.

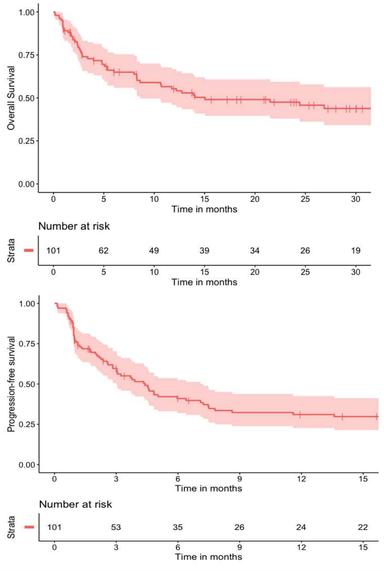
- In univariate analysis, absence of CNS involvement (OR=6.8, p=0.001), IPI score <3 at the time of apheresis (OR=3.4, p=0.003), limited-stage disease at the time of apheresis (OR=3.2, p=0.005), low LDH level at the time of apheresis (OR=5.4, p=<0.001), undergoing HSCT pre-CAR T (OR=3.1, p=0.01), receiving axi-cel (OR=2.7, p=0.01), and not receiving salvage radiotherapy pre-CAR T (OR=4.2, p=0.03) were predictive of achieving CR post-CAR T.

-In multivariate analysis, presence of bulky disease (≥5 cm) post-CAR T infusion was a significant prognostic factor for worse OS (HR=6.2, 95% CI: 2.9-12.8, p<0.001).

-Regarding PFS, high LDH at time of apheresis, age (≥60) at time of apheresis, poor ECOG PS at time of apheresis, advanced-stage disease at time of apheresis, and bulky disease (≥5 cm) post-CAR T infusion were significant prognostic factors for inferior PFS (HR=2.5, 95% CI: 1.17-5.3, p=0.01, HR=3.2, 95% CI: 1.4-7.6, p=0.006, HR=1.8, 95% CI: 1.17-2.7, p=0.007, HR=3.0, 95% CI: 1.07-8.6, p=0.03, HR=3.2, 95% CI: 1.46-7.0, p=0.003, respectively).

Table 2: Cox regression models for PFS and OS prediction

Characteristic	Multivariate analysis			
	PFS		**OS**	
	HR	**p-value**	**HR**	**p-value**
Bulky disease Post-CAR T (≥5 cm	3.2	**0.003**	6.2	**<0.001**
Age at time apheresis (≥60)	3.2	**0.006**	-	-
Elevated LDH at time of apheresis	2.5	**0.01**	1.9	0.05
Poor ECOG PS pre-CAR T infusion	1.8	**0.007**	-	-
High IPI at time apheresis	0.6	0.05	-	-
Advanced stage at time apheresis	3.0	**0.03**	-	-
Bulky disease at time apheresis (≥5 cm)	1.7	0.12	-	-



Summary

-Bulky disease post-CAR T is the most significant prognostic factor that can independently predict survival outcomes among HGBCL patients treated with CAR T-cell therapy.

References

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