Abstract: P1425

Title: REAL-WORLD MANUFACTURING EXPERIENCE OF AXICABTAGENE CILOLEUCEL FOR PATIENTS WITH RELAPSED OR REFRACTORY LARGE B-CELL LYMPHOMA TREATED IN SECOND LINE VERSUS THIRD LINE OF THERAPY AND BEYOND

Abstract Type: Poster Presentation

Topic: Gene therapy, cellular immunotherapy and vaccination - Biology & translational research

Background:

Axicabtagene ciloleucel (axi-cel), an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, is approved in many countries for patients (pts) with relapsed/refractory large B-cell lymphoma (R/R LBCL) within 12 months of first-line chemoimmunotherapy (based on the Phase 3 ZUMA-7 study [NCT03391466]) and in the third-line or later setting (3L+; based on the Phase 2 ZUMA-1 study [NCT02348216]). A higher percentage of naive-like T cells was identified in axi-cel product manufactured in second line (2L; ZUMA-7) vs 3L+ (ZUMA-1) and was associated with improved therapeutic index without impacting the safety profile (Filosto S, et al. *Blood Cancer Discov.* 2024;5:21). With individualized therapies like axi-cel, timely and reliable delivery of product is essential (Tully S, et al. *JCO Clin Cancer Inform.* 2019;3:3). Thus, understanding axi-cel manufacturability for pts in 2L vs 3L+ is of interest, as well as examining the potential impact of line of therapy on product phenotype.

Aims:

To compare the real-world axi-cel manufacturing experience and clinical trial product characteristics for pts with R/R LBCL in 2L vs 3L+.

Methods:

This analysis includes pts with R/R LBCL registered on Kite Konnect® globally and leukapheresed for axi-cel treatment in 2L or 3L+ between April 19, 2022, and January 3, 2024. First-pass manufacturing success rate (FP-MSR) was calculated as the percentage of first-attempt pt lots dispositioned as manufactured within specification out of the total number of first-attempt pt lots dispositioned plus those terminated (excluding those terminated for withdrawn pts) in the time period. Comparison of 2L vs 3L+ FP-MSR was evaluated by fitting a generalized linear model with a binary distribution and performing a fixed effect test. An analysis of apheresis and axi-cel product cell phenotypes, measured as the percentage of cells with naive-like T-cell phenotype (defined as CCR7+CD45RA+ within CD3+ cells), was explored in pts from the pivotal studies ZUMA-7 (2L) and ZUMA-1 (3L+) and statistically analyzed using Wilcoxon rank sum test.

Results:

A total of 4087 pts were analyzed herein, including 1342 pts treated in 2L and 2745 treated in 3L+. The FP-MSR for pts in 2L (96.42%) was significantly higher than for pts in 3L+ (94.68%; P=.01). Per 1000 lots, pts in 2L had 17 more lots of axi-cel product successfully manufactured in the first attempt than pts in 3L+. Among evaluable pts (full analysis set) in 3L+ (ZUMA-1 Cohorts 1+2) vs 2L (ZUMA-7), the median percentage of naive-like T cells in the apheresis was 4.11% (range, 0.09-56.60; n=100) for 3L+ vs 9.28% (range, 0.20-45.07; n=126; P<.0001) for 2L, while the median percentage of naive-like T cells in the product was 18.60% (range, 0.50-74.30; n=101) for 3L+ vs 35.10% (range, 0.06-74.90; n=174; P<.0001) for 2L. In both the apheresis and axi-cel product, pts in 2L displayed a median of ~2 times as many naive-like T cells vs pts in 3L+.

Summary/Conclusion:

In this analysis, a significantly greater proportion of pts with LBCL who received axi-cel in 2L had product successfully manufactured at first attempt vs those in 3L+, with a difference (1.74%) that could result in a

markedly greater number of pts in earlier lines of therapy successfully receiving axi-cel on the first manufacturing attempt. Additionally, pts in the 2L clinical trial setting showed a higher frequency of naive-like T cells in apheresis and product vs pts in 3L+. Overall, these results suggest a benefit in employing axi-cel in earlier lines of therapy, both with respect to manufacturability and product phenotype.

Keywords: Real world data, CAR-T, Diffuse large B cell lymphoma, Cellular therapy