Improvements in Axicabtagene Ciloleucel Manufacturing Result in High Delivery Success and More Predictable Turnaround Time for Patients With Relapsed/Refractory Large B-Cell Lymphoma

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Background

- Axi-cel is an autologous anti-CD19 CAR T-cell therapy approved for patients with R/R LBCL[1,2]
  - Axi-cel has demonstrated curative potential in 2L (ZUMA-7; NCT03391466) and 3L+ (ZUMA-1; NCT02348216) for patients with R/R LBCL[3,4]
- Timely receipt of axi-cel therapy, often quantified as V2VT (time from leukapheresis to product infusion), was associated with favorable responses and survival outcomes for real-world patients with R/R LBCL[5]
- Improvements in the CAR T-cell manufacturing process to maximize successful first-pass manufacturing are essential to reducing V2VT, as they eliminate the need for re-manufacture or re-leukapheresis[6]
  - Patients who received commercial CAR T-cell therapy after re-leukapheresis experienced worse survival outcomes compared with patients who received the product successfully after their first leukapheresis[7]

1. YESCARTA® (axicabtagene ciloleucel) Prescribing information. Kite Pharma, Inc; 2024. 2. YESCARTA® (axicabtagene ciloleucel) [summary of product characteristics]. Amsterdam, The Netherlands: Kite Pharma EU B.V.; 2024. 3. Westin JR, et al. *N Engl J Med.* 2023;389:148-157. 4. Neelapu SS, et al. *Blood*. 2023;141:2307-2315. 5. Locke FL, et al. *Blood*. 2022;140(Suppl 1):7512-7515. 6. Alquist L, et al. *Transplant Cell Ther.* 2024;30(Suppl):S203-S204. 7. Patel R, et al. *J Clin Oncol*. 2024;42(Suppl 16):7044.

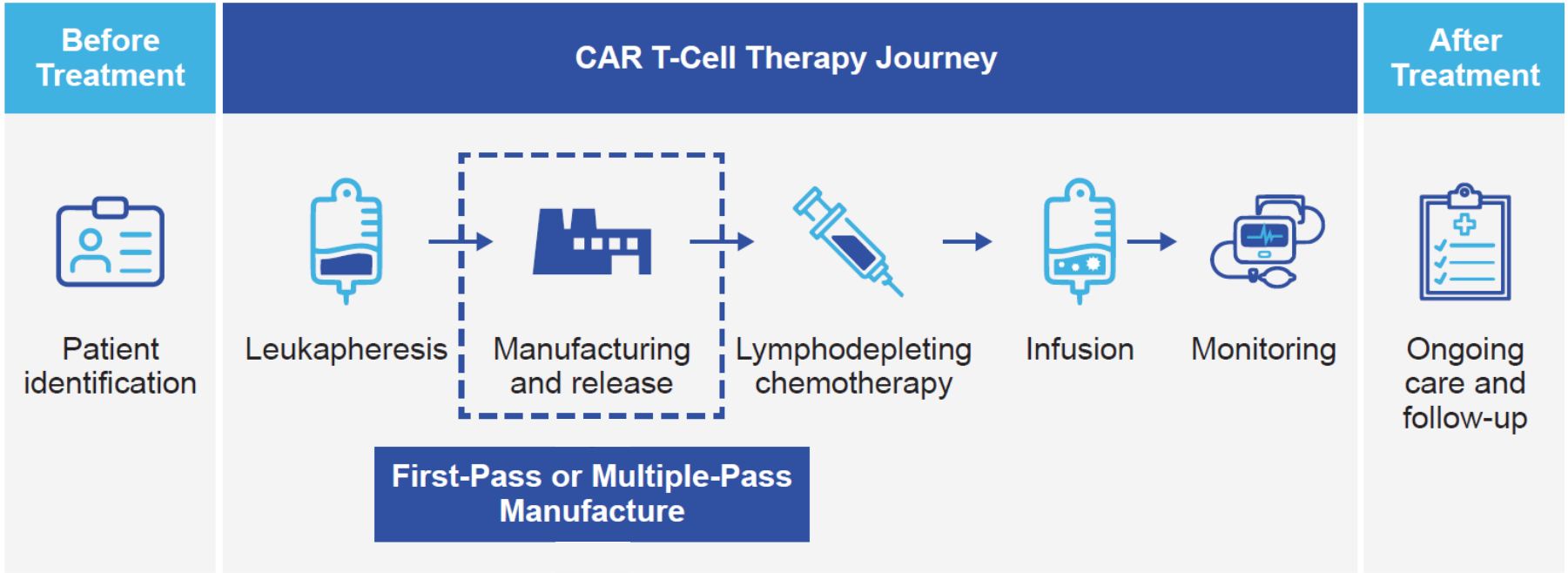
2L, second line; 3L+, third line or later; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; R/R LBCL, relapsed/refractory large B-cell lymphoma; V2VT, vein-to-vein time.

Background (Cont'd)

- In a real-world analysis of patients with R/R LBCL who received commercial axi-cel from April 2022 to January 2024, the first-pass manufacturing success rate was high among all patients, with a greater rate of success for patients treated in 2L versus those in 3L+[1]
- Given the crucial role of efficient and timely manufacturing in optimizing outcomes for patients receiving CAR T-cell therapy, there is a need to understand the impact of improvements to the axi-cel manufacturing process since its approval on manufacturing outcomes

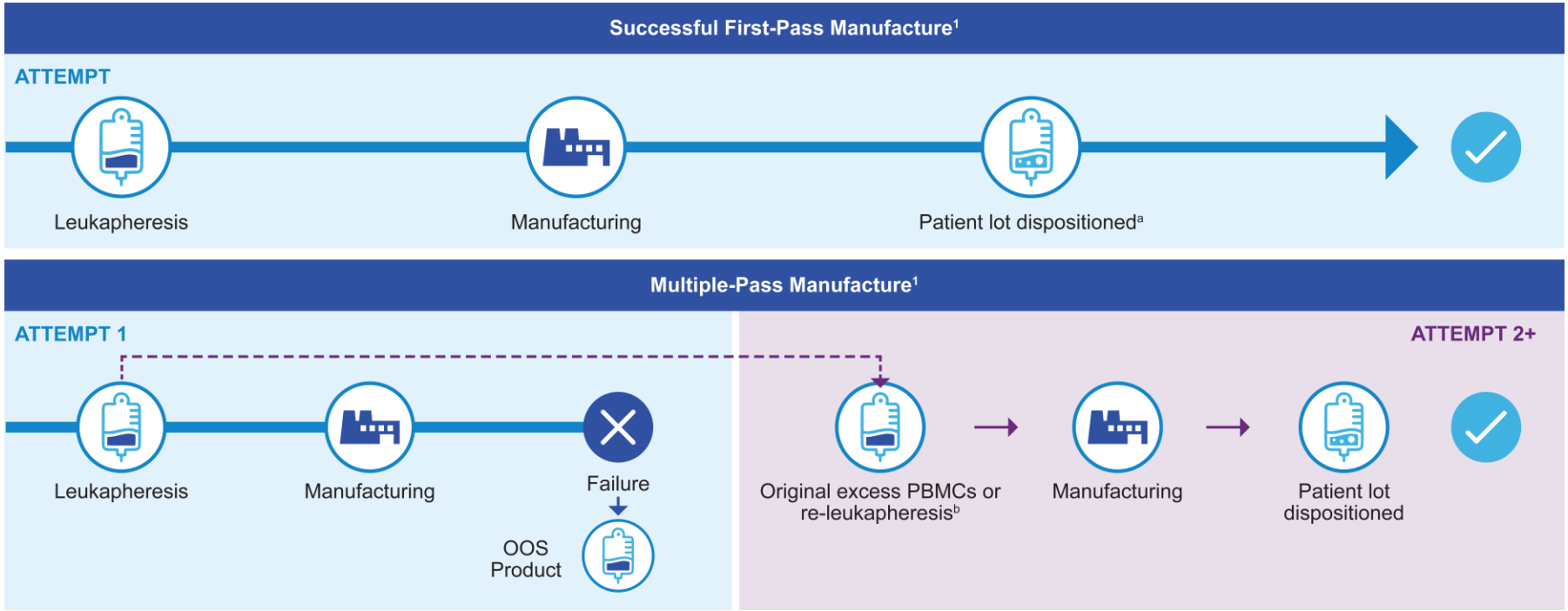
1. Westin JR, et al. *Hemasphere*. 2024;8(Suppl 1):P1425.
2L, second line; 3L+, third line or later; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; R/R LBCL, relapsed/refractory large B-cell lymphoma.

Overview of Axi-Cel Treatment Journey



Axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor.

Overview of Axi-Cel Treatment Journey (Cont'd)



[a] Disposition refers to the systematic determination of axi-cel product release or rejection resulting from evaluation of the relevant set of criteria. [b] In most cases, the subsequent manufacturing attempt is initiated with the excess PBMCs at the manufacturing site from previous leukapheresis (only few patients undergo re-leukapheresis for the following manufacturing attempt).

1. Alquist L, et al. *Transplant Cell Ther.* 2024;30(Suppl):S203-S204.

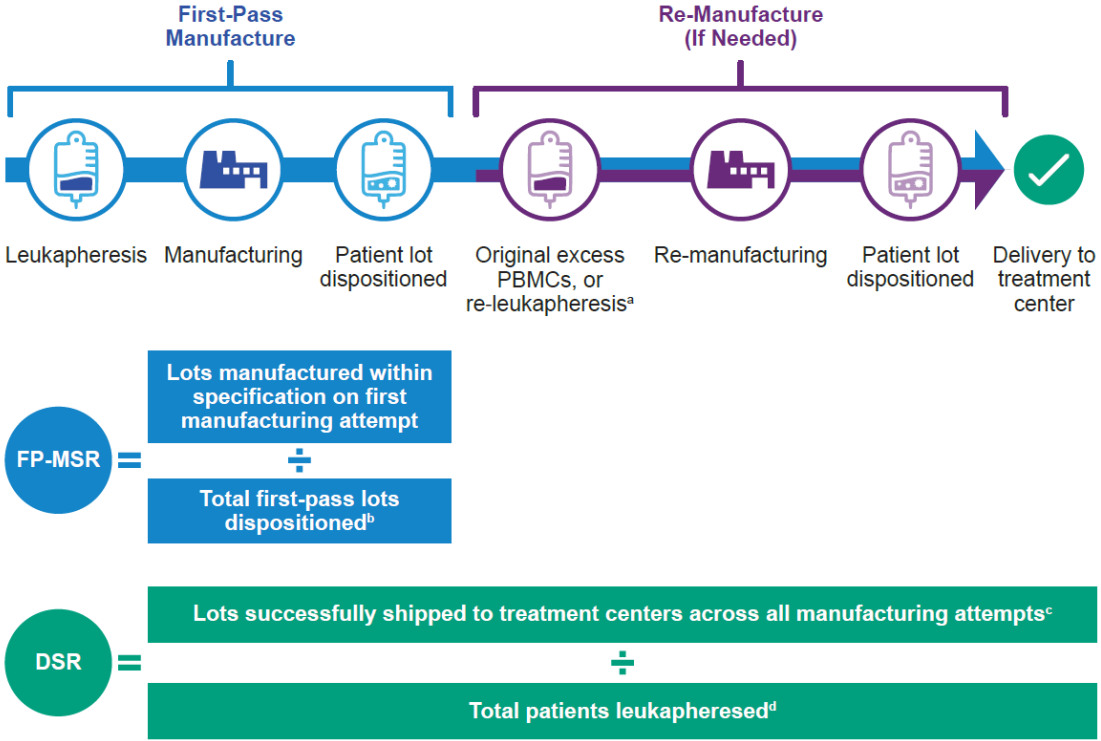
Axi-cel, axicabtagene ciloleucel; OOS, out of specification; PBMC, peripheral blood mononuclear cell.

Objective

- Here, we report the impact of improvements to the axi-cel manufacturing process on global manufacturing metrics in 2018 and 2023 for patients with R/R LBCL treated with axi-cel in 2L or 3L+

2L, second line; 3L+, third line or later; axi-cel, axicabtagene ciloleucel; R/R LBCL, relapsed/refractory large B-cell lymphoma.

Definitions of FP-MSR and DSR



[a] In most cases, the subsequent manufacturing attempt is initiated with the excess PBMCs stored at the manufacturing site from previous leukapheresis. [b] In addition to those lots terminated but not withdrawn. [c] Including out of specification lots that were released for clinical review. [d] Excluding lots in process and withdrawn patients.
DSR, delivery success rate; FP-MSR, first-pass manufacturing success rate; PBMC, peripheral blood mononuclear cell.

Methods

Patients

- Patients with R/R LBCL registered on Kite Konnect® globally for axi-cel in 2L or 3L+ and who were leukapheresed or whose lots were quality dispositioned between January 1, 2018, and December 31, 2023, were included in this analysis
  - Data reported herein are based on indications as entered into Kite Konnect by the healthcare provider

2L, second line; 3L+, third line or later; axi-cel, axicabtagene ciloleucel; R/R LBCL, relapsed/refractory large B-cell lymphoma.

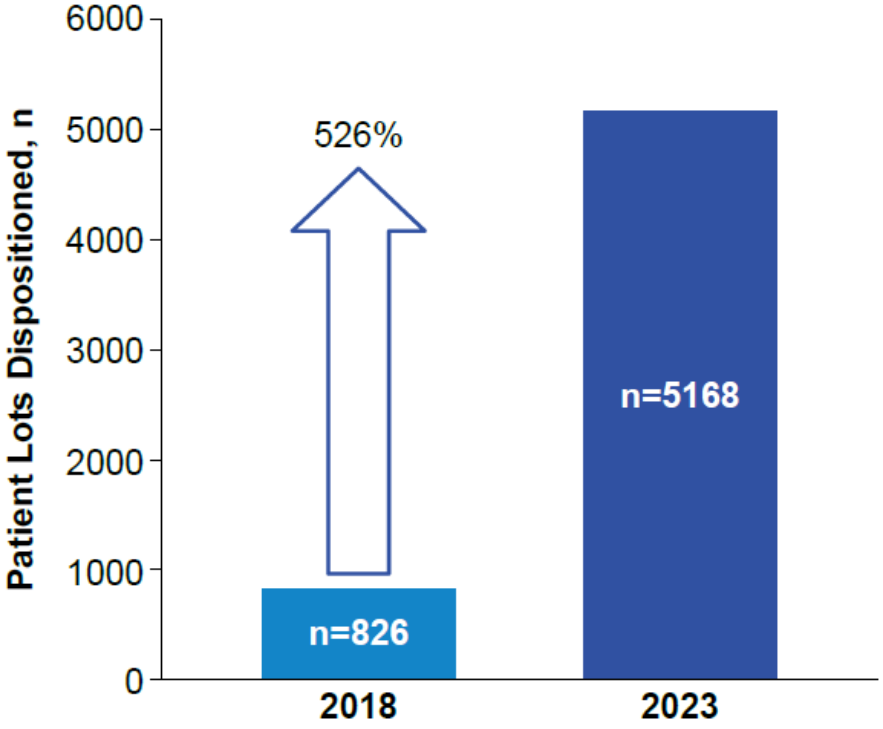
Methods (Cont'd)

Manufacturing Outcomes and Analysis

- **FP-MSR:** The percentage of first-attempt axi-cel lots dispositioned for release out of the total first-attempt lots dispositioned (determination of product release or rejection based on evaluation of release criteria), plus those terminated but not withdrawn, in the time period
- **DSR:** The percentage of axi-cel lots shipped to an authorized treatment center out of the total patients leukapheresed within the time period (excluding lots in process and withdrawn patients)
- **TAT:** Days from date of leukapheresis to date of quality release of final product
- FP-MSR and DSR were examined among all patients in 2018, and in all patients and by line of therapy in 2023; and TAT was examined among all patients from 2018-2023
- The difference in DSR in 2018 versus 2023 was evaluated by fitting a generalized linear model with a binary distribution and performing a fixed effect test, and all calculations were done using SAS (TS1M7)

axicabtagene ciloleucel; DSR, delivery success rate; FP-MSR, first-pass manufacturing success rate; TAT, turnaround time.

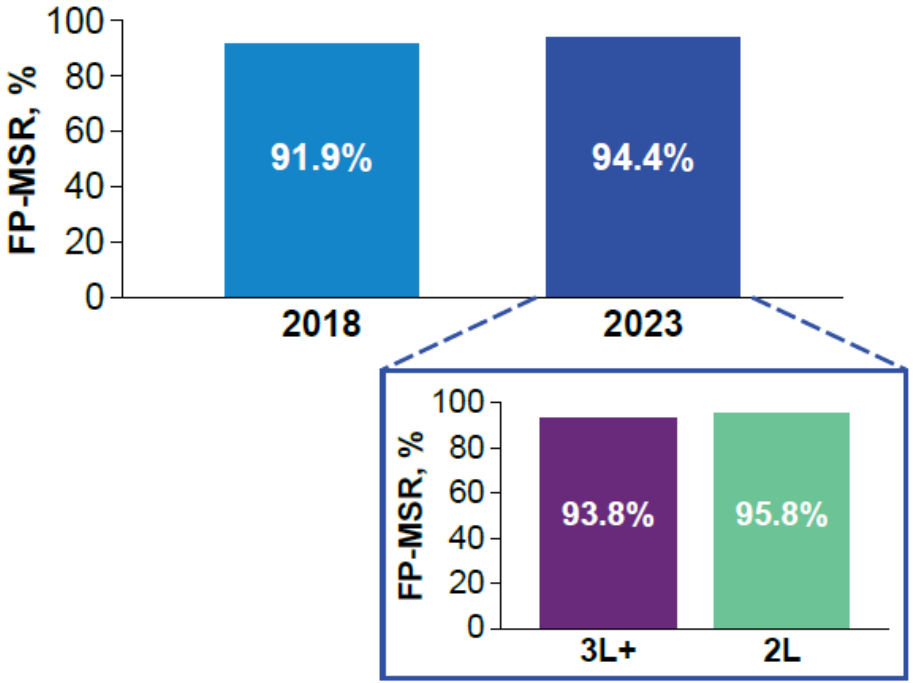
First-Pass Axi-Cel Lots Dispositioned in 2018 and 2023



- In 2018, 826 first-pass axi-cel lots were dispositioned
- In 2023, 5168 first-pass lots were dispositioned, representing a 526% increase from 2018
- Among all lots dispositioned, there was a 502% increase from 2018 (N=877) to 2023 (N=5283)

Axi-cel, axicabtagene ciloleucel.

FP-MSR Among All Patients and by Line of Therapy in 2018 and 2023



- Among all patients, FP-MSR improved from 91.9% (n/N=759/826) in 2018 (only patients in 3L+) to 94.4% (n/N=4880/5168) in 2023 (patients in 2L and 3L+)
- FP-MSR was higher among patients in 2L (95.8%; n/N=1631/1703) than for patients in 3L+ (93.8%; n/N=3249/3465)
  - These results are consistent with a prior analysis which showed a significantly higher FP-MSR for patients in 2L versus patients in 3L+ across all indications for axi-cel[1]

1. Westin JR, et al. *Hemasphere*. 2024;8(Suppl 1):P1425.

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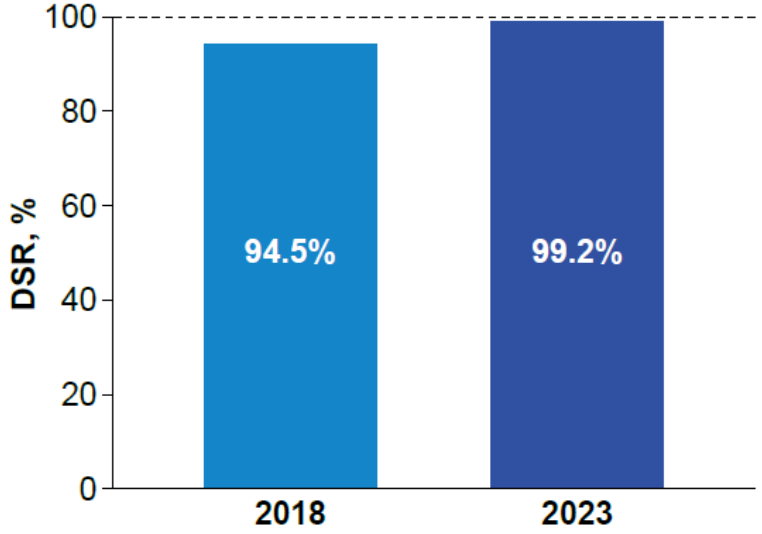
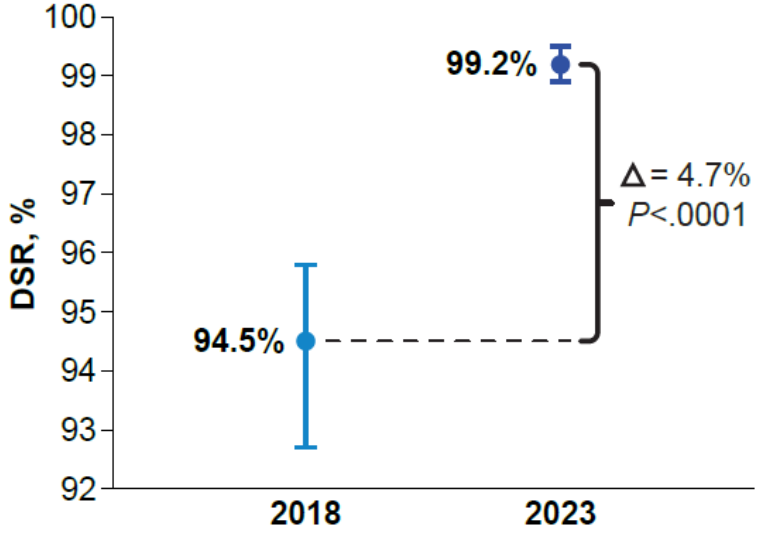
DSR Among Patients in 3L+ in 2018 and 2023

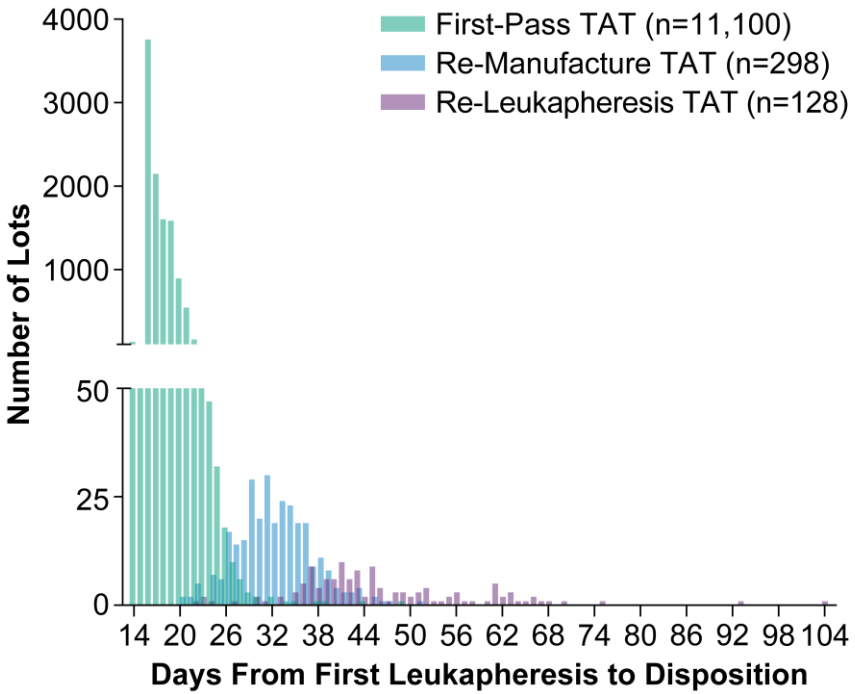




- Among patients in 3L+, there was a statistically significant increase of 4.7% (*P*<.0001) in DSR from 2018 (94.5%; n/N=834/883) to 2023 (99.2%; n/N=3314/3340)
  - Improvements in FP-MSR from 2018 to 2023 likely contributed heavily to the increase in DSR observed across the same time period
- DSR among patients who received axi-cel in both 2L and 3L+ (99.2%; n/N=5039/5082) was very similar to DSR among patients in 3L+ only (99.2%; n/N=3314/3340)

2L, second line, 3L+, third line or later; DSR, delivery success rate.

First-Pass TAT and TAT for Patients Requiring Re-Apheresis or Re-Manufacture From 2018-2023



- Between 2018 and 2023, the global median TAT for all first-pass axi-cel lots manufactured using fresh leukapheresis material (N=11,100) was 17 days (range, 14-49)
  - For patients treated in the United States, median TAT was 16 days
- In the limited cases when re-manufacture using stored leukapheresis material (n=298) or re-leukapheresis (n=128) was required, median TAT increased to 32 and 43 days, respectively
- TATs for patients requiring re-manufacture or re-leukapheresis were more widely variable than those for patients with axi-cel product manufactured successfully at first pass
  - These more variable turnaround times, particularly among patients requiring re-leukapheresis, are likely due in part to clinical factors outside of the manufacturer's control

TAT, turnaround time.

Conclusions

- Physicians require reliable delivery of CAR T-cell therapy to create effective treatment plans for patients with R/R LBCL, which has motivated improvements in the manufacturing of axi-cel between 2018 and 2023
  - After a significant, nearly ~5% improvement in DSR since 2018, axi-cel product was successfully delivered to over 99% of patients in 2023, with an FP-MSR of >94%, demonstrating that physicians can rely on the successful manufacture and delivery of axi-cel when developing treatment plans for patients
  - Axi-cel had a predictable first-pass median TAT of 17 days globally from 2018-2023, which demonstrates that axi-cel manufacturing is not only rapid but reliably delivered, which is critical for timely administration to patients
- These data, along with prior data demonstrating improved axi-cel product attributes and patient outcomes in 2L versus 3L+,[1] suggest a benefit to patients who receive axi-cel in earlier lines of therapy
- Continuous improvements to the axi-cel manufacturing process are ongoing, including the recent United States Food and Drug Administration approval of a manufacturing process change, which is expected to shorten the median TAT for patients in the United States from 16 to 14 days[2]

1. Filosto S, et al. *Blood Cancer Discov.* 2024;5(1):21-33. 2. Kite Receives U.S. FDA Approval of Manufacturing Process Change Resulting in Reduced Median Turnaround Time for Yescarta® CAR T-Cell Therapy. Press release. Kite, a Gilead Company. January 30, 2024. Accessed January 31, 2024. https://www.kitepharma.com/ news/press-releases/2024/1/kite-receives-us-fda-approval-of-manufacturing-process-change-resulting-in-reduced-median-turnaround-time-for-yescarta-car-tcell-therapy.

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- This study was funded by Kite

Plain Language Summary

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QR, Quick Response.