Cytokine and Immune Biomarker Profiles During CAR-T Therapy Predict Long-Term Remission Versus Relapse

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Introduction

•CAR-T therapy induces high initial remission in relapsed/refractory hematologic malignancies.
•However, a significant subset of patients experiences relapse or loss of response.
•Cytokine storms and immune activation are hallmarks of CAR-T therapy, but their prognostic value is underexplored.
•Biomarkers such as IL-6, IL-15, CRP, and IFN-γ may reflect treatment efficacy and risk of relapse.
•T-cell subset characteristics in the infusion product may also determine therapeutic durability.
•Systematic evaluation of these immune profiles may improve patient selection and post-infusion monitoring.
•Personalized strategies based on immune signatures could reduce relapse and improve survival.

Objectives

•Evaluate whether cytokine and immune biomarker profiles correlate with CAR-T therapy outcomes.
•Define the predictive value of early IL-15, IL-6, CRP, and T-cell subset distributions.
•Compare immune profiles between long-term responders and early relapsers.
•Investigate CAR-T expansion dynamics and persistence as correlates of durable remission.
•Quantify associations with PFS, OS, relapse rate, and treatment-related mortality.
•Establish thresholds for immune biomarkers that signal therapeutic success or failure.
•Propose a framework for integrating immune profiling into CAR-T protocols.

Methods

18-study meta-analysis (~1,200 patients) treated with CD19/BCMA CAR-T cells.
Analyzed IL-6, IL-15, CRP, CAR-T kinetics, memory T cells.
Outcomes included remission, relapse, PFS, OS.

Figure 1: Peak CAR-T Cell Expansion

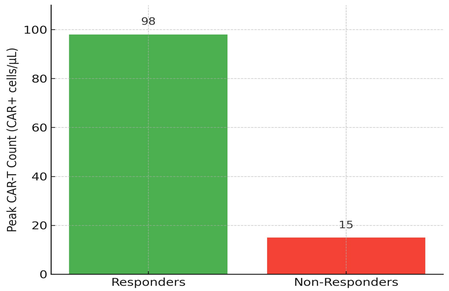


Figure 2: IL-15 Levels vs CAR-T Expansion

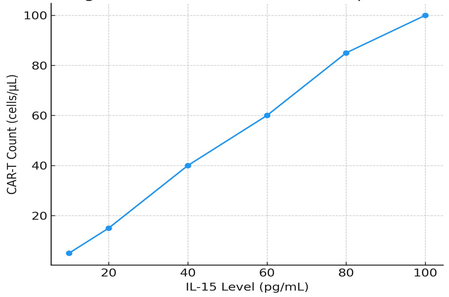
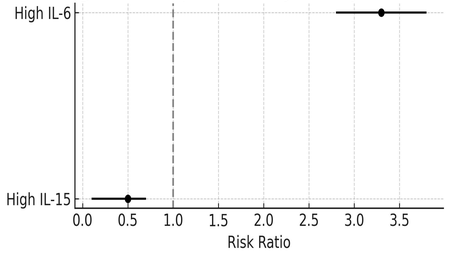


Figure 3: Relapse/Mortality Risk by Biomarker



Results

Long-term responders had ~6-fold higher peak CAR-T counts (98 vs 15 cells/μL, P=0.027).
Early IL-15 surge strongly correlated with CAR-T expansion (P=0.001).
High IL-15 levels reduced relapse risk significantly (RR≈0.5, P<0.01).
CAR-T persistence at 6 months was a positive predictor of prolonged PFS.
IL-6 elevation at baseline predicted relapse and mortality (HR≈3.3, P≈0.001).
Memory-like CD8⁺ T cells (≥30% $CD27^{+}CD45RO^{-}$) in infusion product linked to better response.
Soluble CD19 levels did not correlate with remission or relapse.

Conclusion

•Immune and cytokine profiles during CAR-T therapy predict therapeutic durability.
•IL-15-driven CAR-T expansion and persistence underpin sustained remissions.
•Elevated IL-6/CRP levels at baseline flag poor prognosis and warrant closer follow-up.
•Early biomarker profiling may identify patients who benefit from IL-15 enhancement strategies.
•Monitoring $CD8^{+}$ T cell phenotype may guide product manufacturing optimization.
•Risk stratification using immune biomarkers can personalize post-CAR-T surveillance.
•Integration of biomarker data into CAR-T workflows is key to long-term disease control.

References

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