Annals of Oncology 16 (Supplement 1): i60–i61, 2005
doi:10.1093/annonc/mdi828

ESMO Minimum Clinical Recommendations for diagnosis, treatment and follow-up of relapsed large cell non-Hodgkin's lymphoma

Diagnosis

- Early relapse (<12 months) of a histologically well-established large cell lymphoma does not require repeat biopsy unless clinical presentation mandates exclusion of a second malignancy. In later relapses histological verification of diagnosis is mandatory to exclude the possibility of follicular lymphoma.
- In patients with late relapse or lack of initial adequate immune histochemistry, verification by histology should be done and should include the use of B-cell and T-cell markers since their presence may offer specific treatment options.
- The histological report should give the diagnosis according to the World Health Organisation classification.

Staging and risk assessment

- Patients still amenable to curative therapy should have at least a CT-scan of the abdomen, a chest X-ray or a CT-scan of the chest, and a bone marrow aspirate and biopsy. A diagnostic spinal tap directly combined with a first prophylactic instillation of cytarabine or methotrexate should be considered in high-risk patients showing more than two adverse parameters according to international prognostic index (IPI), especially if involvement of bone marrow, testis, the spine, or the base of the skull is present *[V, D]*.
- A complete blood count, a routine blood chemistry including LDH and uric acid as well as a screening test for HIV and hepatitis B and C are required.
- The staging at relapse is given according to the Ann Arbor system with mentioning of bulky disease *[III, A]*.
- The cumulative dose of anthracyclines used in first line therapy has to be specified (in mg/m^2). If further anthracyclines are to be used, echocardiography or MUGA scans for quantification of the ejection fraction should be done *[V, D]*.
- For prognostic purposes, the IPI should be established *[III, A]*.

Treatment plan

- In CD20-positive B-cell lymphomas the use of rituximab has shown considerable single agent activity even after failed transplantation and may be combined with conventional or high-dose salvage chemotherapy as listed below. However, its impact upon response rate and long-term prognosis still requires confirmation from randomized trials.
- The following recommendations apply to patients with adequate, anthracycline-containing first-line therapy.

Treatment with curative intent

- In suitable patients (no major organ dysfunction, age below approximately 65 years) conventionally-dosed salvage chemotherapy followed by high-dose treatment with stem cell support in responsive patients is recommended *[II, A]*. Any of the published salvage regimens such as (R-) DHAP, (R-) ESHAP, (R-) EPOCH, (R-) ICE, etc. may be adequate since comparative trials are lacking. Also, the choice of the high-dose regimen depends on local experience. Additional involved field or iceberg radiation may be used.

Treatment in patients not suitable for high-dose therapy

- The same conventionally-dosed salvage regimens may be used and may be combined with involved field radiotherapy. Individualized palliative care may be needed in elderly, co-morbid or HIV-positive patients.

Response evaluation

- Adequate radiological tests should be done after 2–4 cycles of salvage therapy, i.e. before autologous stem cell collection and high-dose therapy, and after the end of all therapy.
- An initially-pathologic bone marrow aspirate/biopsy or spinal tap should be repeated at the end of treatment.

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]*.
- Full blood count 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 function (TSH) in patients with irradiation to the neck at 1, 2, and 5 years *[III, C]*.
- After having received chest irradiation at premenopausal age, especially at an age <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 (with a CT scan at least once) at 3, 6, 12, and 24 months, then as needed for evaluation of suspicious symptoms or clinical findings in those patients suitable for further therapy *[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.

Literature

1. Harris NL, Jaffe ES, Stein H et al. A revised European-American classification of lymphoid neoplasms: a proposal from the International Lymphoma Study Group. Blood 1994; 84: 1361–1392.
2. Smithers DW. Summary of papers delivered at the Conference on Staging in Hodgkin's Disease (Ann Arbor). Cancer Res 1971; 31: 1869–1870.
3. Shipp M, Harrington D, Anderson J et al. A predictive model for aggressive non-Hodgkin's lymphoma. N Engl J Med 1993; 329: 987–994.
4. Philip T, Guglielmi C, Hagenbeek A et al. Autologous bone marrow transplantation as compared with salvage chemotherapy in relapses of chemotherapy-sensitive non-Hodgkin's lymphoma. N Engl J Med 1995; 333: 1540–1545.
5. Coiffier B, Haioun C, Ketterer N et al. Rituximab (anti-CD20 monoclonal antibody) for the treatment of patients with relapsing or refractory aggressive lymphoma: a multicenter phase II study. Blood 1998; 92: 1927–1932.
6. Jermann M, Jost LM, Taverna C et al. Rituximab-EPOCH, an effective salvage therapy for relapsed, refractory or transformed B-cell lymphomas: results of a phase II study. Ann Oncol 2004; 15: 511–516.
7. Kewalramani T, Zelenetz AD, Nimer SD et al. Rituximab and ICE as second-line therapy before autologous stem cell transplantation for relapsed or primary refractory diffuse large B-cell lymphoma. Blood 2004; 103: 3684–3688.

Coordinating authors for the ESMO Guidelines Task Force: L. M. Jost[1] & R. A. Stahel[2]

[1]Invited author and member of the task force, Oncology, Kantonsspital, CH-4101 Bruderholz/BL, Switzerland; [2]Assigned task force member, Div. of Oncology, University Hospital, Rämistr. 100, CH-8091 Zürich, Switzerland

Approved by the ESMO Guidelines Task Force: February 2002, last update December 2004.

Correspondence to:
ESMO Guidelines Task Force
ESMO Head Office
Via La Santa 7
CH-6962 Lugano
Switzerland