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Efficacy and safety of CD20×CD3 bispecific antibodies monotherapy in relapsed or refractory large b-cell lymphoma: A systematic review and single-arm meta-analysis

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ADMINISTRATIVE INFORMATION

Support - Chi Mei Hospital, Liouying (CLFHR11432).

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 2 March 2026 and was last updated on 2 March 2026.

INTRODUCTION

Review question / Objective To investigate the efficacy and safety of CD20×CD3 bispecific antibodies in patients with relapsed or refractory large B-cell lymphoma.

Rationale Relapsed or refractory large B-cell lymphoma remains difficult to treat after multiple prior therapies, and outcomes are poor for many patients, including those progressing after CAR T-cell therapy. CD20×CD3 bispecific antibodies are emerging as an off-the-shelf immunotherapy option, but evidence is mainly derived from single-arm trials with heterogeneous populations and reporting. A systematic review and single-arm meta-analysis is therefore needed to synthesize the available data and clarify expected efficacy, durability, and key immune-mediated toxicities in this setting.

Condition being studied The study was designed using a PICO-based framework adapted for single-arm meta-analyses. The population comprised patients with relapsed or refractory large B-cell lymphoma. The intervention included CD20×CD3 bispecific antibodies (epcoritamab, glofitamab, odronextamab, and mosunetuzumab). As this was a single-arm synthesis, no comparator was defined. Outcomes of interest encompassed key measures of clinical efficacy and safety.

METHODS

Search strategy Two reviewers (TSW and SYH) independently performed a systematic search of PubMed, Embase, the Cochrane Library, and ClinicalTrials.gov from database inception to December 24, 2025. The search strategy used combinations of keywords for CD20×CD3 bispecific antibodies and terms related to large B-cell lymphoma.

Participant or population Human participants.

Intervention CD20×CD3 bispecific antibodies.

Comparator Not applicable (single-arm meta-analysis).

Study designs to be included Clinical trials.

Eligibility criteria Studies were included if they: (1) enrolled adults with relapsed or refractory large B-cell lymphoma; (2) investigated CD20×CD3 bispecific antibody monotherapy ; (3) were prospective phase I–II clinical trials; and (4) reported at least one extractable efficacy or safety endpoint.

Information sources Two reviewers (TSW and SYH) independently performed a systematic search of PubMed, Embase, the Cochrane Library, and ClinicalTrials.gov from database inception to December 24, 2025. The search strategy used combinations of keywords for CD20×CD3 bispecific antibodies (epcoritamab, glofitamab, odronextamab, and mosunetuzumab) and terms related to large B-cell lymphoma.

Main outcome(s) Main outcomes were objective response rate (ORR) and complete response (CR), pooled as event rates with 95% confidence intervals.

Additional outcome(s) Additional outcomes included progression-free survival (median PFS) and key safety endpoints, including cytokine release syndrome (CRS; overall and grade ≥3), immune effector cell–associated neurotoxicity syndrome (ICANS), and other selected adverse events (e.g., grade ≥3 hematologic toxicities, pyrexia, and gastrointestinal events) when extractable.

Data management Two reviewers (TSW and SYH) independently extracted data using a standardized form. Information collected included first author and publication year, study sample size, baseline patient characteristics (e.g., sex, age, lymphoma subtype, and number of patients), median duration of response and outcome data for the prespecified primary and additional endpoints. When key data were not available in the published reports, the corresponding authors were contacted to request the missing information.

Quality assessment / Risk of bias analysis Methodological quality was evaluated using an adapted Newcastle–Ottawa Scale for single-arm studies, assessing the domains of selection, comparability, and outcome ascertainment. Because the included studies lacked parallel control groups, the comparability domain was inherently constrained. Overall study quality was determined according to these criteria.

Strategy of data synthesis Given the clinical heterogeneity among the included studies, all pooled estimates were generated using a random-effects model. Statistical analyses were performed with Comprehensive Meta-Analysis software (version 4; Biostat, Inc.).

Subgroup analysis Subgroup analyses were performed by stratifying studies according to the specific CD20×CD3 bispecific antibody evaluated.

Sensitivity analysis To evaluate the robustness of the pooled results, leave-one-out sensitivity analyses were conducted by sequentially omitting each study and reassessing its impact on the overall pooled estimate.

Language restriction No language limit.

Country(ies) involved Taiwan.

Keywords Relapsed or refractory large B-cell lymphoma, CD20×CD3 bispecific antibodies, monotherapy.

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