LymphomaHub

DLBCL, FL

ASH 2018 | Real-world efficacy and safety outcomes with axi-cel in patients with relapsed/refractory large B-cell lymphoma comparable to the ZUMA-1 clinical trial

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On Saturday 1st December 2018, an oral abstract session took place at the 60th American Society of Hematology (ASH) Annual Meeting in San Diego, CA. During Session 627 (Aggressive lymphoma - results from retrospective/observational studies: outcomes with CD-19 CAR-T therapy and checkpoint blockade in the real world setting) Abstract 91 was presented by Loretta J. Nastoupil, University of Texas MD Anderson Cancer Center, Houston, TX.

The study evaluated the real-world outcomes of patients treated with standard of care axicabtagene ciloleucel (axi-cel) under the commercial Food and Drug Administration (FDA) label. Data from 17 US academic centers were retrospectively analyzed.

All patients leukapheresed as of 31st August 2018 (N = 295), with the intention to manufacture commercial axi-cel, were included in the analysis. Of the 295 patients, 274 patients received conditioning chemotherapy and were infused with axi-cel. Median time from leukapheresis to start of conditioning chemotherapy was 21.5 days. Of the 21/295 patients who were not infused with axi-cel: 7 patients went on to receive axi-cel therapy on the ZUMA-9 expanded access trial (NCT03153462) due to non-conforming cell therapy product, 12 patients died secondary to lymphoma, 1 patient had non-measurable disease, and 1 patient experienced infection.

Baseline characteristics

Median age was 60 years (range 21–83) with 96 (33%) patients aged ≥ 65 years old and 65% of patients were male. Performance status (PS) was ECOG 0–1 (81%), ECOG 2 (15%) and ECOG 3–4 (4%). By histology, 68% of patients had diffuse large B-cell lymphoma (DLBCL), 26% had transformed follicular lymphoma (tFL), and 6% had primary mediastinal B-cell lymphoma (PMBCL). Seventy-five percent of patients had received > 3 prior therapies, 35% of patients were primary refractory, 42% of patients were refractory to second line or later, and 33% of patients had relapsed post-autologous stem cell transplant (ASCT).

Bridging therapy between apheresis and infusion was given in 158 (55%) patients, the majority of which consisted of chemotherapy. In total, 43% of patients in this analysis would not have met the eligibility criteria for the ZUMA-1 study at the time of leukapheresis. Common criteria that would have made these patients ineligible for ZUMA-1 included platelets < 75 (n = 13), active deep vein thrombosis/pulmonary embolism (n = 9), prior CD-19 or CAR-T therapy (n = 8), glomerular filtration rate < 60 (n = 8), a history of CNS lymphoma (n = 8), symptomatic pleural effusion (n = 4), left ventricular ejection fraction < 50% (n = 4) and prior allogeneic transplant (n = 2).

Real-world safety results

- Cytokine release syndrome (CRS; Lee criteria used for grading) occurred in 240/274 (92%) patients, with Grade ≥ 3 CRS experienced by 18 (7%) patients. The median time to CRS onset was 3 days
- Neurological toxicity (NT) occurred in 181/274 (69%) patients, with Grade ≥ 3 NT experienced by 85 (33%) patients. The median time to onset of NT was 6 days
- Tocilizumab was administered in 63% of patients and 55% received corticosteroids
- Grade 5 adverse events (AEs) occurred in 7/274 (3%) patients
- Treatment-related deaths: 2/274 (1%) patients
- Deaths due to non-relapse mortality: 7 patients (n = 5 infection; n = 1 hemophagocytic lymphohistiocytosis; n = 1 cerebral edema)
- Median hospital stay was 14 days with 85 (32%) patients requiring admission to the intensive care unit (ICU).

Real-world efficacy results

- Median follow-up: 3.9 months
- Of the 238 patients evaluable at Day 30, overall response rate (ORR) was 80% with 47% complete response (CR)
- Of the 248 patients evaluable at Day 90, best ORR was 81% with 57% CR
- 60 (81%) patients with a CR at Day 30 maintained their response at Day 90
- 22 (37%) patients with a partial response at Day 30 achieved a CR by Day 90
- The majority of patients who had stable disease at Day 30 experienced disease progression by Day 90 (7/9 patients [78%])
- Covariates **NOT** associated with ongoing CR at Day 90: age, disease histology, lymphoma subtype, double-/triple-hit, high risk International Prognostic Index (IPI), bridging therapy, tocilizumab/steroid use, ICU admission.
- Covariates associated with ongoing CR at Day 90:
  - Female (39 [72%] patients) *vs* male (50 [51%] patients) sex, $P = 0.009$
  - ECOG 0–1 (82 [62%] patients) *vs* ECOG ≥ 2 (7 [35%] patients), $P = 0.024$
  - Relapsed (27 [79%] patients) *vs* primary refractory/refractory (24 [47%] / 38 [56%] patients), $P = 0.011$
  - Non-bulky (76 [62%] patients) *vs* bulky (≥10 cm; 13 [42%] patients), $P = 0.040$
  - Met eligibility for ZUMA-1 (62 [65%] patients) *vs* not (27 [47%] patients), $P = 0.037$
- With a median follow-up of 3.9 months, median progression-free survival was 6.18 months (95% CI, 4.57–NA) and 6-month overall survival estimate was 72% (95% CI, 65–80%)

Conclusions

- This multicenter retrospective study delineated the real-world outcomes of axi-cel CAR T-cell therapy for relapsed/refractory aggressive B-cell lymphoma when used as a standard of care.
- Although limited by a short follow-up, 30-day responses in the real-world setting were comparable to the best responses observed in the pivotal ZUMA-1 clinical trial
- Safety appeared comparable to the ZUMA-1 trial despite > 40% of patients failing to meet ZUMA-1 eligibility criteria

- Univariate analysis identified potential predictors of ongoing CRs at 3 months, however longer follow-up and multivariate analyses are needed

References

1. Nastoupil, L.J., *et al*. Axicabtagene ciloleucel (axi-cel) CD19 chimeric antigen receptor (CAR) T-cell therapy for relapsed/refractory large B-cell lymphoma: real-world experience. 01 Dec 2018. Abstract #91. 60th ASH Annual Meeting, San Diego, CA.
