3477 Improvements in Axicabtagene Ciloleucel Manufacturing Result in High Delivery Success and More Predictable Turnaround Time for Patients with Relapsed/Refractory Large B-Cell Lymphoma

Program: Oral and Poster Abstracts
Session: 711. Cell Collection and Manufacturing of HSPCs, CAR-T Cells, and Other Cellular Therapy Products: Poster II
Hematology Disease Topics & Pathways:
Adult, Clinical Practice (Health Services and Quality), Lymphomas, B Cell lymphoma, Chimeric Antigen Receptor (CAR)-T Cell Therapies, Diseases, Treatment Considerations, Biological therapies, Lymphoid Malignancies, Study Population, Human

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Abstract

Introduction:

Axicabtagene ciloleucel (axi-cel) is an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy approved for patients (pts) with relapsed/refractory large B-cell lymphoma (R/R LBCL), with curative potential demonstrated in the second-line (2L; Westin et al. *NEJM.* 2023) and third-line or later settings (3L+; Neelapu et al. *Blood.* 2023). Timely receipt of CAR T-cell therapy, often quantified as vein-to-vein time (V2VT), was associated with favorable responses and survival outcomes for real-world pts with R/R LBCL (Locke et al. ASH 2022). Improving first-pass manufacturing success rate (FP-MSR) is essential to reducing V2VT, as it eliminates the need for re-manufacture or re-leukapheresis (Alquist et al. TCT 2024). Notably, axi-cel demonstrated a high FP-MSR in a real-world analysis, with a greater rate for pts treated in 2L vs 3L+ (Westin et al. EHA 2024). Given the crucial role of timely manufacturing in the axi-cel pt treatment journey, continuous manufacturing process improvements are needed to optimize pt outcomes. Thus, we report the impact of changes to the axi-cel manufacturing process on global manufacturing metrics from 2018 to 2023 for pts with R/R LBCL treated in 2L or 3L+.

Methods:

This analysis included pts with R/R LBCL from KiteKonnect™ who received commercial axi-cel globally from 2018-2023. Outcomes included FP-MSR, delivery success rate (DSR), median turnaround time from leukapheresis to product release (mTAT) among first-pass axi-cel lots manufactured using fresh leukapheresis material, and mTAT for pts with unsuccessful first-pass manufacture who required re-leukapheresis or re-manufacture using stored leukapheresis material (defined as duration from first leukapheresis to product release). FP-MSR was defined as the percentage of first-attempt axi-cel lots dispositioned for release out of the total first-attempt lots dispositioned (plus those terminated but not withdrawn) in the time period. DSR was defined as the percentage of axi-cel lots delivered to an authorized

treatment center out of the total pts leukapheresed within the analysis period (excluding lots in process and withdrawn pts). FP-MSR and DSR were analyzed among 3L+ pts in 2018 (1st complete year after axi-cel approval in 3L+) and 2L or 3L+ pts in 2023 (latest complete year of axi-cel approval in 2L+).

Results:

From 2018 (n=826) to 2023 (n=5168), the number of axi-cel lots dispositioned increased by 526%. Among all pts, FP-MSR improved from 91.9% (n/N=759/826) in 2018 (only pts in 3L+) to 94.4% (n/N=4880/5168) in 2023 (pts in 2L and 3L+). FP-MSR in 2023 was higher among pts in 2L (95.8%; n/N=1631/1703) than for pts in 3L+ (93.8%; n/N=3249/3465). Similarly, among all pts leukapheresed, DSR increased from 94.5% (n/N=834/883) in 2018 for pts in 3L+ to 99.2% (n/N=5039/5082) in 2023 for pts in 2L or 3L+.

Between 2018 and 2023, the global mTAT for all first-pass axi-cel lots manufactured using fresh leukapheresis material (N=11,100) was 17 days (range, 14-49; 16 days for US pts). In the limited cases when re-manufacture using stored leukapheresis material (n=298) or re-leukapheresis (n=128) were required, mTAT increased to 32 and 43 days, respectively, with more widely variable turnaround times for these pts.

Conclusions:

Continuous manufacturing improvements focused on axi-cel from 2018 to 2023 have resulted in reliable FP-MSR and consistent DSR for pts. These data, along with prior data demonstrating improved axi-cel product quality and pt outcomes for pts in 2L vs 3L+, suggest a benefit to pts receiving axi-cel in earlier lines of therapy (Filosto et al. *Blood Cancer Discov.* 2024). Axi-cel has a predictable first-pass mTAT of 17 days (representing >94% of pts in 2023), which is a key factor for physicians to create a reliable treatment plan. Efforts are continually ongoing to further improve axi-cel manufacturing, to optimize the pt treatment journey and outcomes. The successful manufacture and delivery of autologous CAR T-cell therapy products is inherently linked to survival outcomes, and this analysis demonstrates efficiency in these metrics with axi-cel product being successfully delivered for >99% of pts in 2023. These results indicate that most pts who are leukapheresed for axi-cel treatment are receiving this potentially curative therapy.

Disclosures: Miklos: *Kite, a Gilead Company:* Consultancy, Other: Travel Support, Research Funding; *Allogene:* Research Funding; *Adaptive Biotechnologies:* Research Funding; *Novartis:* Consultancy; *Miltenyi:* Consultancy, Research Funding; *Janssen:* Consultancy, Patents & Royalties; *Juno Therapeutics:* Consultancy; *2SeventyBio:* Research Funding; *Fosun Kite Biotechnology:* Honoraria; *Galapagos:* Consultancy; *Bristol Myers Squibb:* Consultancy; *Adicet:* Research Funding. **Tong:** *Kite, a Gilead Company:* Current Employment, Patents & Royalties; *Gilead Sciences:* Current equity holder in publicly-traded company; *AbbVie:* Current equity holder in publicly-traded company. **Kim:** *Kite, a Gilead Company:* Current Employment; *Gilead Sciences:* Current equity holder in publicly-traded company. **Kerr:** *Kite, a Gilead Company:* Current Employment; *Gilead Sciences:* Current equity holder in publicly-traded company. **Neuwirth:** *Kite, a Gilead Company:* Current Employment, Other: Travel Support; *Gilead Sciences:* Current equity holder in publicly-traded company. **Alquist:** *Kite, a Gilead Company:* Current Employment; *Gilead Sciences:* Current equity holder in publicly-traded company.

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