ABCL-360

Clinical, Economic, and Humanistic Outcomes of First-line High-Risk Large B-Cell Lymphoma: A Series of Systematic Literature Reviews

Evan Popoff[1], Hil Hsu[2], Sally W. Wade[3], Markqayne Ray[2], Leah Yang[1], Steve Kanters[1], Liana Nikolaenko[2], Yi Lin[4]

[1]RainCity Analytics, Vancouver, BC, Canada; [2]Kite, a Gilead Company, Santa Monica, CA, USA; [3]Wade Outcomes Research and Consulting, Salt Lake City, UT, USA; [4]Mayo Clinic Comprehensive Cancer Center, Rochester, MN, USA

BACKGROUND

- While treatment options for first-line (1L) large B-cell lymphomas (LBCL) have advanced, unmet need remains high, particularly for high-risk patients.
- The few studies that focused on this high-risk population tend to report poor outcomes, highlighting the need for more effective treatments.

OBJECTIVES

- To conduct systematic literature reviews (SLRs) summarizing clinical literature (trials and real-world evidence [RWE]), healthcare resource use, economic evaluations, and humanistic burden in 1L high-risk LBCL.

METHODS

- SLRs (2017-September 2024) followed PRISMA guidelines and were supplemented by manual searches.
- These global SLRs included broad high-risk LBCL definitions (e.g., international prognostic index [IPI] 4-5, age-adjusted IPI 3, double/triple-hit lymphoma [DHL/THL]) and studies with mixed risk groups (Intermediate-High risk; generally, ≥80% high-risk).
- Two independent reviewers conducted study selection and data extraction.
- Extracted data covered study, patient, treatment characteristics, and clinical, economic, and humanistic outcomes.

RESULTS

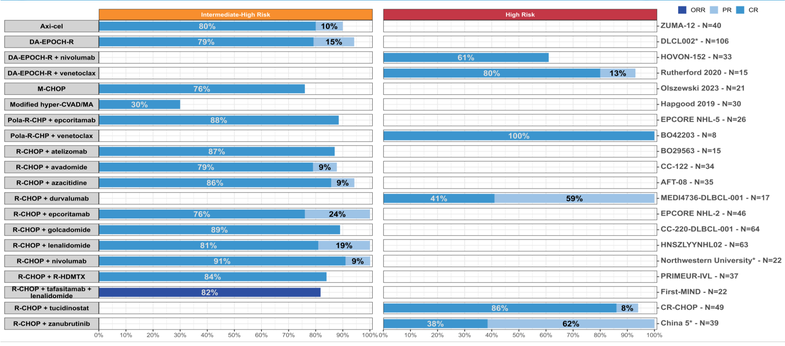
- In trials and RWE, R-CHOP and DA-EPOCH-R were most studied. For R-CHOP, 24-month overall survival (OS) was 61-89% in trials and 38-64% in RWE; for DA-EPOCH-R, 24-month OS was 63-87% in trials and 68-88% in RWE. Emerging combination therapies had promising but limited data.
- Older regimens (in trials) with robust long-term data highlight poor prognosis in double-expressor lymphoma and patients with DHL, while newer therapies, such as axi-cel (in trials) demonstrate potential for improved OS (12m: 91%; 36m: 81%) and progression-free survival (PFS; 12m: 75%; 36m: 75%).
- Among intermediate (IPI 3 or equivalent) - high-risk patients (**Figure 1**), overall response rates (ORR) for R-CHOP-based therapies ranged from 82%-100%, while complete response (CR) rates ranged from 30% with modified hyper-CVAD/MA to 91% in R-CHOP + nivolumab. Despite generally low sample sizes, high-risk patients also showed strong response outcomes, with ORR ranging from 94%-100% and CR 38%-100%.
- Adverse events (AEs) in trials were common in all risk groups, with severe AEs most frequent in venetoclax-, lenalidomide-, and CAR T-based regimens. Cytopenias and infections varied by regimen, and certain newer combinations, like Pola-R-CHP + venetoclax showed more favorable profiles, though conclusions are limited.
- **Table 1** summarizes the economic evaluations which all used lifetime time horizons and varied by IPI status: 2 - IPI ≥2, 1 - IPI 3-5. The two IPI ≥2 cost-utility analyses (CUAs) found that Pola-R-CHP was not cost-effective compared to standard of care (SoC) in both the US and Canada, while it was considered cost-effective in Japan despite higher costs and marginal quality-adjusted life year gains. The IPI 3-5 Norwegian study found Pola-R-CHP was cost-effective vs R-CHOP in high-risk 1L DLBCL patients.

PLAIN LANGUAGE SUMMARY

- Although data are limited, newer treatments for high-risk LBCL show promise. These treatments may also have side effects and not work equally well for everyone.
- More research is needed to understand long-term benefits, costs, and how treatments affect patients' quality of life, so care can be better tailored to each person's needs.

RESULTS

Figure 1. Response Outcomes Across Clinical Trials in Intermediate- to High-Risk Patients



*Note: Studies with * were reported at a specific timepoint rather than best overall. Abbreviations: Axi-cel, Axicabtagene ciloleucel, CR, Complete response; DA-EPOCH-R, Dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab; M-CHOP, Mosunetuzumab cyclophosphamide, doxorubicin hydrochloride, vincristine and prednisone; ORR, Objective response; Pola-R-CHP, Polatuzumab vedotin + rituximab, cyclophosphamide, doxorubicin, and prednisone; PR, Partial response; R-CHOP, Rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine and prednisone*

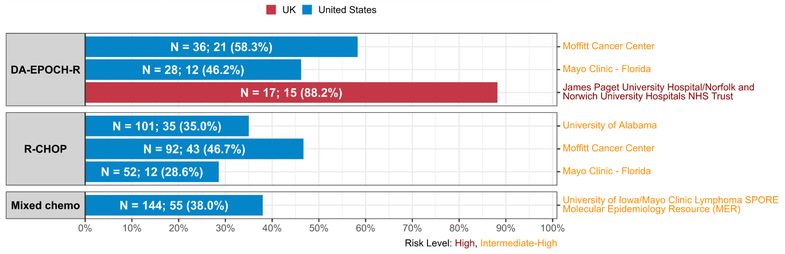
Table 1. Sources of Clinical, Cost, and Utility Inputs for the Economic Models in the SLR

Study name	Population	Type of analysis	Country	Interventions	Clinical trial inputs	Sources of clinical inputs	Sources of costing inputs	Sources of health utility inputs
Mizuoka 2023[1]	Previously untreated DLBCL who had an IPI score of 2-5	CUA	Japan	• Pola-R-CHP • R-CHOP	POLARIX	• Clinical trial	• Costs catalog • Published sources • Expert opinion	• Clinical trial • Published sources • Expert opinion
Vijenthira 2023[2]	Patients with newly diagnosed intermediate- to high-risk (IPI 2-5) DLBCL eligible for curative-intent therapies	CUA	United States and Canada	• Pola-R-CHP • R-CHOP • CAR-T cell • ASCT • SoC	POLARIX	• Clinical trial • Published sources	• Costs catalog • Published sources • Expert opinion	• Published sources
Westermann 2023[3]	Newly diagnosed adult patients with DLBCL non-specified, with IPI 3-5, without known CNS involvement	CUA	Norway	• Pola-R-CHP • R-CHOP	POLARIX	• Clinical trial	• Costs catalog • Published sources	• Clinical trial • Published sources

Abbreviations: ASCT, Autologous Stem Cell Transplant; CAR-T, Chimeric Antigen Receptor T-Cells; CNS, Central Nervous System; CUA, Cost-Utility Analysis; DLBCL, Diffuse Large B-Cell Lymphoma; IPI, International Prognostic Index; *Pola-R-CHP, Polatuzumab Vedotin + Rituximab, Cyclophosphamide, Doxorubicin, and Prednisone; R-CHOP, Rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine and prednisone; SoC, Standard of Care*

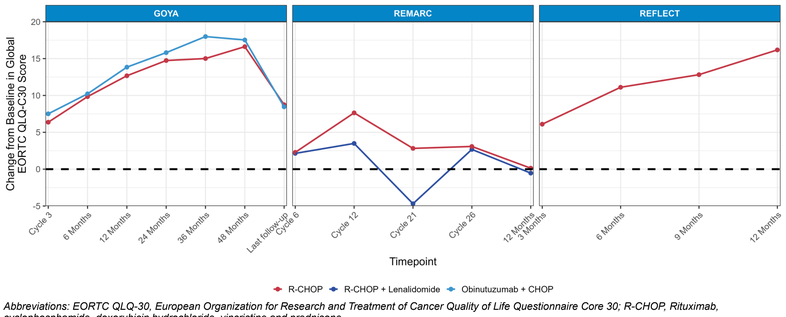
- Five studies assessed inpatient stays during treatment (**Figure 2**), with the proportion of patients with inpatient stays differing across treatments and risk groups. The proportion of patients with inpatient stays was higher in patients who received DA-EPOCH-R (Range: 46.2% - 88.2%) compared to those who received R-CHOP (Range: 28.6% - 46.7%) or chemotherapy (38%).
- Across three studies (**Figure 3**), global health scores significantly improved over time in patients receiving R-CHOP or obinutuzumab + CHOP (GOYA, REFLECT), though declines were seen at long-term follow-up; while no sustained improvement was observed in elderly patients receiving R-CHOP ± lenalidomide (REMARC).

Figure 2. Percentage of Patients With at Least One Inpatient Stay



Abbreviations: DA-EPOCH-R, Dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab; R-CHOP, Rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine and prednisone

Figure 3. Change from Baseline in EORTC QLQ-30 Global Health Status Score



Abbreviations: EORTC QLQ-30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; R-CHOP, Rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine and prednisone

CONCLUSIONS

- Although available data indicate that approved treatments may be beneficial, the clinical burden in 1L high-risk LBCL remains considerable. Furthermore, the literature underscores the need for more clinically effective treatments.
- More clinically effective 1L therapies for high-risk LBCL may also have the potential to reduce the need for subsequent treatment and healthcare utilization.

REFERENCES

1. Mizuoka et al, JME, 2023
2. Vijenthira et al, JCO, 2023
3. Westermann et al, VH, 2023

DISCLOSURES

Dr. Lin holds advisory roles with Janssen, Sanofi, BMS, Regeneron, Genentech, Tessera, Legend, NexT Therapeutics; Steering committees for Janssen, Kite/Gilead; Research funding from Janssen, BMS; Scientific boards for NexImmune, Caribou; DSMB/EDMC for Pfizer. *All funds to Mayo Clinic; no personal compensation.*

This study was funded by Kite, a Gilead company.

Presented at the Society of Hematologic Oncology 2025 Annual Meeting, September 3-5, 2025, Houston, Texas