

CAR T in DLBCL: Optimising Patient Outcomes at EHA 2026

Written by The Life Science Feed Editorial Team · Published 11 June 2026 · Edited by Mara Voss

The application of chimeric antigen receptor (CAR) T-cell therapy in relapsed or refractory diffuse large B-cell lymphoma (DLBCL) has demonstrated curative potential for a subset of patients, yet significant variability in treatment response and toxicity profiles persists.¹ The challenge for clinicians lies in identifying which patients will derive the most benefit and how to mitigate adverse events effectively. Data presented at EHA 2026 highlighted advancements in predictive biomarkers and real-world management strategies aimed at optimising patient outcomes.

KEY TAKEAWAYS

- **The Pivot:** New insights into patient stratification and toxicity management for CAR T-cell therapy in DLBCL.
- **The Data:** Specific biomarkers, such as baseline LDH levels and inflammatory markers, are increasingly correlated with response rates and adverse event incidence.
- **The Action:** Clinicians should integrate refined patient selection criteria and proactive toxicity management protocols to improve CAR T outcomes.

CAR T-cell therapy, specifically autologous anti-CD19 CAR T-cell products, has become a standard of care for adult patients with relapsed or refractory DLBCL after two or more lines of systemic therapy.¹ Diffuse large B-cell lymphoma (DLBCL) is the most common aggressive non-Hodgkin lymphoma, accounting for approximately 30-40% of all adult non-Hodgkin lymphomas. Despite advances in front-line chemoimmunotherapy, a significant proportion of patients experience relapse or become refractory to subsequent treatments, leading to poor prognoses. For these patients, CAR T-cell therapy offers a potentially curative option by genetically engineering a patient's own T-cells to express a chimeric antigen receptor (CAR) that targets the CD19 protein found on lymphoma cells. This targeted approach has demonstrated remarkable efficacy in clinical trials and real-world settings.^{1,2} Despite impressive complete response rates, a substantial proportion of patients do not achieve durable remission, and a significant number experience severe toxicities, including cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS).² The heterogeneity in patient outcomes underscores the need for improved patient selection, pre-treatment optimisation, and post-infusion management strategies.³

Optimising CAR T-cell Therapy in DLBCL

Recent analyses presented at EHA 2026 focused on identifying prognostic factors and refining treatment algorithms. One retrospective cohort study, involving 450 patients treated with commercial CAR T-cell products (axicabtagene ciloleucel, tisagenlecleucel, or lisocabtagene maraleucel) across 25 European centers, investigated the impact of pre-treatment

clinical and biological parameters on overall survival (OS) and progression-free survival (PFS).⁴ The patient population in this study primarily consisted of adults with a median age of 62 years, who had received a median of three prior lines of therapy. The study found that elevated baseline lactate dehydrogenase (LDH) levels (defined as >2x upper limit of normal) were associated with a significantly shorter PFS (Hazard Ratio (HR) 2.15, 95% Confidence Interval (CI) 1.78-2.59, P0.001) and OS (HR 2.30, 95% CI 1.90-2.78, P0.001).⁴ Similarly, patients with a high International Prognostic Index (IPI) score (3) at the time of apheresis demonstrated inferior PFS (HR 1.88, 95% CI 1.56-2.27, P0.001) and OS (HR 1.95, 95% CI 1.61-2.36, P0.001).⁴ These findings reinforce the importance of disease burden and aggressiveness at the time of CAR T-cell collection.

Further data explored the role of inflammatory markers in predicting toxicity. A prospective observational study of 180 patients receiving CAR T-cell therapy for DLBCL reported that pre-infusion C-reactive protein (CRP) levels >10 mg/L were associated with a higher incidence of grade 2 CRS (Odds Ratio (OR) 3.45, 95% CI 1.87-6.36, P0.001) and grade 2 ICANS (OR 2.88, 95% CI 1.49-5.56, P0.001).⁵ Early elevation of ferritin post-infusion (within 72 hours) also correlated with increased severity of CRS and ICANS.⁵ These markers may serve as early indicators for initiating prophylactic or preemptive interventions, such as corticosteroids or tocilizumab, to mitigate severe adverse events.⁵

Another presentation highlighted a real-world analysis of bridging therapy strategies. Among 320 patients who received bridging therapy between apheresis and CAR T-cell infusion, those receiving chemotherapy-based regimens had a higher rate of successful CAR T-cell manufacturing and infusion compared to those receiving radiation therapy or no bridging therapy (88% vs 75% and 70%, respectively, P=0.012).⁶ However, the choice of bridging therapy did not significantly impact PFS or OS in this cohort, suggesting that while it can facilitate timely infusion, its long-term efficacy benefit remains unclear.⁶

Limitations of these analyses include their retrospective nature for some cohorts, which inherently carries risks of selection bias and confounding factors. The reliance on data from multiple centers, while increasing generalizability, also introduces variability in patient management, supportive care, and data recording practices. The heterogeneity of CAR T-cell products and institutional management protocols across centers also introduces variability that can be difficult to control. Future research should focus on prospective, multicenter trials with harmonised data collection to validate these prognostic markers and evaluate the impact of standardised management algorithms. The development of more sophisticated predictive models incorporating multi-omic data, beyond routine clinical parameters, is also warranted to further refine patient selection and personalise treatment approaches.⁷

For a comprehensive overview of haematological practice, including relevant background for advanced therapies like CAR T-cell therapy, readers may consult the Oxford Handbook of Clinical Haematology.

CLINICAL IMPLICATIONS

The EHA 2026 presentations on CAR T-cell therapy in DLBCL underscore a persistent clinical reality: while the therapy is transformative, its application is not universally successful. The data on baseline LDH and IPI scores as predictors of survival, and inflammatory markers for toxicity, are not revolutionary, but they serve as a critical reminder for clinicians. These are readily available parameters that should be rigorously integrated into pre-treatment risk assessments. The temptation to push for CAR T in every eligible patient must be tempered by a clear-eyed evaluation of these established prognostic indicators. Ignoring them is not optimism; it is poor

clinical stewardship.

For the pharmaceutical industry, these insights highlight the ongoing need for more precise patient stratification. Simply expanding indications without refining the selection process will lead to diminishing returns and increased healthcare costs for non-responders. Companies developing next-generation CAR T products or adjunctive therapies should focus on demonstrating efficacy within specific, well-defined patient subgroups, rather than broad populations. The market demands not just innovation, but intelligent application of that innovation. Furthermore, the emphasis on toxicity management suggests a growing opportunity for supportive care interventions and predictive diagnostics that can identify patients at highest risk of CRS and ICANS, potentially reducing the overall burden on healthcare systems.

Ultimately, for patients, these data mean a more informed discussion with their clinicians. While the promise of CAR T-cell therapy is immense, understanding the likelihood of success and the potential for severe side effects is paramount. The goal is not merely to offer a therapy, but to offer the right therapy to the right patient at the right time. This requires a commitment from all stakeholders to move beyond simply administering a treatment to truly optimising the entire patient journey, from initial assessment through long-term follow-up. The data presented at EHA 2026, while incremental, moves us closer to that objective.

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