5-Year Follow-Up Supports Curative Potential of Axicabtagene Ciloleucel in Refractory Large B-Cell Lymphoma (ZUMA-1)

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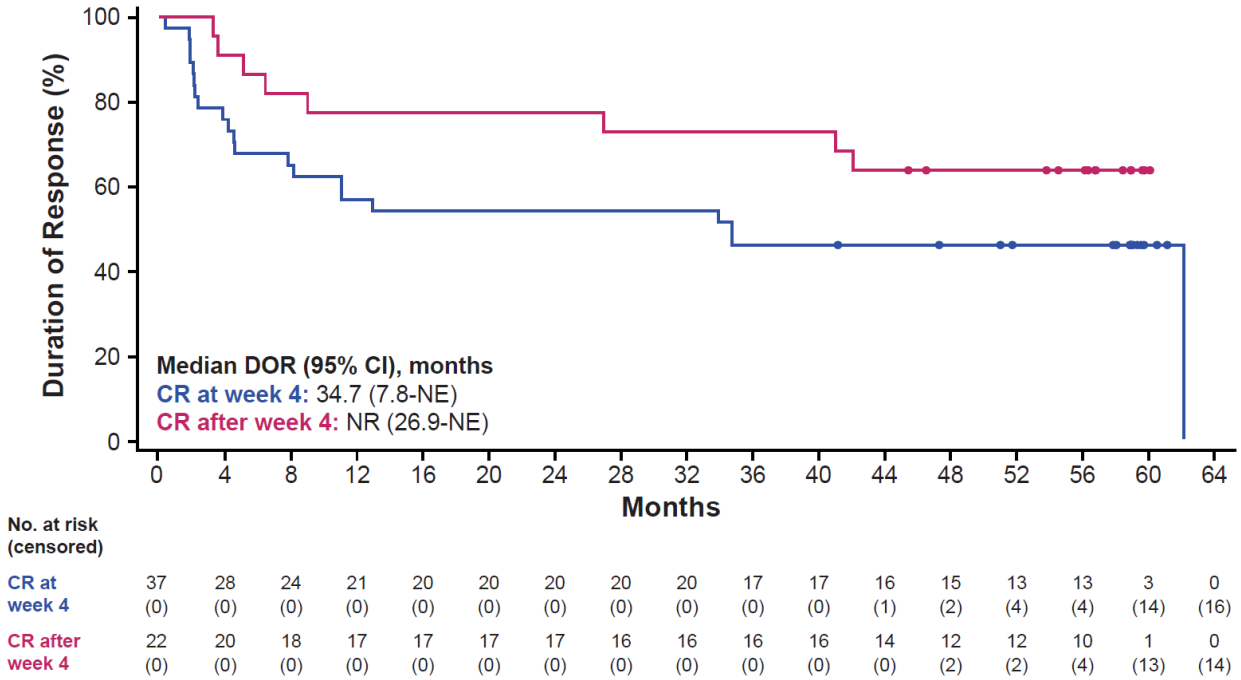
SUPPLEMENTAL DATA

Supplemental Methods

Biomarker analyses

The presence, expansion, and persistence of axi-cel anti-CD19 chimeric antigen receptor (CAR) T cells were measured in peripheral blood mononuclear cells (PBMCs) as previously reported.[1] Briefly, a quantitative polymerase chain reaction assay observed concentration peak anti-CD19 CAR T cells/µL, the area under the curve (AUC) from Day 0 to Day 28 ($AUC_{0\text{-}28}$). B cells were characterized in cryopreserved PBMCs using multicolor flow cytometry. Viable cells were calculated as a percentage of the total number of viable CD45+ leukocytes. B-cell subsets were defined as CD45+CD3−CD14−CD16−CD56−CD19+ and/or CD20+ and further phenotyped as follows: Ig kappa, Ig lambda, class-switched memory (CD20+CD27+IgD−), non–class-switched memory (CD20+CD27+IgD+), naive (CD20+CD27−IgD+CD24lowCD38low), plasmablasts (CD38highCD20−), and transitional (CD20+CD27−IgD+CD24+CD38mid).

Figure S1. Duration of Response by Complete Response at or After Week 4 Postinfusion. This figure shows Kaplan-Meier estimates of DOR in treated patients with LBCL (n=101) in Cohorts 1 and 2 of phase 2 who had a complete response to axi-cel, either at the week 4 disease assessment or afterward. Axi-cel, axicabtagene ciloleucel; CR, complete response; DOR, duration of response; LBCL, large B-cell lymphoma; NE, not estimable.



No. at risk (censored)																	
CR at week 4	37 (0)	28 (0)	24 (0)	21 (0)	20 (0)	20 (0)	20 (0)	20 (0)	20 (0)	17 (0)	17 (0)	16 (1)	15 (2)	13 (4)	13 (4)	3 (14)	0 (16)
CR after week 4	22 (0)	20 (0)	18 (0)	17 (0)	17 (0)	17 (0)	17 (0)	16 (0)	16 (0)	16 (0)	16 (0)	14 (0)	12 (2)	12 (2)	10 (4)	1 (13)	0 (14)

Figure S2. Subgroup Analysis of Median Event-Free Survival.

Figure shows a subgroup analysis of the median EFS in patients treated with axi-cel (n=101) by key patient baseline and clinical covariates. The Clopper–Pearson method was used to calculate the 95% CI. Axi-cel, axicabtagene ciloleucel; DLBCL, diffuse large B-cell lymphoma; EFS, event-free survival; NE, not estimable; PMBCL, primary mediastinal large B-cell lymphoma; TFL, transformed follicular lymphoma.

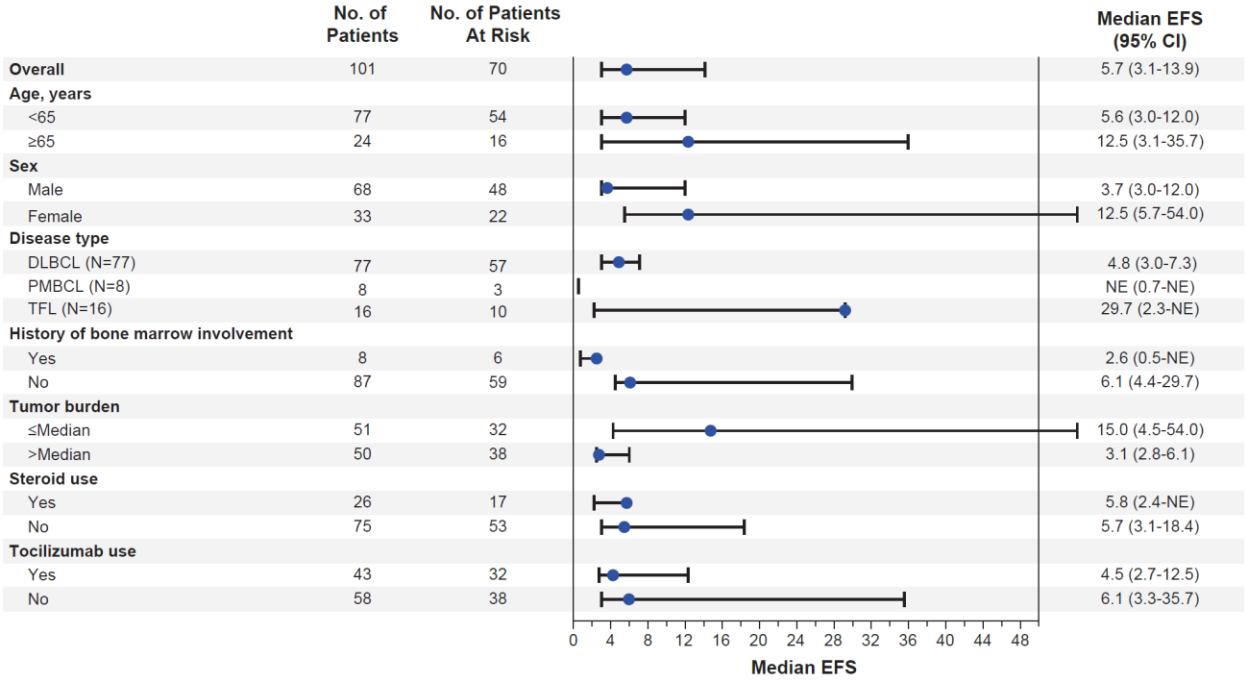


Figure S3. Time to Next Therapy.

This figure shows a Kaplan Meier estimate of time to next therapy among 101 patients with LBCL treated with axi-cel in Cohorts 1 and 2 of phase 2. Axi-cel, axicabtagene ciloleucel; LBCL, large B-cell lymphoma; NE, not estimable.

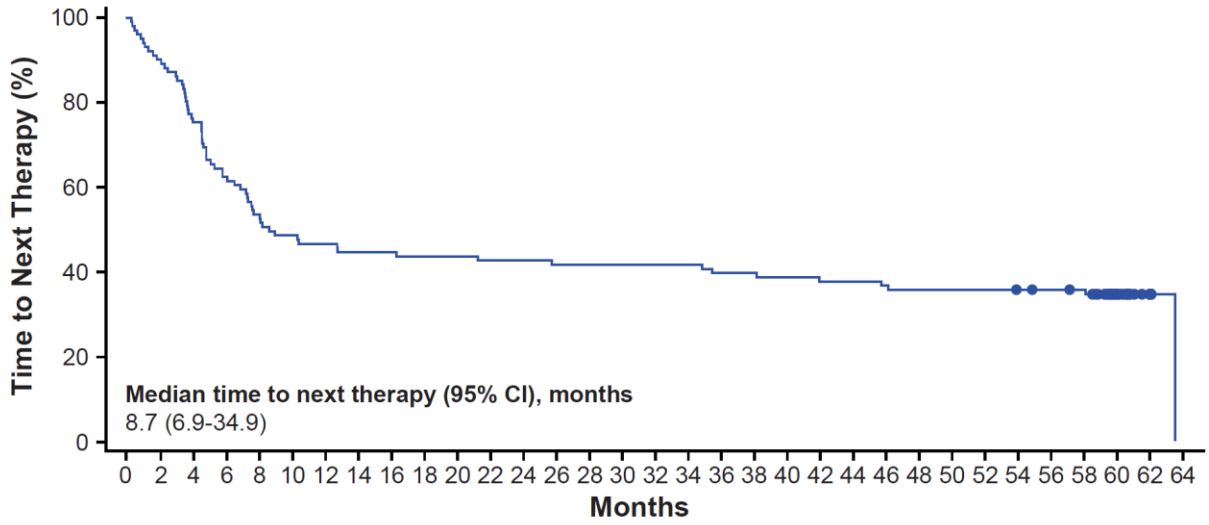


Figure S4. Overall Survival by Event-Free Survival at 12 and 24 Months

This figure shows a Kaplan Meier estimate of OS among 101 patients with LBCL treated with axi-cel in Cohorts 1 and 2 of phase 2, assessed by EFS events by moths 12 and 24. Axi-cel, axicabtagene ciloleucel; EFS, event-free survival; LBCL, large B-cell lymphoma; NE, not estimable; OS, overall survival.

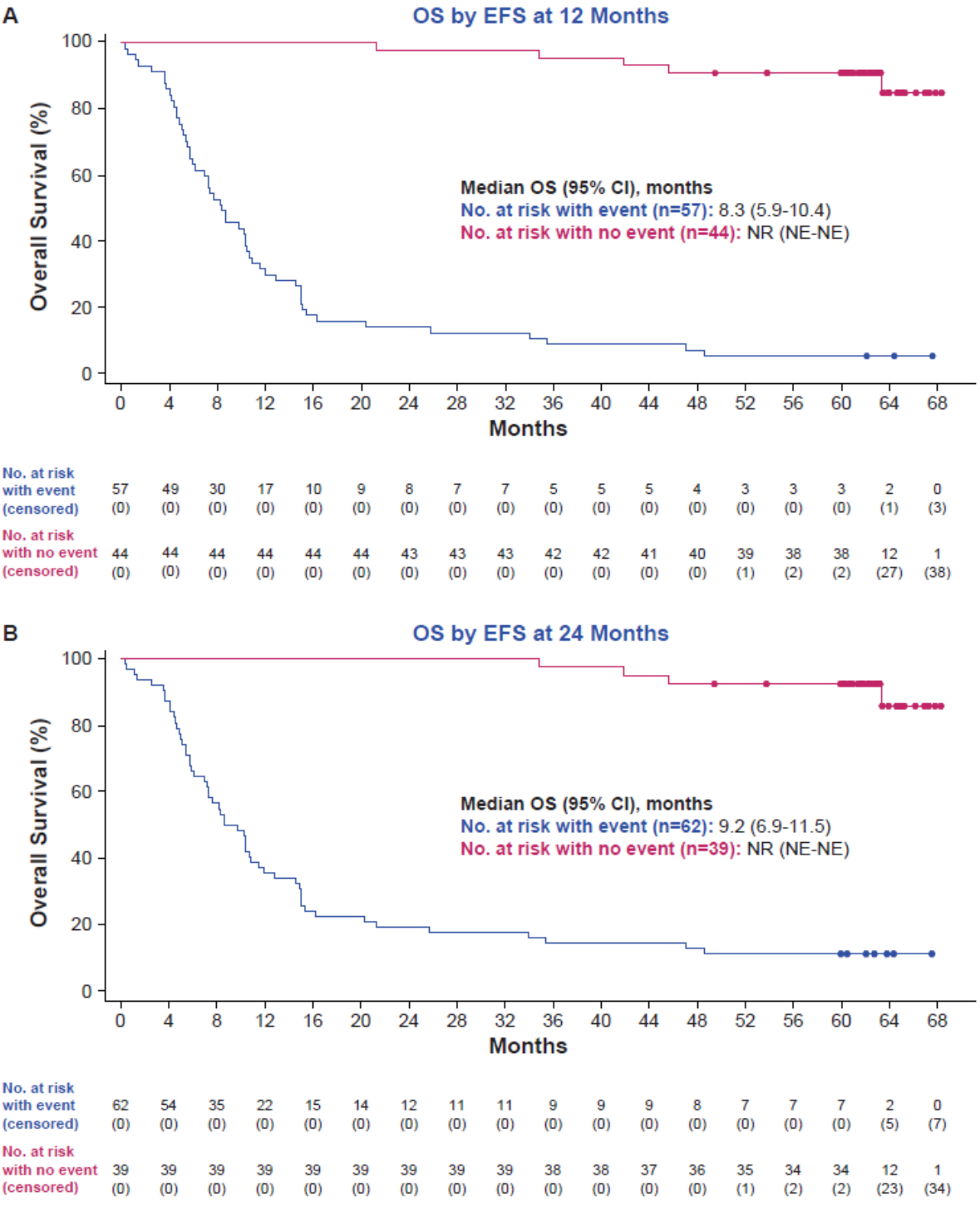
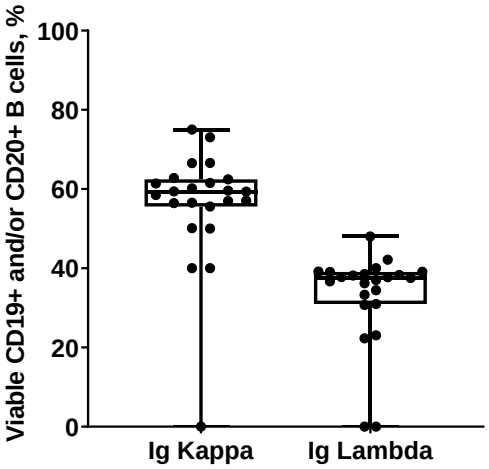


Figure S5. B-Cell Recovery and Diversity.

This figure shows CD19 positive and or CD20 positive B-cell levels by Ig kappa and lambda subtypes as well as B-cell diversity by class at 3-years postinfusion. Ig, immunoglobulin.

B-Cell Recovery



B-Cell Diversity

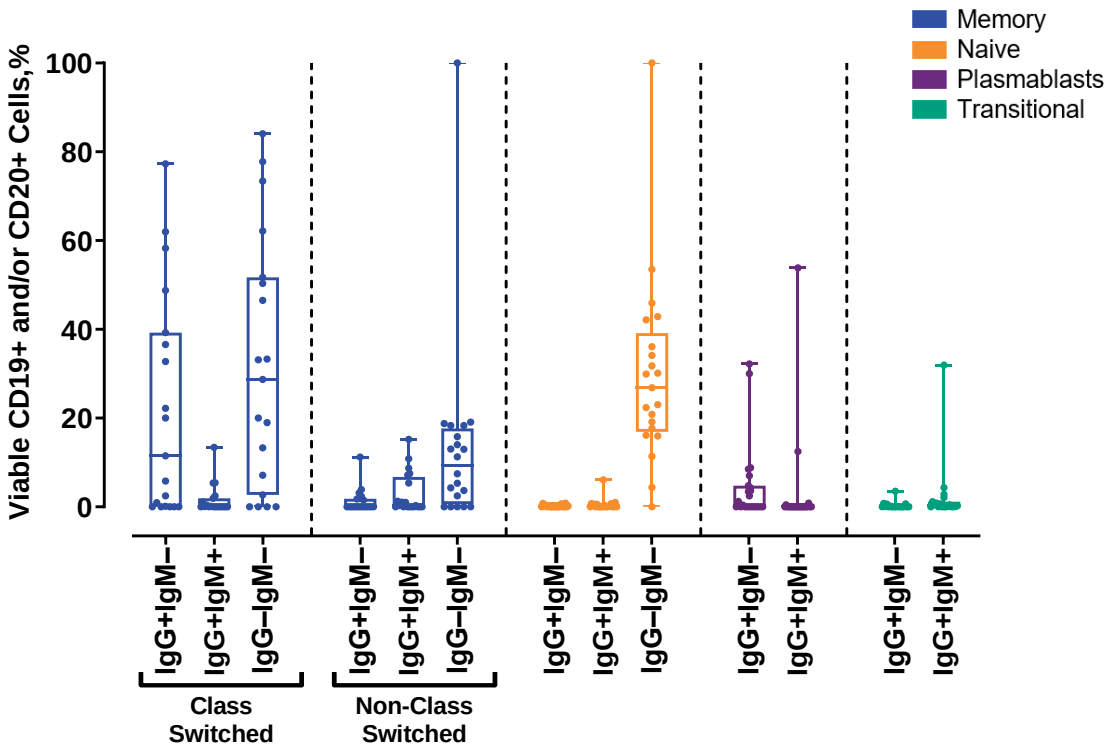


Table S1. Progression-Free and Overall Survival by Response at 3, 6, 12, and 24 Months

	Month 3 N=97	Month 6 N=94	Month 12 N=95	Month 24 N=95
N, median PFS (95% CI) by response, months				
CR	n=42 63.4 (35.6-NE)	n=39 63.4 (NE-NE)	n=39 63.4 (NE-NE)	n=36 63.4 (NE-NE)
PR	n=10 54.0 (4.4-NE)	n=4 NR (54.0-NE)	n=1 54.0 (NE-NE)	n=1 54.0 (NE-NE)
SD	n=7 7.3 (3.7-18.4)	n=1 18.4 (NE-NE)	-	-
PD	n=38 2.6 (1.9-2.8)	n=50 2.8 (2.4-3.0)	n=55 3.0 (2.7-3.1)	n=58 3.0 (2.8-3.3)
Median OS (95% CI) by response, months				
CR	n=42 NR (63.4-NE)	n=39 NR (NE-NE)	n=39 NR (NE-NE)	n=36 NR (NE-NE)
PR	n=10 NR (7.7-NE)	n=4 NR (NE-NE)	n=1 NR (NE-NE)	n=1 NR (NE-NE)
SD	n=7 10.9 (7.3-NE)	n=1 NR (NE-NE)	-	-
PD	n=38 6.5 (5.1-10.3)	n=50 8.5 (5.9-10.7)	n=55 8.7 (6.9-10.9)	n=58 10.0 (7.3-12.0)

CR, complete response; NE, not estimable; NR, not reached; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease.

Table S2. Secondary Malignancies

N (%)	Treated Patients (N=101)
Patients with a new malignancy	5 (5)
Non-melanoma skin cancer	2 (2)
t-MDS*	3 (3)

*t-MDS are events of MDS that have been identified as being likely related to prior chemotherapy (ie, chemotherapy before axi-cel infusion or the first dose of study drug).

MDS, myelodysplastic syndrome; t-MDS, treatment-related myelodysplastic syndrome.

Table S3. Summary of B-Cell Aplasia by Ongoing Response at 60 Months

n (%)	Ongoing Response (n=29)	Relapsed (n=51)	Nonresponder (N=17)
B cells tested at Baseline	23 (79.3)	41 (80.4)	9 (52.9)
No B cells	11 (47.8)	27 (65.9)	6 (66.7)
With B cells	12 (52.2)	14 (34.2)	3 (33.3)
B cells tested at Month 3	27 (93.1)	44 (86.3)	6 (35.3)
No B cells	21 (77.8)	33 (75.0)	4 (66.7)
With B cells	5 (18.5)	9 (20.5)	2 (33.3)
Undetermined	1 (3.7)	2 (4.6)	–
B cells tested at Month 6	24 (82.8)	27 (52.9)	1 (5.9)
No B cells	19 (79.2)	21 (77.8)	–
With B cells	5 (20.8)	5 (18.5)	1 (100)
Undetermined	–	1 (3.7)	–
B cells tested at Month 9	25 (86.2)	20 (39.2)	1 (5.9)
No B cells	10 (40.0)	9 (45.0)	1 (100)
With B cells	15 (60.0)	11 (55.0)	–
B cells tested at Month 12	26 (89.7)	15 (29.4)	–
No B cells	13 (50.0)	7 (46.7)	–
With B cells	13 (50.0)	8 (53.3)	–
B cells tested at Month 15	27 (93.1)	12 (23.5)	–
No B cells	10 (37.0)	6 (50.0)	–
With B cells	17 (63.0)	6 (50.0)	–
B cells tested at Month 18	23 (79.3)	11 (21.6)	–
No B cells	7 (30.4)	5 (45.5)	–
With B cells	16 (69.6)	6 (54.6)	–
B cells tested at Month 24	25 (86.2)	8 (15.7)	–
No B cells	7 (28.0)	1 (12.5)	–
With B cells	18 (72.0)	7 (87.5)	–

REFERENCE

1. Locke FL, Neelapu SS, Bartlett NL, et al: Phase 1 results of ZUMA-1: a multicenter study of KTE-C19 anti-CD19 CAR T cell therapy in refractory aggressive lymphoma. Mol Ther 25:285-295, 2017