Temporal Patterns of Efficacy and Toxicity of CD20×CD3 Bispecific Antibodies in Relapsed/Refractory DLBCL: A Systematic Review

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INTRODUCTION

CD20xCD3 bispecific antibodies represent a paradigm shift in the management of relapsed/refractory (R/R) DLBCL. However, as these therapies transition toward outpatient administration, optimizing the timing of efficacy assessments and the precision of safety monitoring remains a critical challenge.

METHOD

A systematic review was conducted in accordance with PRISMA guidelines to evaluate the temporal dynamics of efficacy and toxicity for CD20xCD3 bispecific antibodies in R/R DLBCL. Comprehensive searches were performed across PubMed, Cochrane and major conference datasets (2022-2026). Primary endpoints included the temporal signature of cytokine release syndrome (CRS) onset and the kinetics of response maturation.

CONCLUSIONS

A distinct temporal pattern was observed in the efficacy and toxicity profiles of CD20xCD3 bispecifics in R/R DLBCL, providing a framework for clinical management. The 2.1–2.7 months maturation window indicates that initial responses often evolve into complete remissions over time, hence clinicians should avoid premature treatment assessment or discontinuation before this window is reached. From a safety perspective, a 24-hour observation period captures the CRS onset peak for most regimens; however, the 72-hour late-onset outlier, mandates risk-stratified monitoring. These findings provide a data driven rationale for optimizing the transition to outpatient administration while ensuring that safety protocols are tailored to the specific agent and administration route.

RESULTS

Across the 11 evaluated studies which met the inclusion criteria, ORR ranged from 42.0% to 85.4%, with CR rates spanning 23.9% to 67.0%, including cohorts with prior CAR-T failure (5.0%–38.9%). Median Duration of Response (DoR) peaked at 26.9 months and 24-month PFS reached 86.0%. While median Duration of Complete Response (DoCR) was largely not reported, available long-term data indicated sustained remissions up to 36.1 months.

Safety analysis revealed agent specific CRS incidences: glofitamab (14.3%–83.0%), mosunetuzumab (14.3%–44.4%) and epcoritamab (49.7%–51.0%). While a rapid median onset of CRS (13.7 to 14 hours) was observed in specific glofitamab and mosunetuzumab cohorts, majority of CRS onset events clustered within a 21–26 hour peak risk window. A late-onset outlier of 72 hours was observed in a mosunetuzumab combination cohort. Efficacy kinetics demonstrated a conversion lag where initial responses at 1.4 months matured into a complete response by 2.1–2.7 months.