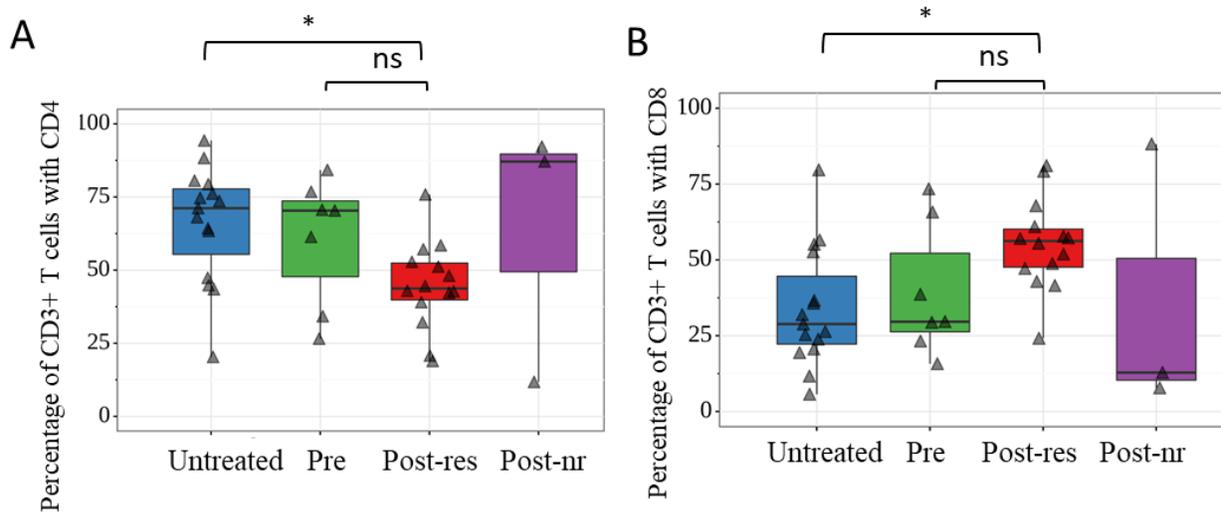
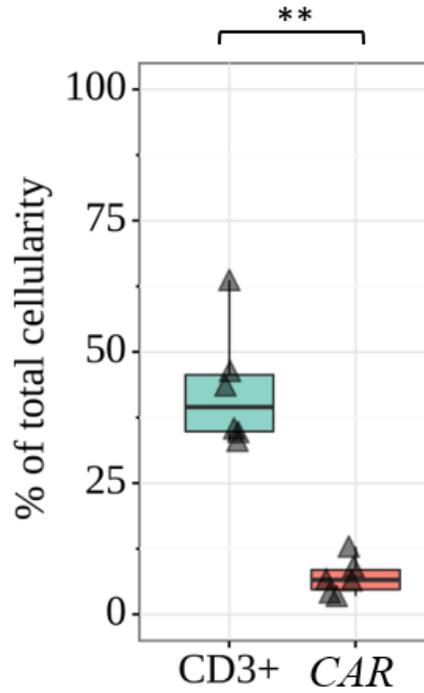


Supplementary Figures



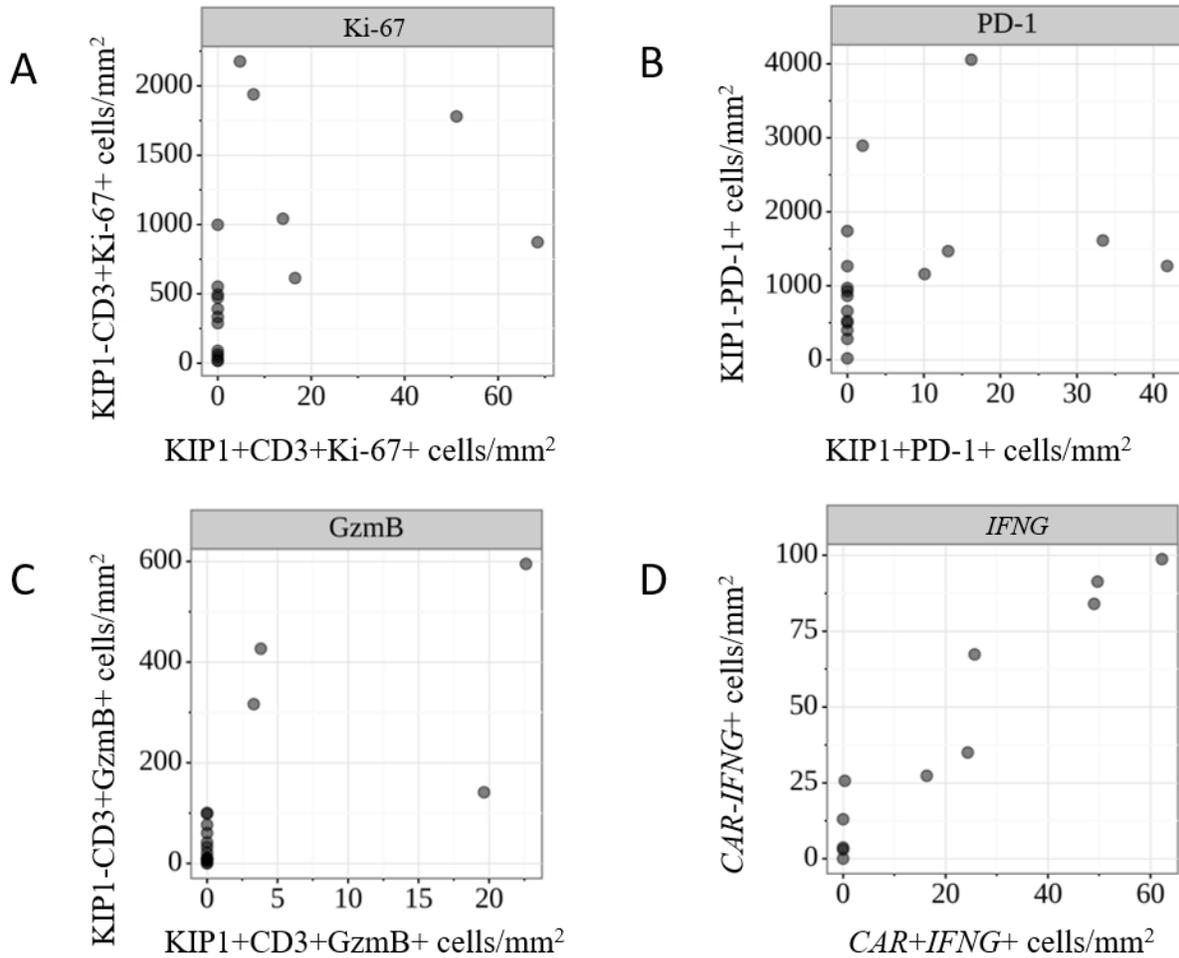
Supplementary Figure 1. CD4⁺ and CD8⁺ T cells as a percentage of total T cells within the DLBCL TME.

Quantified mIF data from groups of DLBCL biopsy samples obtained at diagnosis (Untreated, n=15, *blue*), prior to axicabtagene ciloleucel infusion (Pre, n=7, *green*), and following axicabtagene ciloleucel divided according to a best overall response (Post-res [complete response or partial response], n=14, *red*; Post-nr [stable disease or progressive disease], n=3, *purple*). **A.** The percentage of CD4⁺ cells among total CD3⁺ T cells for the indicated groups. The Kruskal-Wallis (KW) test indicated a significant difference in percentages between conditions ($p = 0.04$), with only the difference between Untreated and Post-res being significant (adjusted $p=0.02$). **B.** The percentage of CD8⁺ among total CD3⁺ T cells for the indicated groups. P values comparing groups were >0.05 from a two-sided Mann-Whitney U test. The KW test indicated a significant difference in percentages between conditions ($p = 0.04$), with only the difference between Untreated and Post-res being significant (adjusted $p=0.02$).



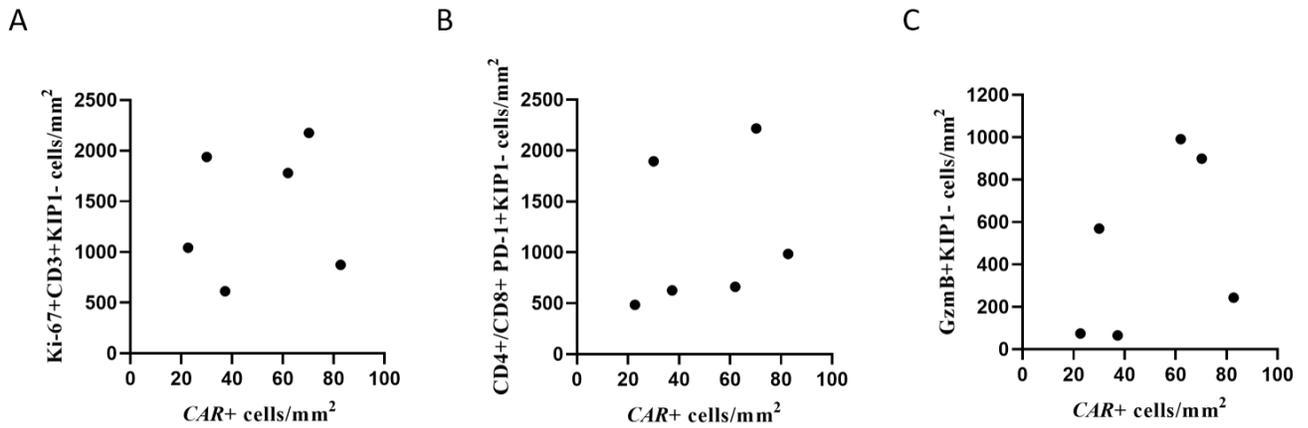
Supplementary Figure 2. Proportion of total T cells and CAR T cells in biopsies following axicabtagene ciloleucel.

The percentage of total cells expressing CD3 and the percentage of total cells expressing *CAR* transcript in biopsies taken after axicabtagene ciloleucel infusion and in which *CAR*-expressing cells were detected. From a two-sided Mann-Whitney U test ** means $p < 0.01$.



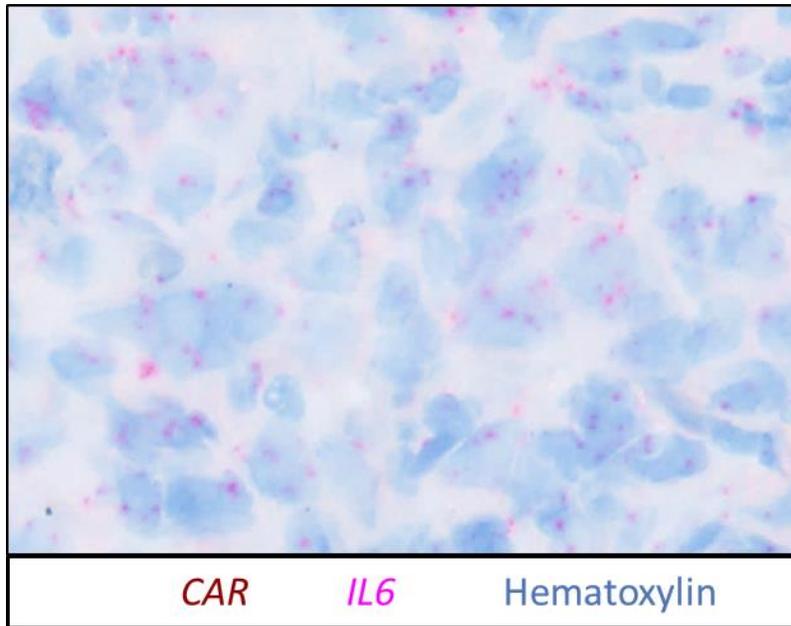
Supplementary Figure 3. Activation markers expressed by CAR and non-CAR T cells in biopsies after axicabtagene ciloleucel infusion.

Comparative quantitative data from mIF and duplex ISH for biopsies obtained after axicabtagene ciloleucel infusion (n=13). **A.** The densities of KIP1⁺CD3⁺Ki-67⁺ cells and KIP1⁻CD3⁺Ki-67⁺ cells (tau=0.51, p=0.007, n=18). **B.** The densities of KIP1⁺PD-1⁺ cells and KIP1⁻PD-1⁺ cells (tau=0.52, p=0.007, n=17). **C.** The densities of KIP1⁺CD3⁺GzmB⁺ cells and KIP1⁻CD3⁺GzmB⁺ (tau=0.60, p=0.002, n=18). **D.** The densities of CAR⁺ IFNG⁺ and CAR⁻ IFNG⁺ cells (tau=0.94, p<0.001, n=11). Kendall tau correlation test applied.



Supplementary Figure 4. CAR+ cells and the expression of activation markers by non-CAR T cells after axicabtagene ciloleucel infusion.

Quantitative ISH and mIF data comparing the densities of CAR+ cells and CD3⁺Ki-67⁺KIP1⁻ cells (A), CD4⁺/CD8⁺ PD-1⁺KIP1⁻ cells (B), and GzmB⁺KIP1⁻ cells (C).



Supplementary Figure 5. *IL6* transcripts in cells with malignant histomorphology.

Supplementary Table 1. Biopsies with Analyzable Tissue from ZUMA-1 Trial

ID	Age	BOR	Pre AC biopsy	Post AC biopsy	days post AC infusion	biopsy site
1	62	CR	Y	Y*	9	gastric fundus
2	66	CR	Y	Y	10	groin LN
3	73	SD	N/A	Y	30	right neck LN
4	35	PR	N/A	Y*	7	right pelvic LN
5	73	PR	N/A	Y	10	Abdominal Mass
6	60	PR	N/A	Y	10	Abdominal LN
7	61	CR	N/A	Y	9	Left Iliac LN
8	76	CR	N/A	Y*	7	Right Groin LN
9	32	CR	N/A	Y	14	Mediastinal Mass
10	64	CR	Y	Y	10	Left Shoulder
11	80	SD	N/A	Y	5	Mediastinal Mass
12	56	PD	N/A	Y	21	Right Leg
13	56	CR	N/A	Y*	9	Mediastinal Mass
14	62	CR	N/A	Y	9	Left cervical LN
15	78	CR	N/A	Y*	9	Right Chest Wall
16	52	PR	N/A	Y	13	Abdominal Mass
17	74	CR	N/A	Y	11	Right Chest Wall Mass
18	63	CR	Y	Y*	7	Right Superficial Back
19	50	CR	Y	N/A	N/A	Right Inguinal LN
20	58	CR	Y	N/A	N/A	Skin, Right Leg
21	68	CR	Y	N/A	N/A	Abdominal Mass

BOR= best overall response, CR= complete response, PR= partial response, SD= stable disease, PD= progressive disease, AC= Axicabtagene ciloleucel
N/A= not available/ not relevant
*= samples with CAR cells detected

Supplementary Table 2. Antibodies used for Multiplex Immunofluorescence Studies

Primary Antibody target	Primary Antibody dilution	Clone	Manufacturer	Species	Opal Fluorochrome
CAR	3000	KIP-1	Kite	rabbit	520
CAR	8000	KIP-3	Kite	rabbit	620
CD3	750	PolyC	Dako	rabbit	540
CD4	250	4B12	Dako	mouse	570
CD8	7000	C8/144B	Dako	mouse	540
PAX5	200	24/Pax-5	BD	mouse	620, 570
PD-1	11000	EH33	DFCI, CST	mouse	690
GZMB	100	GRB-7	Dako	mouse	620
Ki-67	2000	MIB-1	Dako	mouse	690

CST: Cell Signaling Technology

BD: BD transduction laboratories