diffuse large B-cell non-Hodgkin’s lymphoma: ESMO
Clinical Practice Guidelines for diagnosis, treatment and
follow-up

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newly diagnosed diffuse large B-cell
non-Hodgkin’s lymphoma

incidence

Diffuse large B-cell non-Hodgkin’s lymphoma (DLBCL) constitutes 30%–58% of non-Hodgkin’s lymphoma series. The crude incidence in the European Union is 3–4/100 000/year. The incidence increases with age from 0.3/100 000/year (35–39 years) to 26.6/100 000/year (80–84 years).

diagnosis

Diagnosis should be made on the basis of a surgical specimen/excisional lymph node or extranodal tissue biopsy providing enough material for formalin-fixed samples. Core biopsies may be appropriate as the only diagnostic test in the rare patients requiring emergency treatment. Minimal immunohistochemistry (CD45, CD20 and CD3) is mandatory. The collection of fresh frozen material for molecular characterization is recommended although gene expression profiling remains investigational. To ensure adequate quality, processing by an experienced pathology institute has to be guaranteed. The histological report should give the diagnosis according to the current World Health Organization classification.

staging and risk assessment

A complete blood count, routine blood chemistry including lactate dehydrogenase (LDH) and uric acid as well as a screening test for human immunodeficiency virus and hepatitis B and C are required. Protein electrophoresis is recommended.

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or dose-intensive (like R-ACVBp; rituximab, doxorubicin, vindesine, cyclophosphamide, bleomycin, prednisolone given every 2 weeks followed by sequential consolidation) regimens could also be proposed. High-dose chemotherapy with stem-cell transplantation as consolidation treatment after immunochemotherapy remains experimental in first-line therapy but recent phase II trials have shown promising results.

Consolidation by radiotherapy to sites of bulky disease has proved to be of no benefit [III, C]. The role of radiotherapy in partial remission remains to be established in patients treated with rituximab abd evaluated with PET.

**patients aged 60–80 years.** Eight cycles of combination chemotherapy with CHOP treatment combined with eight doses of rituximab given every 21 days is the current standard [I, A]. If rituximab–CHOP is given every 14 days, six cycles of CHOP with eight cycles of rituximab are sufficient. In patients with localized disease, consolidation by radiotherapy has proved to be of no benefit [I, A].

**patients aged >80 years.** R-CHOP treatment could usually be used until 80 years of age in fit patients. Small series have shown that the combination of rituximab with attenuated chemotherapy could induce complete remission and long survival in some very elderly patients.

**CNS prophylaxis.** Patients with high–intermediate- and high-risk IPI, especially those with more than one extranodal site or elevated LDH are at higher risk of CNS relapse. CNS prophylaxis should be recommended in this population but intrathecal injections of methotrexate are probably not an optimal method. Whether some specific involvement sites such as paranasal sinus, upper neck or bone marrow should receive prophylaxis remains to be established. Testicular lymphoma must receive CNS prophylaxis.

**some extra-nodal DLBCLs require special consideration.** Treatment of primary DLBCL of the central nervous system must contain high-dose methotrexate. Addition of high-dose cytarabine seems to improve complete remission rate and outcome. CNS irradiation is usually associated.

Primary DLBCL of the testis is characterized by an increased risk of extranodal relapse. CNS prophylaxis is mandatory. Prophylactic irradiation of the contralateral testis should be considered in localized disease.

Primary mediastinal large B-cell lymphoma (PMBL) is probably a distinct entity. R-CHOP 21 is not established as the definitive treatment option and radiotherapy remains controversial.

**response evaluation**

Abnormal radiological tests at baseline should be repeated after three to four cycles and after the last cycle of treatment. Bone marrow aspirate and biopsy should only be repeated at the end of treatment if initially involved.

PET is highly recommended for post-treatment assessment to define complete remission according to the revised criteria of response. In the case of therapeutic consequences a histological confirmation of PET positivity at this time is strongly recommended. Early PET, performed after one to four cycles of treatment, could be predictive of clinical outcome but its results should not lead to treatment change outside of a clinical trial.
response evaluation

Response criteria are identical to those of first-line treatment evaluation. An evaluation should be performed after three to four cycles of salvage regimen (before high-dose treatment) and after the end of all therapy. Results of PET before high-dose treatment are correlated with clinical outcome.

follow-up

Follow-up of patients in second response could be the same as first response.

note

Levels of Evidence [I–V] and Grades of Recommendation [A–D] as used by the American Society of Clinical Oncology are given in square brackets. Statements without grading were considered justified standard clinical practice by the experts and the ESMO faculty.

literature