Cardiovascular Adverse Event Reporting Patterns With CD19 CAR-T and CD20×CD3 Bispecific Antibodies in Relapsed/Refractory Large B-Cell Lymphoma: A FAERS Disproportionality Analysis

SOHO ANNUAL MEETING 2026

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KEY FINDING: Both CAR-T and CD20×CD3 bispecific antibodies showed disproportionate cardiovascular adverse event reporting in LBCL/DLBCL, with stronger signals for CAR-T therapies that attenuated when analyses were restricted to the shared modern treatment era.

INTRODUCTION

CD19-directed chimeric antigen receptor T-cell (CAR-T) therapies and CD20×CD3 bispecific antibodies have transformed the treatment landscape of relapsed/refractory large B-cell lymphoma (LBCL), offering effective immune-effector approaches for patients with otherwise limited options.[1] Cardiovascular adverse events, including arrhythmias, heart failure, thromboembolic events, and hemodynamic complications, are increasingly recognized with T-cell–directed therapies and may occur in association with, or independently of, cytokine release syndrome.[12]

Recent pharmacovigilance data have also identified cardiovascular safety signals with CD20×CD3 bispecific antibodies, including hypotension and arrhythmias.[3] However, comparative cardiovascular reporting patterns between CAR-T and bispecific antibody platforms within the same LBCL/DLBCL treatment population remain incompletely characterized.

METHODS

1. **FAERS data window:** Retrospective pharmacovigilance disproportionality analysis of deduplicated FAERS reports from 2017Q4–2026Q1, using product-specific post-approval windows.
2. **Population and Exposure Definition:** Retrospective pharmacovigilance disproportionality analysis of deduplicated FAERS reports from 2017Q4–2026Q1, using product-specific post-approval windows.
3. **Cardiovascular Outcome Definition:** Core cardiovascular adverse events were identified using a prespecified MedDRA Preferred Term dictionary covering arrhythmias, thromboembolic events, heart failure/cardiomyopathy, cardiac arrest/shock, ischemic events, pulmonary vascular events, and myocarditis/pericarditis.
4. **Disproportionality Analysis:** Reporting odds ratios (RORs) with 95% confidence intervals were calculated versus the full deduplicated FAERS background and in direct CAR-T versus bispecific antibody comparisons within the selected immune-effector cohort.
5. **Signal Definition:** An ROR-based disproportionality signal was defined as a **lower 95% confidence limit >1**.
6. **Sensitivity Analysis and Visualization:** A common-era analysis from June 15, 2023 through 2026Q1 was performed to harmonize reporting windows across both treatment platforms and assess the robustness of platform-level differences. Figures were generated in GraphPad Prism 11.

Figure 1. Platform-Level Disproportionality of CardiovascularAdverse Events

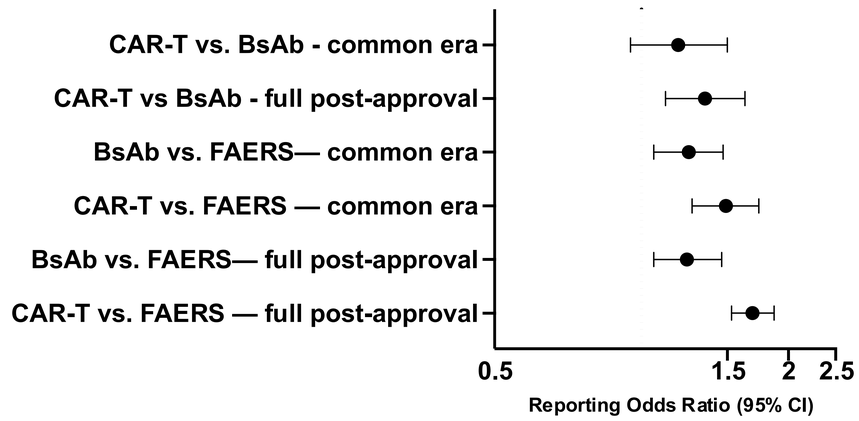
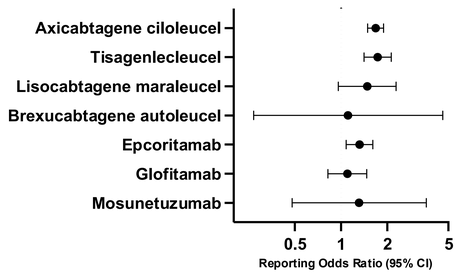


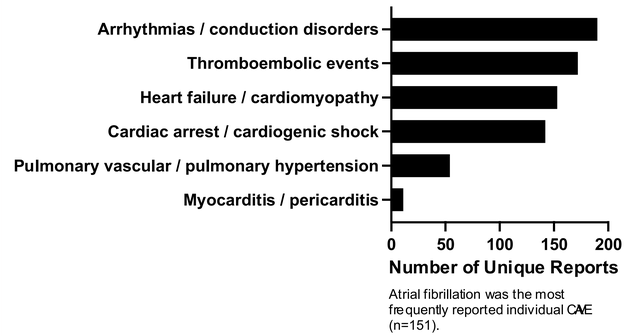
Figure 2. Drug-Level Disproportionality of CardiovascularAdverse Events



KEY RESULTS

- Among **9,948 unique selected-product reports**, 615 contained ≥1 core CVAE. Platform-specific counts were non-mutually exclusive; **49 reports contained both CAR-T and bispecific antibody products**.
- Compared with the overall FAERS background, cardiovascular disproportionality was greater for CAR-T therapies (**ROR 1.69; 95% CI 1.53–1.87)** than for CD20×CD3 bispecific antibodies **(ROR 1.24; 95% CI 1.06–1.46).**
- In direct within-cohort comparisons, CAR-T therapies showed higher relative CVAE reporting during the full post-approval period **(ROR 1.35; 95% CI 1.12–1.63).** However, this difference attenuated in the shared modern treatment era **(ROR 1.19; 95% CI 0.95–1.50).**
- The most frequently reported phenotypes were **arrhythmias/conduction disorders, thromboembolic events, heart failure/cardiomyopathy, and cardiac arrest/cardiogenic shock**.

Figure 3. Spectrum of Reported Cardiovascular Adverse Events



Atrial fibrillation was the most frequently reported individual CAE (n=151).

SENSIVITY ANALYSIS

- In the **common-era analysis (June 15, 2023–2026Q1)**, CAR-T remained disproportionate versus all FAERS (**ROR 1.49; 95% CI 1.27–1.74**) and bispecific antibodies remained disproportionate (**ROR 1.25; 95% CI 1.06–1.47**).
- The direct CAR-T vs bispecific difference attenuated from **ROR 1.35 (1.12–1.63)** in the full period to **ROR 1.19 (0.95–1.50)** in the common era.

CONCLUSIONS

Cardiovascular surveillance should remain part of routine care for both CAR-T and CD20×CD3 bispecific therapies in LBCL/DLBCL.

The stronger full-period CAR-T signal, together with attenuation in the shared modern era, suggests that **treatment platform and reporting era should both be considered when interpreting cardiovascular toxicity patterns**.

LIMITATIONS

- FAERS is a spontaneous reporting system and is subject to **underreporting, stimulated reporting, and reporting bias**.
- Lack of reliable exposure denominators prevents estimation of **incidence or absolute risk**.
- Residual confounding from underlying malignancy and prior or concomitant immunosuppressive therapies cannot be excluded.
- Disproportionality signals are **hypothesis-generating and do not establish causality**.

References:
1 Munir M, Sayed A, Addison D, Epperla N. Cardiovascular toxicities associated with novel cellular immune therapies. Blood Adv. 2024;8(24):6282-6296. doi:10.1182/bloodadvances.2024013849.
2 Goldman A, Maor E, Bomze D, et al. Adverse cardiovascular and pulmonary events associated with chimeric antigen receptor T-cell therapy. J Am Coll Cardiol. 2021;78(18):1800-1813. doi:10.1016/j.jacc.2021.08.044.
3 Munir M, Sayed A, Lee DH, et al. Cardiovascular adverse events associated with bispecific antibodies in relapsed or refractory B-cell non-Hodgkin lymphomas. J Hematol Oncol. 2026;19(1):33. doi:10.1186/s13045-026-01809-3.

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