

The Impact of Ethnicity and Obesity on CAR T-cell Therapy Outcomes

Supplemental Tables and Figures

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SUPPLEMENTAL TABLES

Table S1: Characteristics and Response of 11 Patients Treated with 2 CARs at NCI

| Ethnicity | Sex | CAR #1 | CAR #2 | CAR Interval (Days) | Baseline Disease Burden #1 | Baseline Disease Burden #2 | BMI #1 | BMI #2 | Max CRS Grade #1 | Max CRS Grade #2 | NTX #1 | NTX #2 | MRD Neg CR #1 | MRD Neg CR #2 |
|--------------|-----|---------|---------|---------------------|----------------------------|----------------------------|--------|--------|------------------|------------------|--------|--------|---------------|---------------|
| Hispanic | M | CD19 | CD22 | 53 | M3 | M3 | 21.7 | 20 | 0 | 3 | No | Yes | No | No |
| Hispanic | M | CD19 | CD22 | 404 | M3 | M1 | 28.2 | 23.7 | 4 | 0 | Yes | No | Yes | No |
| Non-Hispanic | M | CD19 | CD22 | 236 | M3 | M3 | 15.6 | 16.4 | 1 | 2 | No | No | No | No |
| Hispanic | F | CD22 | CD19 | 217 | M1 | M3 | 19.5 | 23 | 1 | 1 | No | No | Yes | No |
| Non-Hispanic | M | CD19 | CD22 | 408 | M1 | M1 | 24.6 | 26.5 | 1 | 1 | No | No | Yes | Yes |
| Non-Hispanic | M | CD19 | CD22 | 108 | M1 | M3 | 24.3 | 20.2 | 3 | 1 | Yes | No | Yes | Yes |
| Non-Hispanic | M | CD19/22 | CD22 | 70 | M3 | M2 | 19.9 | 20.1 | 0 | 2 | No | No | No | Yes |
| Non-Hispanic | M | CD19/22 | CD22 | 59 | M3 | M3 | 15.7 | 16 | 1 | 2 | No | Yes | No | No |
| Non-Hispanic | M | CD22 | CD19/22 | 175 | M1 | M1 | 19.1 | 20.5 | 3 | 0 | No | No | Yes | Yes |
| Non-Hispanic | F | CD22 | CD22 | 813 | M3 | M3 | 16.5 | 15.1 | 0 | 2 | No | No | No | No |
| Non-Hispanic | F | CD22 | CD22 | 469 | M1 | M3 | 19.6 | 18.8 | 1 | 1 | No | No | Yes | Yes |

Each CAR infusion was an independent treatment event (separate apheresis). CAR interval represents elapsed time between first and second CAR infusions. M = male, F = female, BMI = body mass index (kg/m²), CRS = cytokine release syndrome (ASTCT grade), NTX = neurotoxicity, MRD neg CR = measurable residual disease negative complete remission.

Table S2: CAR T-cell Outcomes by BMI Class

| | Underweight (n=7) | Normal Weight (n=91) | Overweight (n=20) | Obese (n=21) |
|--|-------------------|----------------------|-------------------|--------------|
| | | | | |

| | | | | |
|----------------------------|----------|-----------|-----------|-----------|
| ASTCT CRS Grade (%) | | | | |
| None | 1 (14.3) | 22 (24.2) | 6 (30.0) | 4 (19.0) |
| 1 | 2 (28.6) | 28 (30.8) | 11 (55.0) | 6 (28.6) |
| 2 | 4 (57.1) | 23 (25.3) | 2 (10.0) | 5 (23.8) |
| 3 | 0 (0.0) | 14 (15.4) | 1 (5.0) | 5 (23.8) |
| 4 | 0 (0.0) | 4 (4.4) | 0 (0.0) | 1 (4.8) |
| Neurotoxicity (%) | 1 (14.3) | 20 (22.0) | 4 (20.0) | 4 (19.0) |
| CR (%) | | | | |
| Yes | 6 (85.7) | 62 (68.1) | 11 (55.0) | 15 (71.4) |
| No | 1 (14.3) | 28 (30.8) | 9 (45.0) | 6 (28.6) |
| Not Evaluable | 0 (0.0) | 1 (1.1) | 0 (0.0) | 0 (0.0) |

ASTCT = American Transplantation and Cellular Therapy Consortium, CRS = cytokine release syndrome, CR = complete remission. One patient with grade 4 CRS died due to grade 5 capillary leak syndrome and was not evaluable for CR.

| Table S3: Cytokine Release Syndrome (Gr 3-5 vs. 0-2) of B-ALL Patients (n=139) | | | | |
|---|---------------------------|----------------|---------------------------|----------------|
| Variable (Risk Group vs. Ref) | Univariate | | Multivariable | |
| | OR (95% CI) | p-value | OR (95% CI) | p-value |
| Age (yrs) | 1.13 (1.06 - 1.21) | 0.0002 | 1.14 (1.05 - 1.24) | 0.001 |
| Ethnicity (Hispanic vs. non-Hispanic) | 2.84 (1.16 - 6.93) | 0.02 | 3.69 (1.29 - 10.6) | 0.01 |
| Disease Burden (M2/3 vs. M1) | 4.61 (1.30 - 16.3) | 0.02 | 5.54 (1.42 - 21.6) | 0.01 |
| BMI (Continuous) | 1.1 (1.02 - 1.18) | 0.01 | 1.01 (0.91 - 1.12) | 0.85 |

OR = odds ratio, CI = confidence interval, B-ALL = B-cell acute lymphoblastic leukemia

| Table S4: Neurotoxicity of B-ALL Cohort (n=139) | | |
|--|----------------------------|----------------|
| Variable (Risk Group vs. Ref) | Univariate | |
| | OR (95% CI) | p-value |
| Age (yrs) | 1.04 (0.988 - 1.10) | 0.13 |
| Sex (Male vs. Female) | 3.17 (1.026 - 9.78) | 0.04 |

| | | |
|--|---------------------|------|
| Race/Ethnicity (Hispanic vs. White non-Hispanic) | 0.95 (0.38 – 2.34) | 0.92 |
| Other non-Hispanic vs. White non-Hispanic | 0.33 (0.07 – 1.54) | 0.16 |
| Prior HSCT (yes vs. no) | 1.18 (0.515 - 2.70) | 0.69 |
| Prior CART (yes vs. no) | 1.32 (0.58 – 3.0) | 0.52 |
| Disease Burden (M2/3 vs. M1) | 1.80 (0.705 - 4.58) | 0.22 |
| BMI (O/O vs. Non O/O) | 0.89 (0.358 - 2.21) | 0.80 |
| Obese vs. non-obese | 0.88 (0.27 – 2.84) | 0.82 |
| CAR (CD22 vs. CD19) | 1.36 (0.566 - 3.26) | 0.49 |
| CD19/22 vs. CD19 | 0.24 (0.028 - 1.99) | 0.18 |

OR = odds ratio, CI = confidence interval, O/O = overweight/obese, MM = multiple myeloma, ALL = B-cell acute lymphoblastic leukemia, NHL = B-cell non-Hodgkin lymphoma, HSCT = allogenic hematopoietic stem cell transplant, CAR = chimeric antigen receptor

| Table S5: Complete Remission of B-ALL Cohort (n=139) | | |
|--|---------------------------|-------------|
| Variable (Risk Group vs. Ref) | Univariate | |
| | OR (95% CI) | p-value |
| Age (yrs) | 1.02 (0.97 - 1.07) | 0.49 |
| Sex (Male vs. Female) | 0.60 (0.26 - 1.37) | 0.22 |
| Race/Ethnicity (Hispanic vs. White non-Hispanic) | 0.67 (0.30 – 1.50) | 0.33 |
| Other non-Hispanic vs. White non-Hispanic | 0.81 (0.29 – 2.25) | 0.67 |
| Prior HSCT (yes vs. no) | 0.72 (0.35 - 1.49) | 0.37 |
| Prior CART (yes vs. no) | 0.94 (0.45 – 1.95) | 0.86 |
| Disease Burden (M2/3 vs. M1) | 0.38 (0.16 - 0.88) | 0.02 |
| BMI (O/O vs. Non O/O) | 0.74 (0.34 - 1.60) | 0.44 |
| Obese vs. non-obese | 1.20 (0.43 – 3.34) | 0.72 |
| CAR (CD22 vs. CD19) | 1.43 (0.67 - 3.08) | 0.36 |

| | | |
|------------------|--------------------|------|
| CD19/22 vs. CD19 | 2.15 (0.62 - 7.48) | 0.23 |
|------------------|--------------------|------|

OR = odds ratio, CI = confidence interval, O/O = overweight/obese, MM = multiple myeloma, ALL = B-cell acute lymphoblastic leukemia, NHL = B-cell non-Hodgkin lymphoma, HSCT = allogenic hematopoietic stem cell transplant, CAR = chimeric antigen receptor

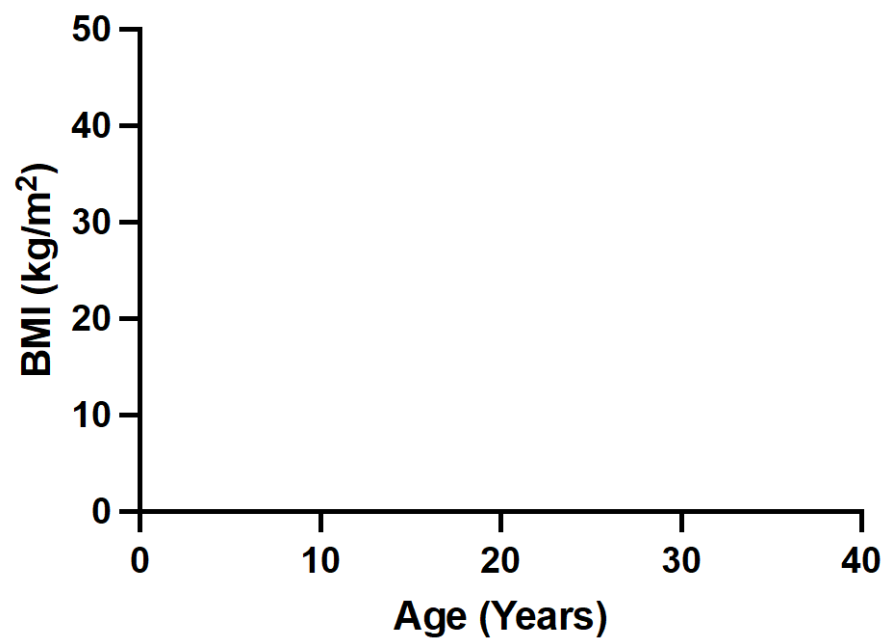
| Table S6: Toxicity and Response of MM and NHL Patients | | | | | |
|--|----------------|----------------|---------------------|-------------------------|----------------------|
| | | Ethnicity | | BMI | |
| NHL (%) | Overall (n=23) | Hispanic (n=2) | non-Hispanic (n=21) | Overweight/Obese (n=13) | Normal Weight (n=10) |
| Severe CRS | 6 (26.1) | 1 (50.0) | 5 (23.8) | 5 (38.5) | 1 (10.0) |
| Developed Neurotoxicity | 3 (13.0) | 1 (50.0) | 2 (9.5) | 3 (23.1) | 0 |
| CR | 10 (43.5) | 1 (50.0) | 9 (42.9) | 7 (53.8) | 3 (30.0) |
| MM (%) | Overall (n=24) | Hispanic (n=3) | non-Hispanic (n=21) | Overweight/Obese (n=17) | Normal Weight (n=7) |
| Severe CRS | 6 (25.0) | 1 (33.3) | 5 (23.8) | 4 (23.5) | 2 (28.6) |
| Developed Neurotoxicity | 3 (12.5) | 0 | 3 (14.3) | 3 (17.6) | 0 |
| CR | 2 (8.3) | 0 | 2 (9.5) | 1 (5.9) | 1 (14.3) |

Severe CRS defined as grade ≥ 3 by ASTCT criteria. NHL = non-Hodgkin lymphoma, MM = multiple myeloma, BMI = body mass index, CRS = cytokine release syndrome, CR = complete remission

SUPPLEMENTAL FIGURES

Figure S1: Correlation of Age and BMI among B-ALL Patients

B-ALL BMI on Age



Scatterplot showing the relationship between body mass index (BMI) and age among B-ALL patients. $R^2=0.33$

Figure S2: CRS Severity by Treatment Year

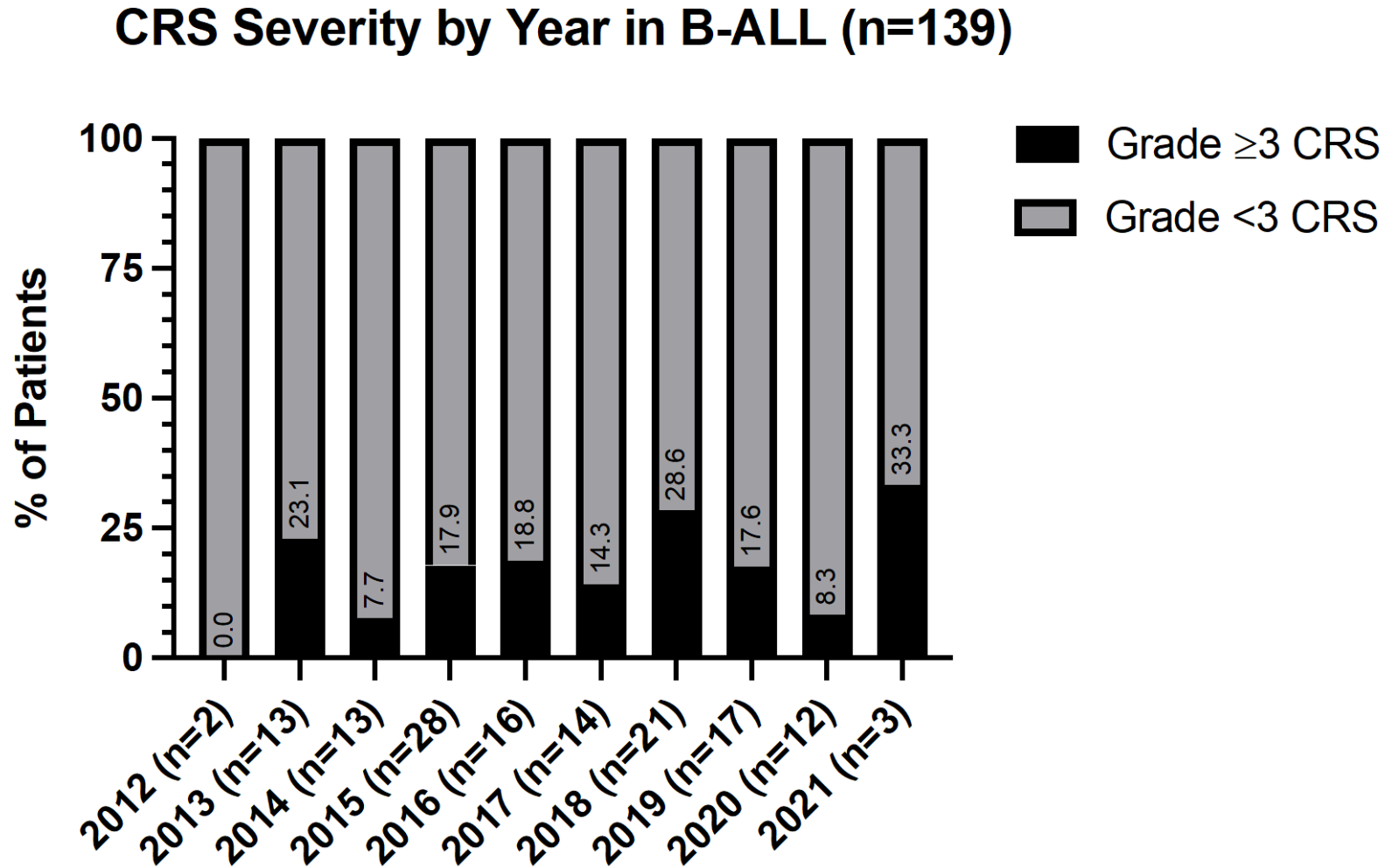
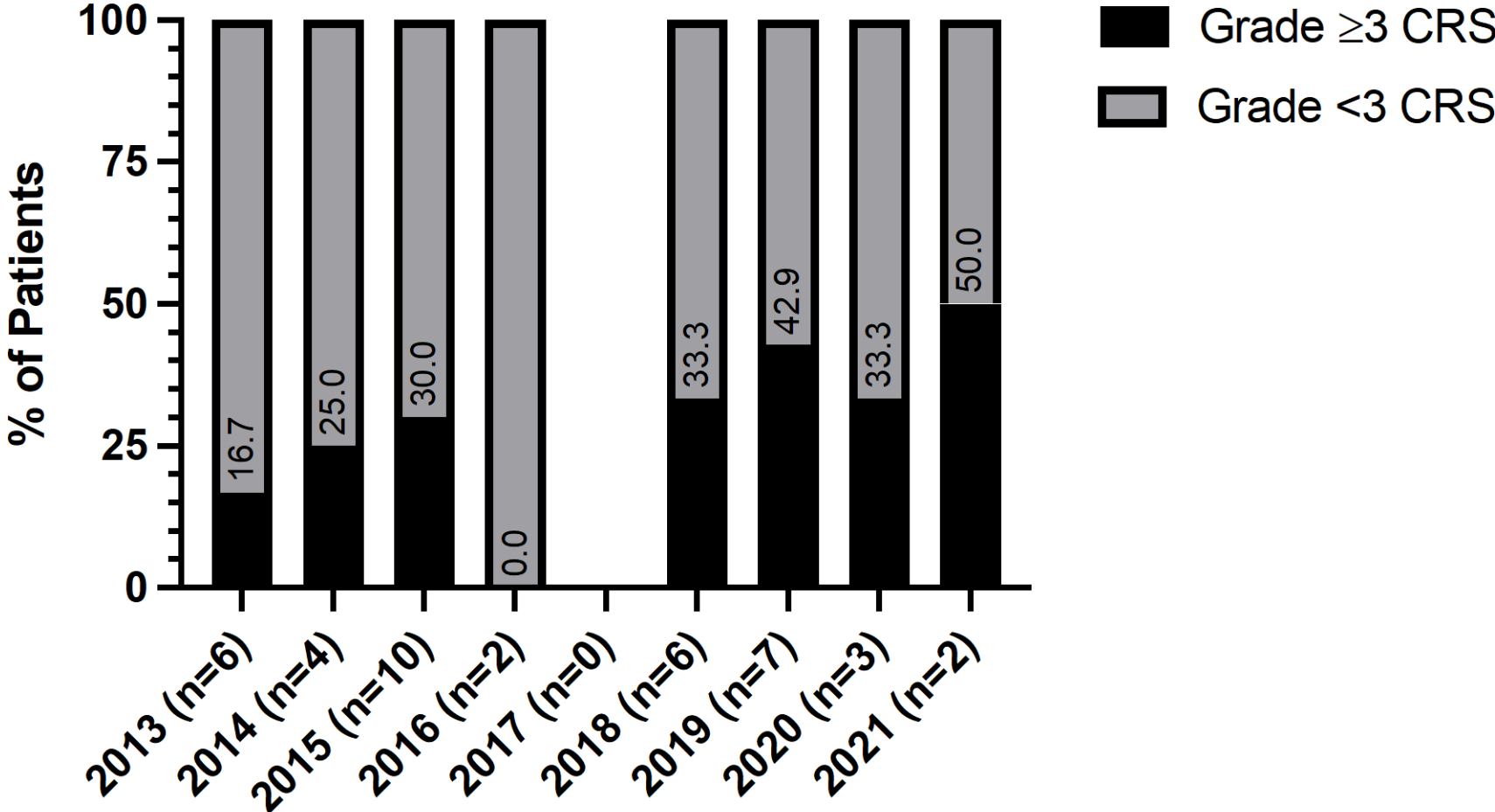


Figure S3: Percentage of B-ALL patients who experienced severe (grade ≥ 3) CRS by year of treatment. Patients included in this analysis were treated from July 2012 to March 2021. Chi-Square p-value = 0.87. CRS = cytokine release syndrome.

Figure S3: CRS Severity by Treatment Year for Hispanic Patients

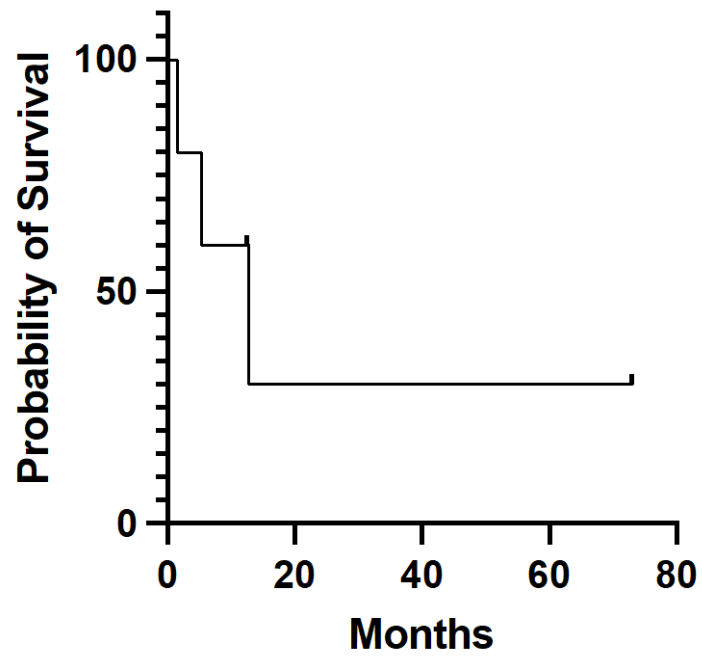
CRS Severity by Year in Hispanic B-ALL Patients (n=40)



Percentage of Hispanic B-ALL patients who experienced severe (grade ≥ 3) CRS by year of treatment. CRS = cytokine release syndrome.

Figure S4: Survival of Black B-ALL Patients

B-ALL Survival of Black Patients (n=5)



Kaplan-Meier Survival Curve of 5 Black or African American B-ALL patients. Index date (t=0) time of CAR T-cell infusion

