ESMO minimum clinical recommendations for diagnosis, treatment and follow-up of newly diagnosed large cell non-Hodgkin's lymphoma

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Incidence

- Large Cell Lymphoma constitutes 30–58% of non-Hodgkin's lymphoma series. The crude incidence in the European Union is 3–4/100 000 per year. The incidence increases with age from 0.3/100 000 per year (35–39 y) to 26.6/100 000 per year (80–84 y).

Diagnosis

- Diagnosis should almost always be based on a surgical specimen/excisional lymph node biopsy providing enough material for fresh frozen and formalin-fixed samples. To ensure adequate quality, immediate processing by an experienced pathology institute has to be guaranteed.
- Fine needle aspirations or core biopsies may be appropriate as the only diagnostic test in the rare patients requiring emergency treatment or those not suitable for curative therapy.
- The histological report should give the diagnosis according to the WHO classification with use of CD20 immunohistochemistry.

Staging and risk assessment

- Patients amenable to curative therapy should have at least a chest X-ray and a CT-scan of the abdomen, as well as a bone marrow aspirate and biopsy. A diagnostic spinal tap directly combined with a first prophylactic instillation of cytarabine or methotrexate shall be considered in high-risk patients [patients with more than two adverse parameters according to international prognostic index (IPI)] with e.g. involvement of bone marrow, testis, the spine, or the base of the skull *[V, D]*.
- A complete blood count, routine blood chemistry including LDH and uric acid as well as a screening test for HIV and hepatitis B and C are required. Protein electrophoresis is recommended for B-cell lymphomas.
- The staging is given according to the Ann Arbor system with mentioning of bulky disease *[III, A]*. For prognostic purposes, the IPI should be established *[III, A]*.

Treatment plan

- A multidisciplinary treatment planning is required:
  Treatment with curative intent: CHOP-treatment combined with rituximab given every 21 days for usually 8 cycles is the current standard for CD20+ large-cell non-Hodgkin's lymphoma of all stages *[II, A]*. In T-cell lymphoma, CHOP remains the standard. Shortening the interval between CHOP cycles to two weeks with growth factor support may be considered *[II, B]*.
- High-dose chemotherapy with stem cell transplantation in poor risk patients remains experimental.
- Consolidation by radiotherapy to sites of bulky disease has not proven its benefit *[III, C]*.
- Dose reductions due to hematological toxicity should be avoided and febrile neutropenia justifies prophylactic use of hematopoietic growth factors in patients treated with curative intent.

Response evaluation

- Adequate radiological tests should be done after 2 to 4 cycles and after the last cycle of CHOP or CHOP + radiotherapy, and whenever there are doubts regarding adequate response.
- An initially pathologic bone marrow aspirate/biopsy or spinal tap should be repeated at the end of treatment.
- Patients with incomplete or lacking response should be evaluated for early salvage regimens.

Follow-up

- History and physical examination every 3 months for 2 years, every 6 months for 3 more years, and then once a year with attention to development of secondary tumors *[V, D]*. High-risk patients still with curative options, such as high-dose chemotherapy with stem cell support, may mandate more frequent controls.
- Blood count and LDH at 3, 6, 12, and 24 months, then only as needed for evaluation of suspicious symptoms or clinical findings in those patients suitable for further therapy *[V, D]*.
- Evaluation of thyroid dysfunction (TSH) in patients with irradiation to the neck at 1, 2, and at least at 5 years *[III, A]*.
- After having received chest irradiation at premenopausal age, especially at an age below 25 years, women should be screened for secondary breast cancers clinically *[III, A]* and, after the age of 40–50 years, by mammography *[III, C]*.
- Minimal adequate radiological examinations at 6, 12, and 24 months after end of treatment, by CT scan when indicated by site of disease *[V, D]*.

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.

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