haematologica
Journal of the Ferrata Storti Foundation

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Received: June 11, 2025.
Accepted: December 16, 2025.

Citation: Ronit Marcus, Abraham Avigdor, Uri Greenbaum, Samantha Brown, Shalev Fried, Noa Golan-Accav, Noga Shem-Tov, Ronit Yerushalmi, Ivetta Danylesko, Elad Jacoby, Arnon Nagler, Avichai Shimoni, Orit Itzhaki, Jonathan Esensten, Ori Ben Valid, Annamaria Ballweg, Xavier Deschênes-Simard, Efrat Luttwak, Gunjan Shah, Michael Scordo, Parastoo Dahi, Miguel-Angel Perales, Tsila Zuckerman, Sean M Devlin, Dana Yehudai-Ofir, Hazim Khatib, Nivin Shibli, Roni Shouval and Ofrat Beyar-Katz. Locally manufactured versus commercial CAR T therapy for large B-cell lymphoma: a multi-center propensity score-matched analysis. Haematologica. 2025 Dec 24. doi: 10.3324/haematol.2025.288419 [Epub ahead of print]

Locally manufactured versus commercial CAR T therapy for large B-cell lymphoma : a multi-center propensity score-matched analysis

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This work has been presented in part as an oral presentation at the 67th ASH annual meeting.

Funding

The reported research was supported in part by the National Institutes of Health/National Cancer Institute (NIH/NCI) award number P01CA023766 and Memorial Sloan Kettering Cancer

Center Support Grant (P30 CA008748). RS reports grant support from an NIH-NCI K08CA282987, the Long Island Sound Chapter, Swim Across America, The Lymphoma Research Foundation, and Comedy vs. Cancer.

COI

RS reports speaker honoraria from Incyte, MSD, andSanofi.

OBK reports speaker honoraria from Gilead and Novartis.

JHE reports sponsored research funding from Lonza, Inc. for the development of point-of-care cellular therapy manufacturing devices.

XDS: He has served on advisory boards for Gilead, and has received speaker honoraria from Bristol Myers Squibb and Hoffmann-La Roche.

Dr. Perales reports honoraria from Adicet, Allogene, Caribou Biosciences, Celgene, Bristol-Myers Squibb, Equilium, Exevir, ImmPACT Bio, Incyte, Kite/Gilead, Merck, Miltenyi Biotec, MorphoSys, Nektar Therapeutics, Novartis, Omeros, OrcaBio, Pierre Fabre, Sanofi, Syncopation, Takeda, VectivBio AG, and Vor Biopharma. He serves on DSMBs for Cidara Therapeutics and Sellas Life Sciences. He has ownership interests in Omeros and OrcaBio. He has received institutional research support for clinical trials from Allogene, Genmab, Incyte, Kite/Gilead, Miltenyi Biotec, Nektar Therapeutics, and Novartis.

Authors contribution

RM, AA, UG, SB, OBK and RS- designed and conducted the study, performed the analysis and interpretation of data. All other authors (SB, SF, NGA, NST, RY, ID, EJ, AN, AS, OI, JE, OBV, AB, XDS, EL, GS, MS, PD, MAP, TZ, SMD, DYO, HK, NS) contributed to data analysis and critically revised the manuscript. All authors read and approved the final version of the manuscript.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ABSTRACT

Locally manufactured chimeric antigen receptor T-cell (CAR T) therapy enables rapid manufacturing and a substantially shorter vein-to-vein time. However, its clinical efficacy compared to commercial CAR T products remains unclear. This retrospective study compared outcomes in patients with Large B-cell lymphoma (LBCL) treated with a CD19-directed autologous locally manufactured CAR T product (CD28-based co-stimulation) versus axicabtagene-ciloleucel (axi-cel) or tisagenlecleucel (tisa-cel) across three academic centers. All patients had received at least two prior lines of therapy. Propensity score analysis for CAR T product adjusted for age, karnofsky performance status, lactate dehydrogenase (LDH) level, primary refractory disease, and transformed histology were performed to account for underlying differences in treatment groups. Among 330 patients (132 axi-cel, 104 tisa-cel, 94 locally manufactured), those treated with locally manufactured CAR T were younger, had higher performance status, and were more likely to present with elevated LDH and primary refractory disease. Median time from apheresis to CAR T infusion was significantly shorter with locally manufactured CAR T (11 days) than with axi-cel (38 days) or tisa-cel (44 days) ($p<0.001$). In adjusted analyses for progression-free survival (PFS), there was a trend to improved PFS in locally manufactured versus axi-cel (weighted hazard ratio [WHR], 1.54; 95% CI, 1.00–2.37; $p=0.051$) and no significant difference between locally manufactured versus tisa-cel (HR 0.71, 95% CI 0.45–1.11; $p=0.13$). Overall survival was comparable across groups: locally manufactured vs axi-cel (HR 1.35, 95% CI 0.87–2.10; $p=0.18$) and locally manufactured vs tisa-cel (HR 0.85, 95% CI 0.53–1.34; $p=0.48$). Rates of grade ≥2 cytokine release syndrome were lower with locally manufactured CAR T. These findings support locally manufactured CAR T as a clinically comparable alternative to commercial products in LBCL, with the potential advantage of rapid availability for patients with aggressive disease.

INTRODUCTION

Chimeric antigen receptor T-cell (CAR T) therapies targeting CD19 have transformed the treatment landscape for B-cell malignancies, offering potential cure for patients with otherwise poor prognosis[1]. However, widespread use of commercial CAR T products is constrained by high costs, limited availability, and extended production times, particularly for patients with rapid disease progression[2–4]. A promising alternative is locally manufactured cell production, which may alleviate some of these limitations.

Although establishing facilities for locally manufacturing requires significant investment in infrastructure and personnel, production cost are substantially lower, logistical processes are minimized by eliminating the need for complex multi-step shipping and traceability[5], and the quality control period may be more efficient and shortened [6,7]. Importantly, the time from apheresis to infusion is considerably shorter with locally manufactured- cells compared to 30-40 days for most commercial products. Additionally, the use of fresh cells, without freezing and storage, may improve product quality and efficacy [8].

Despite these potential advantages, locally manufactured products can pose challenges. Smaller centers may find it difficult to justify the high start-up costs and training requirements. Moreover, the lack of standardization across such facilities and the operator-dependent nature of production may raise concerns about product consistency and safety[9–11]. Locally manufactured products often rely on decentralized production settings with greater variability in protocols, instrumentation, and operator expertise. This variability can affect multiple critical aspects of product quality. For instance, differences in T-cell subset composition, transduction efficiency, and expansion kinetics may lead to inconsistencies in potency, persistence, and in vivo expansion of the final product—key factors that influence clinical outcomes[12]. Additionally, locally manufactured products may also be more susceptible to contamination or batch failure, due to less robust infrastructure and automation. To date, large-scale comparative data on the safety and efficacy of locally manufactured versus commercial CAR T therapies are lacking.

Sheba medical center has operated a locally manufactured CAR T program since 2016, using an anti-CD19 construct with CD28-based co-stimulation[13]. With the availability of commercial CAR T products in Israel, a subset of patients with large B-cell lymphoma (LBCL) have received either locally manufactured or commercial therapies based on factors such as insurance coverage, clinical urgency, and manufacturing availability.

This international multicenter study provides the first direct comparison of locally manufactured and commercial CAR T products in LBCL, analyzing key clinical outcomes such as efficacy and toxicity, along with logistical considerations like time to infusion. A retrospective study using an inverse probability weights design was conducted to evaluate an autologous CD19 locally manufactured CAR T product in comparison to commercial alternatives in patients with LBCL who had received at least two prior lines of therapy.

METHODS

Patient Population and Study Design:

Adults with relapsed/refractory (R/R) aggressive B-cell lymphomas who had failed at least two prior treatment lines were included in this study. Included histologies were diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), high-grade B-cell lymphoma, primary mediastinal B-cell lymphoma, and transformed follicular lymphoma. Patients with primary central nervous system lymphoma, Burkitt lymphoma, and Richter transformation were excluded.

Patients treated with locally manufactured products were treated at Sheba hospital between 2016 and 2024. The locally manufactured product, a CD28-based academic CAR T and FMC63-scFv directed against CD19, was administered as part of a phase I/II clinical trial (NCT02772198)[13]. Patients received fresh 1 × 10^6 CAR-positive cells/kg following lymphodepletion.

Commercial CAR T products were administered at Sheba hospital, Memorial Sloan Kettering Cancer Center (MSKCC) and Rambam Health Care Campus between 2017 and 2024. The treatment was administered in accordance with the product leaflet and local protocols. For axi-cel and tisa-cel products, lymphodepletion included fludarabine 30 mg/m2 × 3 days (days −5 to −3) and cyclophosphamide 300-500 mg/m2 × 3 day (days −5 to −3). In some cases, bendamustine 90 mg/m2 × 2 day (days −4 to −3) was administered. For locally manufactured products, lymphodepletion included fludarabine 25 mg/m2 × 3 days (days −4 to −2) and cyclophosphamide 900 mg/m2 × 1 day (day −2).

The study was approved by the local institutional review boards of all participating centers.

Data Collection and Definitions:

Data were collected using the REDCap database[14,15]. Response to therapy was assessed by investigators using PET-CT scans at 100 days post-CAR T infusion, according to Lugano response criteria[16]. Overall response rate (ORR) at day 100 was defined as the proportion of patients achieving complete response (CR) or partial response (PR). Overall survival (OS) was measured from CAR T infusion to death. Progression-free survival (PFS) was measured from CAR T infusion to first documented progression or death; Patients were censored at time of next treatment without a preceding progression or at last follow-up. Time to relapse was defined from CAR T infusion until relapse, such that death without relapse was considered a competing event; Time to non-relapse mortality (NRM) was defined from CAR T infusion until death without a preceding relapse, where relapse was considered a competing event. Toxicities, including cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), were recorded per the American Society of Transplantation and Cellular Therapy (ASTCT) consensus guidelines[17].

Statistical Analysis:

Continuous variables were reported as median and range, while categorical data are presented as percentages. Baseline characteristics were compared using Pearson's chi-squared, Fisher's exact, and Kruskal-Wallis rank sum tests, as appropriate. Propensity score modeling for CAR T product assignment (locally manufactured versus axicabtagene ciloleucel [axi-cel] and locally manufactured versus tisagenlecleucel [tisa-cel]) was conducted using logistic regression models that adjusted for the following factors: age, transformed lymphoma, primary refractory disease prior to apheresis, LDH levels before lymphodepletion, and karnofsky performance scale (KPS). OS and PFS were estimated using Kaplan-Meier methods. Associations between CAR T products and survival endpoints were calculated using Cox proportional hazards models. Relapse and non-relapse mortality were estimated using the cumulative incidence function. Associations between CAR T products and relapse and NRM were calculated using the cause-specific hazards approach for competing risks regression, which were weighted using the inverse probabilities derived from the propensity score models. Associations between CAR T products and CRS and ICANS were estimated using logistic regression models. To account for potential differences in CAR T product assignment, all models were inverse probability weighted (IPW) using the estimated propensity scores. Presenting both sets of estimates allows readers to assess the impact of adjustment, evaluate the robustness of the findings, and better understand the influence of patient selection on outcomes. For sensitivity analysis, unadjusted

estimates are reported as well. Statistical significance was set at a two-sided p-value <0.05. Data were analyzed using R version 4.3.2.

RESULTS

Patient Characteristics

Data were collected from 330 patients treated with anti-CD19 CAR T ~~cells~~ at participating centers. The CAR T products used were axi-cel (n=132, 40%), tisa-cel (n=104, 32%), and Sheba locally manufactured (locally manufactured, n=94, 28%). The most common diagnosis across the groups was DLBCL NOS, with frequencies of 77%, 86%, and 76% for axi-cel, tisa-cel, and locally manufactured, respectively (**Table 1**).

Patients receiving locally manufactured CAR T were younger, with a median age of 51 years, compared to 62 years for axi-cel and 69 years for tisa-cel (p<0.001). Additionally, they had better KPS, with 71% of locally manufactured patients having a KPS≥90, compared to 48% for axi-cel and 50% for tisa-cel (p=0.001). Locally manufactured patients had higher rates of elevated LDH levels (64%) before lymphodepletion compared to 46% and 45% in the axi-cel and tisa-cel groups, respectively (p=0.015). Furthermore, locally manufactured patients had a higher rate of primary refractory disease (54%) compared to 48% in axi-cel and 36% in tisa-cel (p=0.024). The frequencies of CAR-T cell therapy product by site are shown in Supplemental Table 1.

Production efficiency of locally manufactured product was 98.6%[13], but data are unavailable for commercial products. The time from apheresis to infusion ("vein-to-vein time") was significantly shorter for locally manufactured, with a median of 11 days (IQR 10-11), compared to 38 days (IQR 30-46) for axi-cel and 44 days (IQR 38-53) for tisa-cel (p<0.001). Consequently, only 21% of locally manufactured patients received bridging therapy (primarily steroids) compared to 67% for axi-cel and 78% for tisa-cel (p<0.001). Most patients had progressive or stable disease before CAR T infusion across all groups, with 72%, 74%, and 72% in the axi-cel, tisa-cel, and locally manufactured groups, respectively.

Lymphodepletion therapy was primarily composed of fludarabine and cyclophosphamide in 99% of axi-cel patients, 96% of tisa-cel patients, and 100% of locally manufactured patients. Bendamustine was used as lymphodepletion for 1 patient (0.8%) in the axi-cel group and 4 patients (3.8%) in the tisa-cel group.

Response

Disease response at day 100 is shown in Supplemental Table 2. ORR was highest with axi-cel (64% CR, 17% PR), followed by tisa-cel (50% CR, 11% PR) and locally manufactured (42% CR, 22% PR). In adjusted analyses using IPW, locally manufactured was associated with a significantly lower overall response compared to axi-cel (weighted odds ratio [WOR], 0.17; 95% CI, 0.07–0.38; $p<0.001$). No significant difference was observed between locally manufactured and tisa-cel (WOR, 0.41; 95% CI, 0.15–1.03; $p=0.075$).

Overall survival and progression-free survival

Median follow-up was 39 months (95% CI: 29–46), 35 months (95% CI: 31–51) and 49 months (95% CI: 43–51) for axi-cel, tisa-cel and locally manufactured respectively.

Median OS was longest with axi-cel (31 months [95% CI, 20–not reached]), followed by tisa-cel (16 months [13– not reached]) and locally manufactured (15 months [9–38]) (**figure 1a**). In IPW-adjusted Cox models for OS (**figure 2a**), there were no significant differences between locally manufactured and the commercial CAR T products (locally manufactured vs axi-cel weighted hazard ratio [WHR], 1.35; 95% CI, 0.87–2.10; $p=0.18$; locally manufactured vs. Tisa-cel (WHR, 0.85; 95% CI, 0.53–1.34; $p=0.48$). Unadjusted Cox models yielded similar results, with no significant associations found.

Median PFS was also longest with axi-cel (11 months [95% CI, 7.5–27]), followed by tisa-cel (3.3 months [95% CI, 2.5–6.6]) and locally manufactured (95% CI, 3.0 months [2.0–17]) (**figure 1b**). In IPW models (**figure 2b**), a trend to improved PFS with axi-cel was found when comparing locally manufactured to axi-cel (WHR, 1.54; 95% CI, 1.00–2.37; $p=0.051$) and no difference with locally manufactured compared to tisa-cel (WHR, 0.71; 95% CI, 0.45–1.11; $p=0.13$). Results were similar in the unadjusted models.

Relapse and non-relapse mortality

At 1-year post-infusion, the cumulative incidence of relapse (**figure 1c**) was highest with tisa-cel (67% [95% CI, 56–75]), followed by locally manufactured (57% [44–67]) and axi-cel (46% [38–55]). In both unadjusted and IPW analyses (**figure 2c**), relapse risk was higher with locally manufactured compared to axi-cel (WHR, 1.71; 95% CI, 1.08–2.70; $p=0.021$), but comparable to tisa-cel (WHR, 0.68; 95% CI, 0.43–1.07; $p=0.095$).

The 1-year cumulative incidence of NRM (**figure 1d**) was 7.8% (95% CI, 3.1–15.0) with locally manufactured, 6.5% (3.0–12.0) with axi-cel, and 5.1% (1.9–11.0) with tisa-cel. In unadjusted and IPW analyses (**figure 2d**), NRM risk with locally manufactured was comparable to both axi-cel (WHR, 1.02; 95% CI, 0.38–2.77; *p*=0.96) and tisa-cel (WHR, 0.98; 95% CI, 0.28–3.37; *p*=0.97).

Toxicity

Grade ≥2 CRS occurred in 26% of patients treated with locally manufactured (n=24), 52% with axi-cel (n=68), and 37% with tisa-cel (n=38, **table 2**). In both unadjusted and weighted logistic regression models, the risk of grade ≥2 CRS was lower with locally manufactured compared to axi-cel (weighted odds ratio [WOR], 0.31; 95% CI, 0.17–0.56; *p*<0.001). Locally manufactured was also associated with a lower odds of grade ≥2 CRS compared to tisa-cel in unadjusted analysis (*p*=0.018), but was comparable in the IPW model (WOR, 0.57; 95% CI, 0.28–1.14; *p*=0.12).

Grade ≥2 ICANS was least common in patients treated with tisa-cel (12%, n=12), followed by locally manufactured (29%, n=27) and axi-cel (36%, n=47). The odds of grade ≥2 ICANS with locally manufactured was comparable to axi-cel (WOR, 0.60; 95% CI, 0.33–1.09; *p*=0.10), while patients treated with locally manufactured had significantly higher odds of grade ≥2 ICANS in comparison to tisa-cel (WOR, 4.85; 95% CI, 1.90-14.4; p=0.002).

DISCUSSION

This international multicenter study provides the first direct comparison of a locally manufactured CAR T product with commercially available CD19-directed CAR T therapies in patients with LBCL treated after at least two prior lines of therapy. Our findings demonstrate that despite being administered to a younger and more high-risk population—characterized by superior performance status, elevated lactate dehydrogenase levels, and a higher incidence of primary refractory disease—the localy manufactured product yielded clinical outcomes comparable to tisa-cel and, in some respects, approaching those of axi-cel. Notably, locally manufactured CAR T was associated with a substantially shorter vein-to-vein time and lower rates of high-grade CRS. PFS and OS were similar when compared to commercially available

CAR T. These results suggest that locally manufactured CAR T therapies can offer a viable and timely alternative to commercial products.

These findings are consistent with other reports on local manufacturing CAR T programs. The high rate of successful cell production and the short vein-to-vein times in our cohort—ranging from 7 to 13 days—align with previous studies[18,19]. Recently, a systematic literature review and meta-analysis assessed vein-to-vein time in patients with R/R LBCL treated with commercial CAR T therapies: axi-cel, tisa-cel, and liso-cel. Axi-cel was associated with the shortest median vein-to-vein time (30.6 days), compared to tisa-cel (48.4 days) and liso-cel (35.9 days). Moreover, longer vein-to-vein time (40+ days) was associated with significantly lower CR rates and worse OS compared to shorter vein-to-vein time (<28 days or 28 to <40 days), highlighting the potential benefits of earlier infusion with CAR T therapies[20]. Over the past few years, there has been remarkable development in producing CAR T within just 24–48 hours, representing a dramatic shift from traditional timelines[21–23]. These advances not only support faster production but also preserve greater stemness in the CAR T, potentially improving long-term persistence and efficacy.

Notably, during the COVID-19 pandemic, centers in Spain with local manufacturing programs were able to continue administering CAR T therapy despite global supply chain disruptions, further demonstrating the logistical advantages of local production[24]. Toxicity and efficacy outcomes in these studies were also comparable to both our cohort and real-world data from commercial CAR T products.

The differences between locally manufactured and commercial products observed in our cohort, particularly prior to adjustment for patient-related variables, could be explained by a distinct patient population receiving locally manufactured therapy. As commercial CAR T products became available, only patients who did not meet the approved indications, had rapidly progressing disease, faced production failures, or lacked insurance coverage were enrolled in the Sheba locally manufactured clinical trial. Consequently, locally manufactured patients tended to have higher tumor burdens and may have received additional treatments prior to CAR T therapy, as reflected in the baseline characteristics (**table 1**). Furthermore, tumor burden in this study was assessed using LDH levels, which are less informative than metabolic tumor volume (MTV) and may have limited the accuracy of comparisons.

A noteworthy feature of the locally manufactured product used is the absence of cryopreservation during manufacturing. Preclinical and early clinical studies suggest that

cryopreservation may negatively impact CAR T efficacy[8,18]. While our study did not directly address this issue, future research is needed to explore the potential benefits of using fresh, non-cryopreserved cells.

Another key finding was the lower proportion of patients in the locally manufactured cohort receiving bridging therapy, likely due to the shorter vein-to-vein times. Delaying CAR T infusion for additional bridging therapy cycles increases the risk of disease progression or therapy-related complications[25]. However, the impact of foregoing bridging therapy entirely remains unclear, especially in patients with high disease burden[26]. In our study, patients in the locally manufactured cohort generally had more advanced disease, raising the question of whether a single cycle of bridging therapy may benefit certain high-burden patients, while others with less aggressive disease could benefit from faster production and infusion times[27,28].

Importantly, our study demonstrated that locally manufactured therapy is safe. While it is well established that CD28-containing CAR T are associated with a higher toxicity burden, our cohort showed lower rates of high-grade CRS compared to both axi-cel and tisa-cel, as well as fewer high-grade ICANS compared to axi-cel.

This study highlights a central role of academic locally manufactured models in overcoming some of the limitations of commercial CAR T, while also complementing their use. Academic networks can drive innovation and address unmet needs, but collaboration with the pharmaceutical industry is likely necessary for scaling production and ensuring broader availability. A hybrid approach that combines academic research with industry infrastructure could provide a balanced solution to expand global access to CAR T therapies[6,10]. Notably, A phase II multicenter study is evaluating the feasibility and efficacy of locally manufactured CAR T (ARI-0001) versus commercial axi-cel in relapsed or refractory DLBCL. Success could further support local production as a way to improve access and quality(NCT05641428).

This study has several limitations. First, its retrospective design introduces the potential for selection bias and residual confounding, despite the use of propensity score weighting to adjust for key baseline differences. Unmeasured variables—such as disease kinetics, comorbidities, or center-level practices—may have influenced treatment allocation and outcomes. Second, the study included only patients treated in the third-line setting or beyond, and results may not generalize to earlier lines of therapy. Given the markedly shorter manufacturing time of locally manufactured CAR T, earlier use—particularly in the second-line setting—may yield even

greater clinical benefit. Finally, there is no data on CAR T expansion and persistence that could be associated with therapeutic response and toxicity. Prospective, randomized studies will be needed to definitively establish the relative effectiveness of locally manufactured versus commercial CAR T therapies, though such trials may be constrained by logistical and funding barriers.

To our knowledge, this is the first multicenter, matched comparison of a locally manufactured CD19-directed CAR T therapy with commercial products in patients with relapsed or refractory LBCL. Despite being administered to a higher-risk population, the locally manufactured product demonstrated comparable efficacy and safety to commercial therapies, while offering the logistical advantage of markedly shorter manufacturing times. These findings suggest that locally manufactured manufacturing can serve as a clinically effective and operationally feasible alternative, particularly for patients requiring expedited treatment. As global demand for CAR T therapies continues to rise, scalable and timely delivery models such as locally manufactured may play an increasingly important role in expanding equitable access.

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Table 1: Patient characteristics:

Characteristic	**Axicabtagene ciloleucel**, N = 132, n (%); Median (IQR)	**Tisagenlecleucel**, N = 104 , n (%); Median (IQR)	**Local manufacture**, N = 94, n (%); Median (IQR)	**p-value**[1]
Pre-CAR-T Age	62 (52, 69)	69 (60, 75)	51 (38, 63)	<0.001
Sex				0.070
Male	89 (67%)	55 (53%)	55 (59%)	
Female	43 (33%)	49 (47%)	39 (41%)	
Pre-CAR-T KPS (categorized)				0.001
>=90	63 (48%)	51 (50%)	66 (71%)	
<90	67 (52%)	52 (50%)	27 (29%)	
Unknown	2	1	1	
Diagnosis				
DLBCL NOS	101 (77%)	89 (86%)	71 (76%)	
High-grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangement	10 (7.6%)	8 (7.7%)	5 (5.3%)	
Primary mediastinal B-cell lymphoma	11 (8.3%)	0 (0%)	13 (14%)	
High-grade B-cell lymphoma, NOS	6 (4.5%)	4 (3.8%)	4 (4.3%)	
EBV-positive DLBCL	1 (0.8%)	1 (1.0%)	0 (0%)	
T-cell rich DLBCL	2 (1.5%)	2 (1.9%)	1 (1.1%)	
Intravascular large B-cell lymphoma	1 (0.8%)	0 (0%)	0 (0%)	
Transformed NHL				0.3
De-novo LBCL	76 (58%)	70 (67%)	61 (65%)	
Transformed LBCL	55 (42%)	34 (33%)	33 (35%)	
Unknown	1	0	0	
Cell of origin				0.038

Characteristic	**Axicabtagene ciloleucel**, N = 132, n (%); Median (IQR)	**Tisagenlecleucel**, N = 104 , n (%); Median (IQR)	**Local manufacture**, N = 94, n (%); Median (IQR)	**p-value**[1]
non-GCB	53 (45%)	62 (63%)	37 (51%)	
GCB	64 (55%)	37 (37%)	35 (49%)	
Unknown	15	5	22	
Disease stage at apheresis				0.5
<=II	29 (23%)	28 (27%)	19 (20%)	
III-IV	98 (77%)	75 (73%)	74 (80%)	
Unknown	5	1	1	
LDH range pre-lymphodepletion				0.015
Normal	68 (54%)	53 (55%)	33 (36%)	
Elevated	58 (46%)	44 (45%)	58 (64%)	
Unknown	6	7	3	
Bulky disease (a mediastinal mass >1/3 intra-thoracic diameter on PA chest x-ray or any mass ≥ 10 cm) pre-apheresis	22 (17%)	10 (9.7%)	13 (14%)	0.3
Previous auto-HCT	35 (27%)	24 (23%)	25 (27%)	0.8
Previous allo-HCT	6 (4.5%)	3 (2.9%)	4 (4.3%)	0.8
Primary refractory - pre-apheresis	64 (48%)	37 (36%)	49 (54%)	0.024
Unknown	0	0	4	
Bridging	89 (67%)	81 (78%)	20 (21%)	<0.001
Pre-CAR-T disease response				0.13
CR	4 (3.0%)	9 (8.7%)	2 (2.1%)	
PR	33 (25%)	18 (17%)	24 (26%)	
SD/PD	95 (72%)	76 (74%)	68 (72%)	
Unknown	0	1	0	
Lymphodepletion				0.070

Characteristic	**Axicabtagene ciloleucel**, N = 132, n (%); Median (IQR)	**Tisagenlecleucel**, N = 104 , n (%); Median (IQR)	**Local manufacture**, N = 94, n (%); Median (IQR)	**p-value**[1]
Cyclophosphamide/Fludarabine	131 (99%)	100 (96%)	94 (100%)	
Bendamustine	1 (0.8%)	4 (3.8%)	0 (0%)	
Days from apheresis to CAR-T infusion	38 (30, 46)	44 (38, 53)	11 (10, 11)	<0.001

[1] Kruskal-Wallis rank sum test; Pearson's Chi-squared test; Fisher's exact test

Abbreviation: KPS: Karnofsky Performance Status, DLBCL NOS: Diffuse Large B-Cell Lymphoma, Not Otherwise Specified**,** LBCL: Large B-Cell Lymphoma, GCB: Germinal Center B-Cell-like**,** LDH: lactate dehydrogenase , PA: Posteroanterior, HCT: Hematopoietic Cell Transplant, CR: complete response, PR: partial response, SD: satble disease, PD: progressive disease

Table 2: CAR-T associated toxicities:

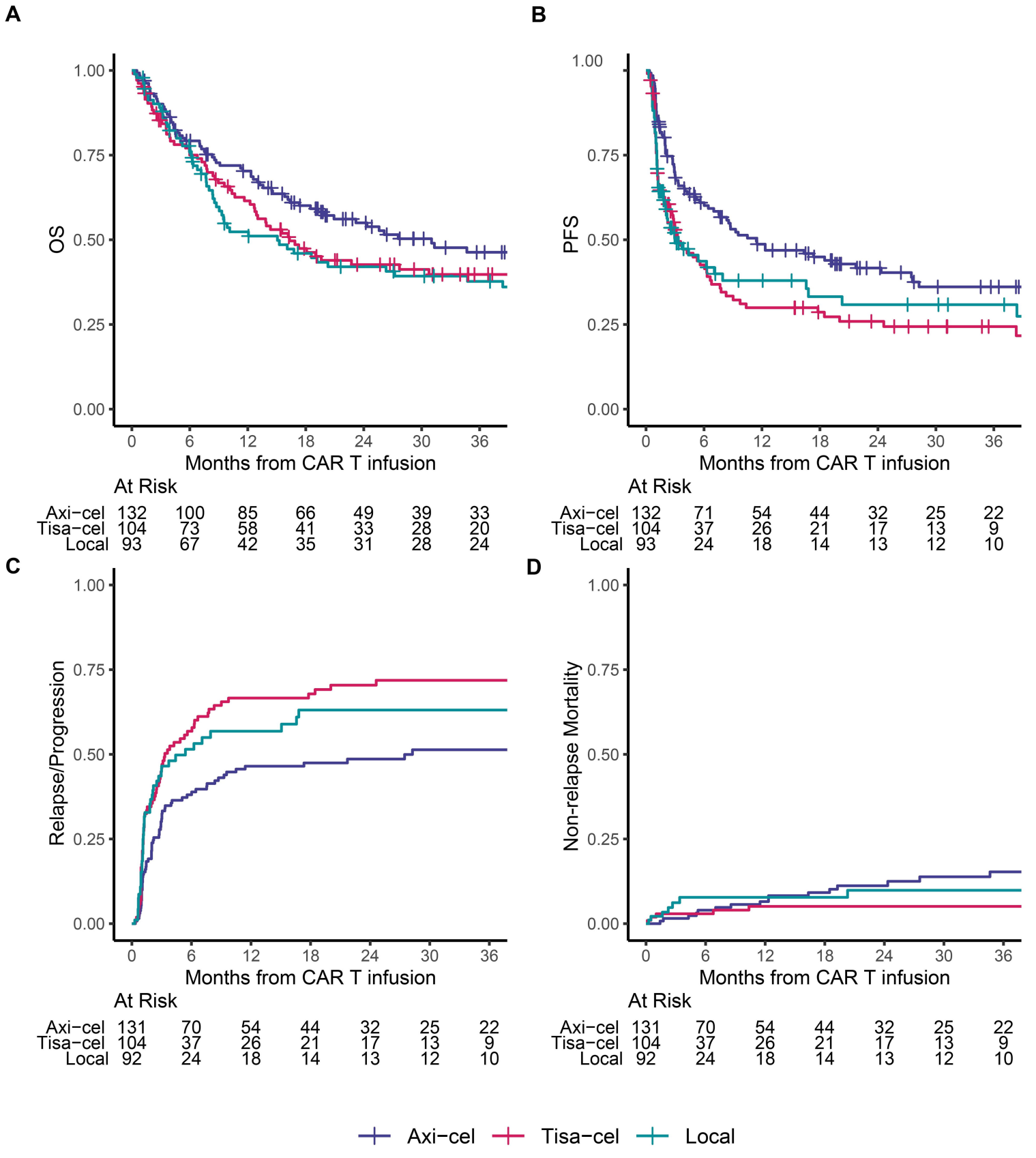
Characteristic	**Axicabtagene ciloleucel**, N = 132, n (%)	**Tisagenlecleucel**, N = 104, n (%)	**Local manufacture**, N = 94, n (%)
CRS			
0	12 (9.1%)	30 (29%)	13 (14%)
1	52 (39%)	36 (35%)	57 (61%)
2	45 (34%)	25 (24%)	13 (14%)
3	21 (16%)	11 (11%)	8 (8.5%)
4	2 (1.5%)	1 (1%)	2 (2.1%)
5	0 (0%)	1 (1%)	1 (1.1%)
ICANS			
0	74 (56%)	84 (81%)	57 (61%)
1	11 (8.3%)	7 (6.8%)	10 (11%)
2	15 (11%)	8 (7.8%)	4 (4.3%)
3	27 (20%)	4 (3.8%)	18 (19%)
4	5 (3.8%)	0 (0%)	5 (5.3%)
Unknown	0 (0%)	1 (0.9%)	0 (0%)
ICU admission within first 30 days post CAR-T infusion	17 (14%)	6 (6.1%)	3 (3.4%)
Unknown	13	5	7

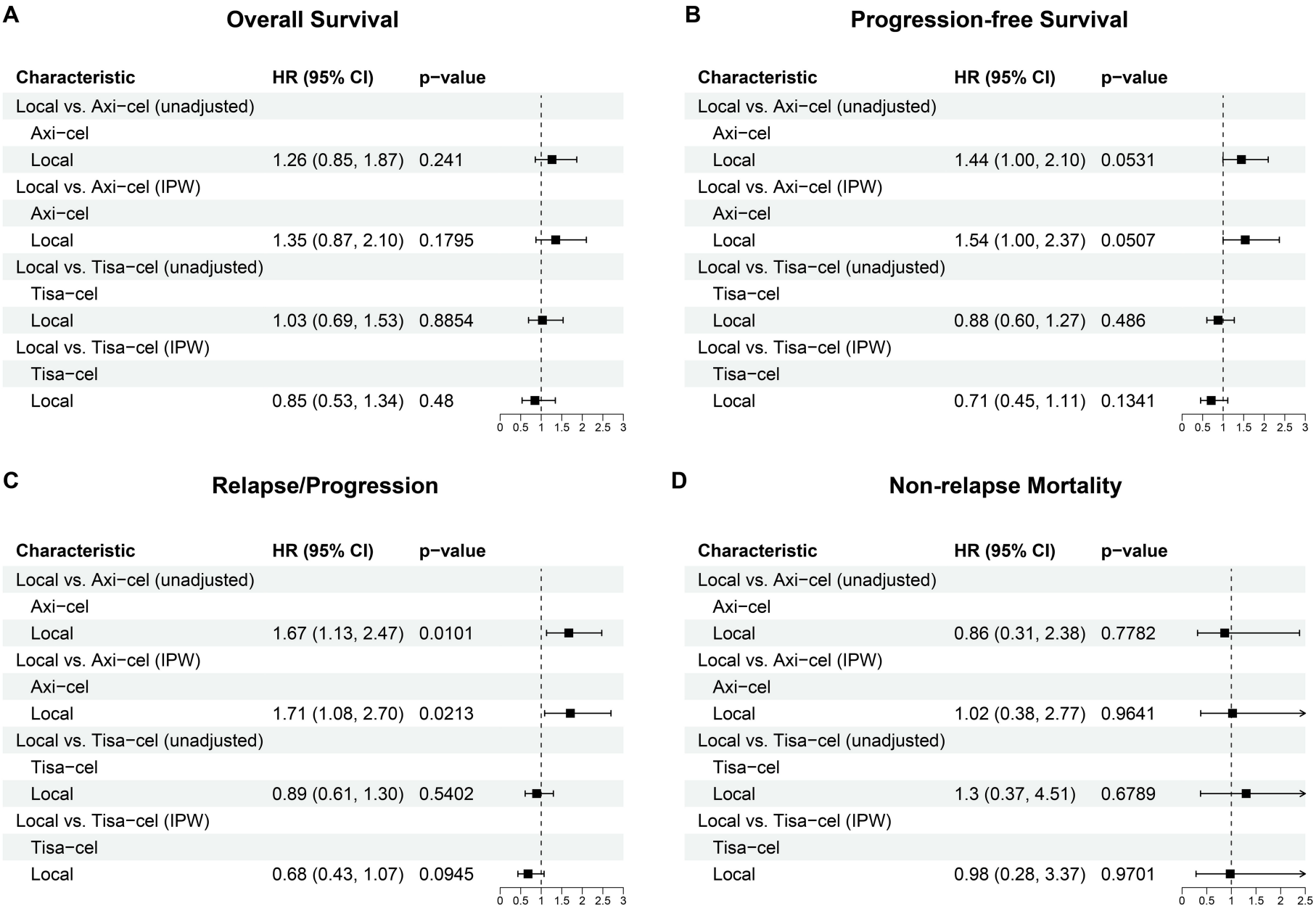
Abbreviation: CRS: Cytokine Release Syndrome, ICANS:Immune Effector Cell-Associated Neurotoxicity Syndrome, ICU: Intensive Care Unit

Figure legends:

Figure 1. Unadjusted Clinical Outcomes by CAR T Product. (A) Overall survival (OS) and (B) progression-free survival (PFS) by CAR T product, estimated using Kaplan-Meier methods. (C) Cumulative incidence of relapse or progression, and (D) non-relapse mortality, stratified by CAR T product and analyzed using competing risks methodology. *One patient who received locally manufactured CAR T with incomplete survival data is excluded from Figures 1A-D. One additional patient who received locally manufactured CAR T and one patient who received axi-cel were excluded from the Figures 1C and 1D due to incomplete relapse data.

Figure 2. Hazard Ratios for Outcomes by CAR T Product. (A) Overall survival (OS) and (B) progression-free survival (PFS) by CAR T product, estimated using unadjusted and inverse probability weighted (IPW)-adjusted Cox models. (C) Cumulative incidence of relapse or progression and (D) non-relapse mortality (NRM), analyzed using IPW-adjusted Cox models stratified by CAR T product.


A
OS
1.00
0.75
0.50
0.25
0.00
0
6
12
18
24
30
36
Months from CAR T infusion
At Risk
Axi−cel 132 100 85 66 49 39 33
Tisa−cel 104 73 58 41 33 28 20
Local 93 67 42 35 31 28 24
B
PFS
1.00
0.75
0.50
0.25
0.00
0
6
12
18
24
30
36
Months from CAR T infusion
At Risk
Axi−cel 132 71 54 44 32 25 22
Tisa−cel 104 37 26 21 17 13 9
Local 93 24 18 14 13 12 10
C
Relapse/Progression
1.00
0.75
0.50
0.25
0.00
0
6
12
18
24
30
36
Months from CAR T infusion
At Risk
Axi−cel 131 70 54 44 32 25 22
Tisa−cel 104 37 26 21 17 13 9
Local 92 24 18 14 13 12 10
D
Non−relapse Mortality
1.00
0.75
0.50
0.25
0.00
0
6
12
18
24
30
36
Months from CAR T infusion
At Risk
Axi−cel 131 70 54 44 32 25 22
Tisa−cel 104 37 26 21 17 13 9
Local 92 24 18 14 13 12 10
Axi−cel
Tisa−cel
Local


A
Overall Survival
Characteristic
HR (95% CI)
p−value
Local vs. Axi−cel (unadjusted)
Axi−cel
Local
1.26 (0.85, 1.87)
0.241
Local vs. Axi−cel (IPW)
Axi−cel
Local
1.35 (0.87, 2.10)
0.1795
Local vs. Tisa−cel (unadjusted)
Tisa−cel
Local
1.03 (0.69, 1.53)
0.8854
Local vs. Tisa−cel (IPW)
Tisa−cel
Local
0.85 (0.53, 1.34)
0.48
0 0.5 1 1.5 2 2.5 3
B
Progression-free Survival
Characteristic
HR (95% CI)
p−value
Local vs. Axi−cel (unadjusted)
Axi−cel
Local
1.44 (1.00, 2.10)
0.0531
Local vs. Axi−cel (IPW)
Axi−cel
Local
1.54 (1.00, 2.37)
0.0507
Local vs. Tisa−cel (unadjusted)
Tisa−cel
Local
0.88 (0.60, 1.27)
0.486
Local vs. Tisa−cel (IPW)
Tisa−cel
Local
0.71 (0.45, 1.11)
0.1341
0 0.5 1 1.5 2 2.5 3
C
Relapse/Progression
Characteristic
HR (95% CI)
p−value
Local vs. Axi−cel (unadjusted)
Axi−cel
Local
1.67 (1.13, 2.47)
0.0101
Local vs. Axi−cel (IPW)
Axi−cel
Local
1.71 (1.08, 2.70)
0.0213
Local vs. Tisa−cel (unadjusted)
Tisa−cel
Local
0.89 (0.61, 1.30)
0.5402
Local vs. Tisa−cel (IPW)
Tisa−cel
Local
0.68 (0.43, 1.07)
0.0945
0 0.5 1 1.5 2 2.5 3
D
Non-relapse Mortality
Characteristic
HR (95% CI)
p−value
Local vs. Axi−cel (unadjusted)
Axi−cel
Local
0.86 (0.31, 2.38)
0.7782
Local vs. Axi−cel (IPW)
Axi−cel
Local
1.02 (0.38, 2.77)
0.9641
Local vs. Tisa−cel (unadjusted)
Tisa−cel
Local
1.3 (0.37, 4.51)
0.6789
Local vs. Tisa−cel (IPW)
Tisa−cel
Local
0.98 (0.28, 3.37)
0.9701
0 0.5 1 1.5 2 2.5

Supplemental Table 1: Frequency of CAR-T cell therapy product by site

Characteristic	MSKCC, N = 128[1]	Rambam Health Care Campus, N = 19[1]	Sheba Medical Center, N = 183[1]
CAR-T product			
Axicabtagene ciloleucel	71 (55%)	10 (53%)	51 (28%)
Tisagenlecleucel	57 (45%)	9 (47%)	38 (21%)
Sheba POC anti CD19	0 (0%)	0 (0%)	94 (51%)

[1] n (%)

Supplemental Table 2: Disease response at day 100 by CAR-T cell therapy product

Characteristic	Axicabtagene ciloleuce, N = 132[1]	Tisagenlecleucel, N = 104[1]	Sheba POC anti CD19, N = 94[1]
Response at Day 100 Post-CAR-T			
CR	42 (45%)	30 (34%)	10 (18%)
PR	5 (5.3%)	3 (3.4%)	0 (0%)
SD	2 (2.1%)	0 (0%)	0 (0%)
POD	45 (48%)	54 (62%)	45 (82%)
Unknown	38	17	39
Response of CR or PR at Day 100 Post-CAR-T	47 (50%)	33 (38%)	10 (18%)
Unknown	38	17	39
Response of CR at Day 100 Post-CAR-T	42 (45%)	30 (34%)	10 (18%)
Unknown	38	17	39

[1] n (%)

Abbreviations: complete response (CR), partial response (PR), stable disease (SD), progression of disease (POD).