Impact of Obesity on Efficacy, Safety, and Expansion Kinetics of Chimeric Antigen Receptor T-cell (CAR T) Therapy in Patients with R/R Large B Cell Lymphoma (LBCL)

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Introduction

- Obesity causes low-grade inflammation and immune escape
- This T-cell exhaustion has led to better responses to immune checkpoint blockade therapy in patients with higher body mass index (BMI)
- Previous studies have shown no significant association of obesity with safety or efficacy of CAR T therapy in hematologic malignancies
- Data on outcomes in LBCL and CAR T expansion kinetics is limited

Objectives

To investigate the effect of obesity on efficacy and safety outcomes, healthcare utilization, and CAR T expansion in patients with relapsed or refractory LBCL treated with Axicabtagene Ciloleucel (axi-cel).

Methods

- 189 patients were divided into 87 underweight/normal (≤24.99kg/m^2), 56 overweight (>25kg/m^2 and ≤29.99kg/m^2), and 46 obese (>30kg/m^2)
- CAR T expansion was measured by real-time flow cytometry with anti-idiotype-FMC63 conjugated to Dylight 650
- Calculated areas under the curve (AUCs) using linear trapezoidal method on raw values, then log10 transformed
- Continuous outcomes were compared using a Kruskal-Wallis test, categorical outcomes using Chi-square tests, and time-to-event outcomes using the Kaplan-Meier estimator and the log-rank test

Results

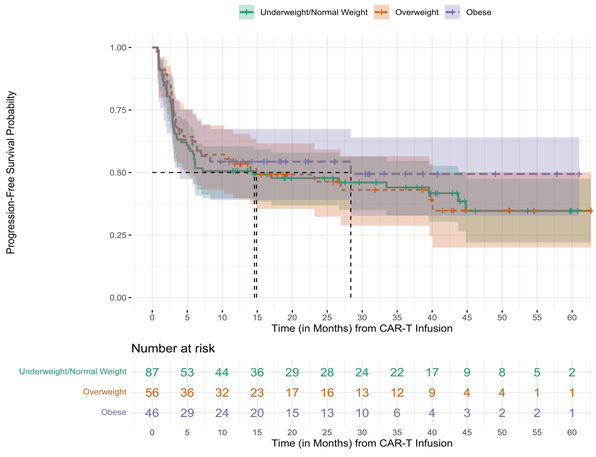


Figure 1. Progression-free survival stratified by BMI

- Median progression-free survival (PFS) was 14.6 months (IQR 4.93, 44.81) for underweight/normal weight, 14.89 months (IQR 5.82, 40.07) for overweight, and 28.37 months (IQR 3.88, NA) for obese (p=0.800)
- Complete response and overall response were not significantly different for their best response at 12 months (p=0.989 and p=0.802, respectively)

	Underweight/Normal Weight (n=87)	Overweight (n=56)	Obese (n=46)	P-Value
Any CRS Event	90.8% (n=79)	92.9% (n=52)	100% (n=46)	P=0.086
CRS Grade 3+	2.3% (n=2)	0% (n=0)	0% (n=0)	NA
Any ICANS Event	47.1% (n=41)	55.4% (n=31)	52.2% (n=24)	P=0.610
ICANS Grade 3+	14.9% (n=13)	16.1% (n=9)	19.6% (n=9)	P=0.794
Length of Stay	13 (IQR: 10-15) days	13 (IQR: 10.8-15.3) days	14 (IQR: 11-16.8) days	P=0.473
ICU Utilization	9.2% (n=8)	12.7% (n=7)	8.7% (n=4)	P=0.818
Tocilizumab Use	77.0% (n=67)	71.4% (n=40)	76.1% (n=35)	P=0.747
Anakinra Use	12.1% (n=8)	14.0% (n=6)	16.7% (n=6)	P=0.746
Steroid Use	79.3% (n=69)	83.9% (n=47)	78.3% (n=36)	P=0.505

Results (cont.)

- Median overall survival (OS) was 44.81 months (IQR 18.18, NA) for underweight/normal weight, 40.07 months (IQR 23.18, NA) for overweight, and not achieved for obese (p=0.348)
- No significant difference in overall incidence or when graded as severe (>3) in CRS or ICANS, nor healthcare utilization variables
- Differences in day 7 and day 14 CAR T expansion were not statistically significant (p=0.754 and p=0.355, respectively)

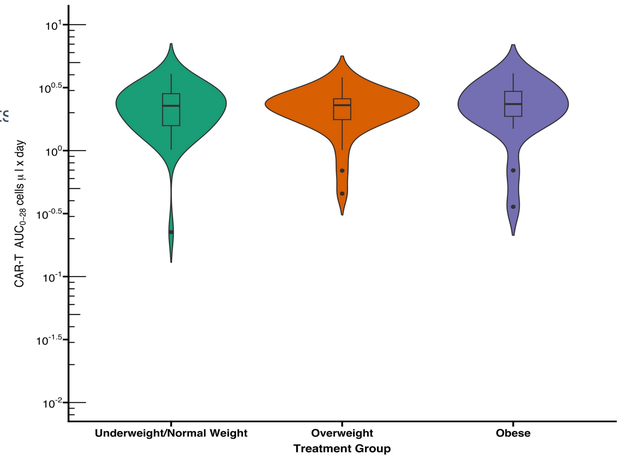


Figure 2a. Violin plot of AUC of log10-transformed CAR-T expansion

For AUC, there were no statistically significant differences (CD4: p=0.828, CD8: p=0.870, CD4 +CD8: p=0.882)

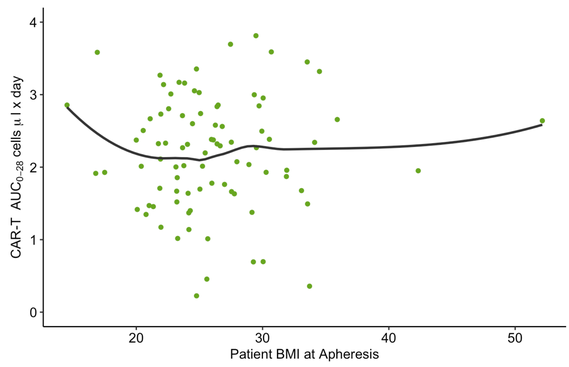


Figure 2b. Scatter plot of Patient BMI by Log10-transformed CAR-T AUC

Discussion

- Contrary to the effect of obesity on response to therapies like checkpoint inhibitors, we demonstrate that BMI does not significantly impact patients treated with CAR T
- Despite weight-based dosing for axi-cel, correlative studies on CAR T expansion kinetics did not indicate any significant difference
- CAR T therapy is an effective treatment option for lymphoma regardless of BMI

References

1. **Wang Z, Aguilar EG, Luna JI, et al.** Paradoxical effects of obesity on T cell function during tumor progression and PD-1 checkpoint blockade. *Nat Med. 2019 Jan;25(1):141-51.*
2. **Faruqi AJ, Ligon JA, Borgman P, et al.** The impact of race, ethnicity, and obesity on CAR T-cell therapy outcomes. *Blood Adv. 2022 Dec 13;6(23):6040-50.*
3. **Wudhikarn K, Bansal R, Khurana A, et al.** The impact of obesity and body weight on the outcome of patients with relapsed/refractory large B-cell lymphoma treated with axicabtagene ciloleucel. *Blood Cancer J. 2021 Jul 1;11(7):124.*

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