NEW EHA 2025 GUIDELINES ON THE MANAGEMENT OF LARGE B CELL LYMPHOMAS

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A multidisciplinary panel of 23 experts from Europe have developed a new set of EHA guidelines for the management of LBCL.[1]

These include a new recommendation for CAR-T cell therapy in patients who are primary refractory or relapse within 12 months of 1L treatment.[1]

Recommendations for Stage I–IV LBCL with 0 or 1 additional risk factor (high LDH or poor performance status) are to treat with 4-6 cycles of R-CHOP21.* Patients with Stage III–IV disease and >2 risk factors should receive Pola-R-CHP x6 or R-CHOP21 ×6.

1L LBCL

- Stage I–II + 0 risk factors, <80 years → R-CHOP21 ×4 (6 cycles if tumour ≥7.5 cm)
- Stage III, IV, or I/II + 1 risk factor, <80 years → R-CHOP21 ×6
- Stage III–IV + ≥2 risk factors, <80 years → Pola-R-CHP x6 or R-CHOP21 ×6

2L R/R LBCL

Stratification of patients by time-to-relapse. Biopsy recommended

1L refractory or relapse <12 months

Stratification by CAR-T cell eligibility

- CAR-T eligible → Liso-cel or axi-cel
- No intention to proceed to CAR-T → Glofitamab-GemOx, clinical trial, 2L therapy,** or best supportive care

Patients who do not respond to 1L treatment or relapse within 12 months should be offered CAR-T cell therapy with liso-cel or axi-cel if eligible. This is a change from the previous recommendation[2] to offer HCT to eligible patients.

Relapse >12 months

- Transplant eligible → Immunochemotherapy*** followed by HDT/ASCT if CR/PR
- No intention to proceed to transplant → Glofitamab-GemOx, clinical trial, 2L therapy,** or best supportive care

Patients who relapse >12 months should receive immunochemotherapy** + HCT if CR/PR (if eligible) or glofitamab-GemOx, clinical trial, 2L therapy, or supportive care

3L R/R LBCL

Biopsy strongly recommended

3L treatment decision should be influenced by prior treatments, disease condition, and patient's overall status, and a biopsy is strongly reccomended

CAR-T, bispecifics, loncastuximab tesirine, tafasitamab-LEN, Pola-BR
In limited stage: IS-RT
Clinical trials
Best supportive care

*Special considerations should be given to treatment of high-grade (double- or triple-hit) lymphoma, primary mediastinal B cell lymphoma, primary testis lymphoma, intravascular LBCL and patients at high risk for CNS relapse or frailty. Alternative or more-intensive treatment regiments and additional assessments are recommended in these cases.[1]
**2L therapy: epcoritamab+GemOx when available; tafasitamab+LEN in non-refractory patients. R-chemotherapy: R-DHAX, R-ICE, R-GDP, R-ESHAP, Pola-BR.
***2L immunochemotherapy before HDT/ASCT: R-DHAX (P or C), R-ICE, R-GDP, R-ESHAP. In case of CMR, go to HDT/ASCT.

At Diagnosis

- Use a combination of haematopathology, full IHC panels, and access to molecular testing per WHO/ICC standards to diagnose LBCL.
- IHC and FISH are essential to distinguish high-risk subtypes.
- PET-CT is the gold standard to define local and disseminated disease, outperforming bone marrow biopsy.
- IPI is mandatory and CNS-IPI strongly recommended.
- Comprehensive supportive care is essential and frailty should be assessed.
- Cell-of-origin classification has no therapeutic implications.

After Treatment

- Assess response with PET imaging using Lugano criteria.[3]
- Interim PET (after 2–4 R-CHOP cycles) helps assess early R-CHOP chemosensitivity.
- EoT biopsy and further follow-up is recommended for unclear lesions on EoT PET.

Conclusion

New EHA treatment guidelines for LBCL now recommend CAR-T cell therapy as 2L treatment instead of HDT/ASCT in eligible patients who do not respond to 1L therapy or relapse within 12 months. For patients who relapse >12 months after 1L treatment, the guidelines recommend immunochemotherapy followed by HDT/ASCT in transplant-eligible patients.

Abbreviations

1L: first-line; 2L: second-line; 3L: third-line; ASCT: autologous stem cell transplantation; axi-cel: axicabtagene ciloleucel; CMR: complete metabolic response; CR: complete response; CNS-IPI: central nervous system- International Prognostic Index; EHA: European Hematology Association; EoT: end-of-treatment; FISH: fluorescence in situ hybridisation; GemOx: gemcitabine and oxaliplatin; HDT: high-dose therapy; ICC: International Consensus Classification of Myeloid Neoplasms and Acute Leukemias; IHC: immunohistochemistry; IPI: International Prognostic Index; IS-RT: involved site radiotherapy; LEN: lenalidomide; LDH: lactate dehydrogenase; liso-cel: lisocabtagene maraleucel; R-CHOP21: rituximab + cyclophosphamide + doxorubicin + vincristine + prednisolone; R-DHAX, rituximab + dexamethasone + cytarabine + oxaliplatin; R-ESHAP: rituximab + etoposide + solu-medrone + high-dose cytarabine + cisplatin; R-GDP: rituximab + gemcitabine + dexamethasone + cisplatin; R-ICE: rituximab + ifosfamide + carboplatin + etoposide; R/R: relapsed/refractory; Pola-BR: polatuzumab vedotin + bendamustine + rituximab; Pola-R-Chp: polatuzumab vedotin + rituximab + cyclophosphamide + doxorubicin + prednisolone; PR: partial response

References

1. Thieblemont C. Presentation p571-2. EHA. 12-15 June, 2025.
2. Tilly H et al. Ann Oncol. 2015;26(Suppl 5):v116-25.
3. Cheson BD et al. J Clin Oncol. 2014;32(27):3059-68.