Long-Term Safety and Activity of Axicabtagene Ciloleucel in Refractory Large B-Cell Lymphoma (ZUMA-1): A Single-Arm, Multicenter, Phase 1-2 Trial.

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Background: Large B-cell lymphoma (BCL) patients often face poor outcomes after first or second-line therapy failures. Chimeric antigen receptor (CAR) T-cell therapies targeting CD19 are a promising treatment for relapsed or refractory (R/R) BCL. The ZUMA-1 trial assessed the efficacy of axicabtagene ciloleucel, an autologous anti-CD19 CAR T-cell therapy, in treating R/R BCL.

Methods: ZUMA-1, a single-arm multicenter trial spanning 22 US and Israeli centers, enrolled adults with histologically confirmed R/R BCL post-autologous stem-cell transplantation. Participants, with Eastern Cooperative Oncology Group status 0 or 1, received one dose of axicabtagene ciloleucel (2×10^6 CAR T cells/kg) after fludarabine and cyclophosphamide conditioning. Primary endpoints included phase 1 safety and phase 2 objective response rate.

Results: By August 11, 2018, 101 patients were assessable with a median follow-up of 27.1 months. Median patient age was 58 years; 67% were male. Treatment-emergent adverse events (TEAEs) were universal; most common were pyrexia (87%), anemia (68%), hypotension (58%), and vomiting (34%). Grade ≥3 TEAEs occurred in 98%, with cytokine release syndrome in 11% and neurological events in 32%. Serious adverse events affected 48%, yet were manageable and reversible. Disease progression caused 50 deaths. Investigator-assessed objective responses were noted in 83% (59 complete, 25 partial), and independent review committee (IRC) assessment confirmed 74% (55 complete, 20 partial), with 10 patients stable.

Conclusion: Axicabtagene ciloleucel demonstrated durable responses and over two years of median overall survival with a manageable safety profile in R/R BCL patients. However, further studies are needed to understand the mechanisms of treatment resistance.