

BACKGROUND

Relapsed or refractory large B-cell lymphoma (R/R LBCL) carries poor outcomes after multiple prior therapies, including CAR T-cell therapy. Epcoritamab, a subcutaneous CD3×CD20 bispecific antibody, shows clinically meaningful activity in heavily pretreated R/R LBCL, but long-term durability and safety require further evaluation.

OBJECTIVE

To systematically review long-term outcomes of epcoritamab in R/R LBCL, including response durability, survival, minimal residual disease, and safety.

METHODS

- Systematic search of PubMed and Scopus from inception to 2026, conducted per PRISMA 2020.
- Eligible: original clinical studies reporting long-term efficacy or safety outcomes of epcoritamab in R/R LBCL.
- Included: three multicenter, single-arm, open-label trial reports (2020–2022), median follow-up 2–3 years.
- Population: median age 64–68 years, heavily pretreated and high-risk, with frequent primary refractory disease.
- Outcomes: ORR, CR, duration of response, PFS, OS, MRD status and adverse events.
- Appraisal: study design, limitations, risk of bias and applicability assessed for each report.

RESULTS

- Three long-term follow-up reports were identified, from the EPCORE NHL-1 and NHL-3 trials.
- ORR 56%–63.1% and CR 40.1%–47%; benefit was concentrated among complete responders, with prolonged duration of complete response and improved PFS and OS.
- MRD negativity occurred in 45%–57% of evaluable patients and correlated with improved outcomes.
- Cytokine release syndrome, pyrexia, fatigue, injection-site reactions, neutropenia and infections were most common; no new safety signals emerged with longer follow-up.

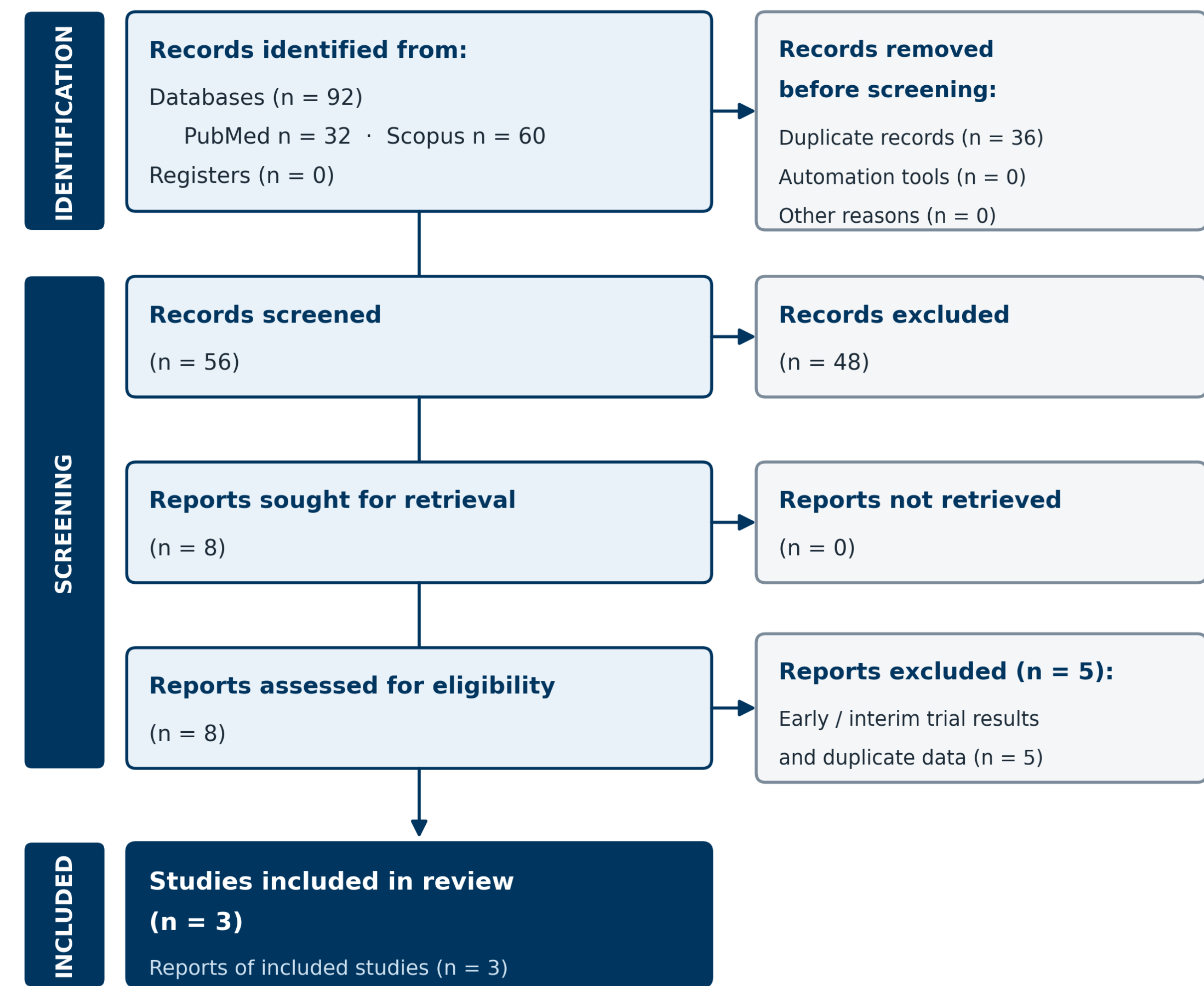
CONCLUSIONS

- Long-term data support epcoritamab as an effective therapy for R/R LBCL.
- Benefit is greatest among patients achieving complete response or MRD negativity.
- Comparative and real-world studies are needed.

LIMITATIONS

- All three reports were single-arm, with no direct comparator.
- Long-term follow-up cohorts were small (7–27 patients).
- The two EPCORE NHL-1 reports share an overlapping cohort.
- One cohort was Japanese-only, limiting generalizability.
- Survival endpoints were reported at differing timepoints, precluding pooling.

STUDY SELECTION

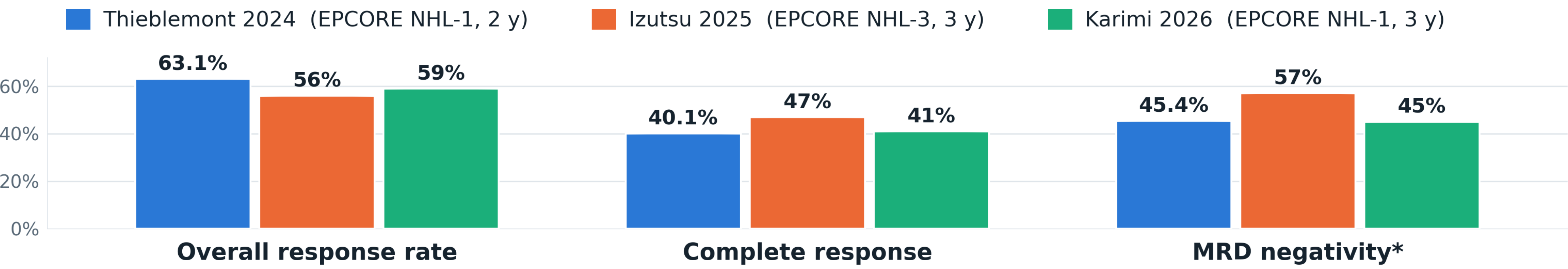


OUTCOMES AND KEY FINDINGS

Study	Response outcomes	Survival outcomes	MRD findings	Safety outcomes	Key takeaway
Thieblemont 2024	ORR 63.1%; CR 40.1%; 64.2% of complete responders remained in CR at 24 months	24-month PFS 27.8%; OS 44.6%; among CR patients, PFS 65.1% and OS 78.2%	MRD negativity in 45.4%; associated with longer PFS and OS	CRS 51.0%, pyrexia 24.8%, fatigue 24.2%, neutropenia 23.6%	Durable 2-year benefit, especially among complete responders
Izutsu 2025	ORR 56%; CR 47%; median DOR 15.2 months; DOR in CR not reached	Median PFS/OS 4.1/14.9 months overall; 3-year PFS/OS 25%/39%; among CR patients 53%/71%	MRD negativity in 57%; associated with longer PFS	CRS 83%, injection-site reaction 69%, neutropenia 39%; no fatal TEAEs	Confirms long-term activity and manageable safety in Japanese R/R DLBCL
Karimi 2026	ORR 59%; CR 41%; median DOR 20.8 months; median DOCR 36.1 months	Median PFS 4.2 months overall and 37.3 months in CR patients; median OS 18.5 months overall and not reached in CR patients	MRD negativity in 45% of evaluable patients	CRS 51%, fatigue 25%, pyrexia 25%, grade 3 infections 24%; no new safety signals	Sustained 3-year disease control in complete responders

ORR, overall response rate; CR, complete response; DOR, duration of response; DOCR, duration of complete response; PFS, progression-free survival; OS, overall survival; MRD, minimal residual disease; CRS, cytokine release syndrome; TEAE, treatment-emergent adverse event.

RESPONSE, COMPLETE RESPONSE AND MRD NEGATIVITY ACROSS THE THREE REPORTS



*MRD negativity among patients evaluable for minimal residual disease. Values as reported in each publication; cohorts of the two EPCORE NHL-1 reports overlap.

CRITICAL APPRAISAL

Study	Design strengths	Limitations	Risk of bias	Applicability
Thieblemont 2024	Pivotal trial; long follow-up; subgroup and MRD data	Single-arm design; no direct comparator	Moderate	High applicability to heavily pretreated R/R LBCL
Izutsu 2025	3-year follow-up; country-specific data; MRD analysis	Small sample size; Japanese-only cohort	Moderate to high	Useful for Japanese and Asian R/R DLBCL populations
Karimi 2026	Longest EPCORE NHL-1 follow-up; mature survival and safety	Single-arm design; overlapping cohort with the 2024 report	Moderate	Highly relevant for long-term epcoritamab outcomes

LONG-TERM FOLLOW-UP COHORTS

EPCORE NHL-1 157 patients enrolled; 27 (17.2%) in follow-up at 2 years and 18 (11%) at 3 years
EPCORE NHL-3 36 patients enrolled; 7 (19.4%) in follow-up at 3 years

REFERENCES

1. Thieblemont C, et al. Leukemia. 2024;38(12):2653-62. 2. Izutsu K, et al. Int J Clin Oncol. 2025;30(8):1631-40. 3. Karimi YH, et al. Ann Hematol. 2026;105(3):79. 4. Page MJ, et al. BMJ. 2021;372:n71.

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