Hodgkin’s lymphoma: ESMO Clinical Recommendations for diagnosis, treatment and follow-up

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incidence

The incidence of Hodgkin’s lymphoma (HL) in western countries is 2–3/100,000 per year resulting in ~7500 new cases annually in the USA. There is an age-related bimodal incidence. Most patients are in their third decade of life, and a second smaller rise in incidence occurs after the age of 55 years.

diagnosis

The diagnosis of HL always requires a lymph node biopsy. Hodgkin’s lymphoma is peculiar in that the number of tumor cells (Hodgkin–Sternberg cells or lymphocytic and histiocytic (L & H) cells with various appearance) represent only 0.1–1% of the entire cell population with a heterogeneous admixture of lymphocytes, histiocytes, eosinophils, plasma cells, fibroblasts and other cells. According to the updated WHO classification, two major subtypes can be distinguished.

I. Lymphocyte predominant Hodgkin’s lymphoma (LPHL; ~5%). The malignant cells (L & H cells) have a different immunophenotype (CD15–/CD30–/CD20+) as compared with classical HL (CD15+/CD30+/CD20–).

II. Classical Hodgkin’s lymphoma (cHL)

- Lymphocyte rich
- Nodular sclerosing
- Mixed cellularity
- Lymphocyte depleted
- Hodgkin’s lymphoma, unclassifiable
- Staging and risk assessment.

Patients should be carefully asked for the presence of B-symptoms, such as fever, night sweat and weight loss. Most patients with HL (>60%) initially observe enlarged cervical lymph nodes. Since other lymphoid organs such as spleen, liver, bone marrow and lung can be involved, a comprehensive staging procedure including bone marrow biopsy and CT scans of the abdomen and thorax are needed.

- A liver biopsy should be restricted to cases with elevated alkaline phosphatase or other clinical suspicion. Explorative laparotomy and splenectomy are generally no longer recommended.

- The staging is based on the Cotswolds classification, a modification of the Ann Arbor staging system. Based on additional risk factors such as large mediastinal mass (more than one-third of horizontal chest diameter) extranodal disease, high ESR (>50 with B symptoms; >30 without B symptoms) and three or more involved lymph node areas, patients are being allocated to the following risk groups:
  - early favorable risk group: stage I and II without risk factors;
  - early unfavorable risk group: stage I and II with risk factors;
  - advanced risk group: stage III, IV and IIb with large mediastinal mass or extranodal involvement.

treatment of limited disease

Standard treatment for patients with early favorable HL is a combined chemoradiotherapy consisting of two cycles of ABVD (doxorubicin/bleomycin/vinblastine/dacarbazine) followed by 30 Gy involved field (IF) radiotherapy based on the German Hodgkin Study Group (GHSG) HD7 and HD10 trials as well as the EORTC trials H7F and H8F. These trials also showed that the addition of chemotherapy to radiotherapy substantially reduces the number of relapses. Moreover, two cycles of ABVD is not inferior to four cycles of ABVD when combined with 30 Gy IF radiotherapy. Thus, $2 \times ABVD + 30$ Gy is currently the treatment of choice. The major focus of ongoing trials is the additional reduction of toxicity but studies eliminating drugs from the ABVD backbone or reducing the radiation dose are not yet conclusive. An alternative to combined modality treatment (CMT) is chemotherapy only. Depending on the response to treatment and the presence of risk factors, usually four to six cycles of ABVD are being given. Currently, there is only very limited data from larger prospectively randomized trials supporting this approach.

Lymphocyte predominant Hodgkin’s lymphoma (LPHL) presents more often in early stages with an indolent course but a tendency to recur. Stage I LPHL patients can be treated with IF radiotherapy (30 Gy) only. Rituximab is an option for relapsed LPHL.

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treatment of early unfavorable disease

Standard of care for patients with early unfavorable HL (intermediate-stage risk group) is four cycles of ABVD followed by 30 Gy IF radiotherapy. Tumor control and overall survival in excess of 85% or 90% at 5 years. Radiotherapy in extended field (EF) technique or six cycles of chemotherapy are of similar efficacy but more toxic. Experimental approaches include the use of more aggressive chemotherapy such as BEACOPP_{escalated}: a reduction in radiation dose from 30 to 20 Gy IF, and the use of chemotherapy only. The potential impact of PET to discriminate low- and high-risk patient groups need to be studied prospectively.

follow-up

History, physical examination and laboratory analysis should be performed every 3 months for the first year, every 6 months for years 2 and 3 and then once a year. CT scan is needed to confirm a complete remission, additional CT scans are not recommended except for evaluation of residual disease. After radiotherapy to breast tissue women should be screened for secondary breast cancer clinically and by mammography at age >40 years.

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