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Acute myeloblastic leukemia in adult patients: ESMO Clinical Recommendations for diagnosis, treatment and follow-up

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incidence

The incidence of acute myeloblastic leukemia (AML) in adults in Europe is 5–8 cases/100 000/year. The mortality is ∼4–6 cases/100 000/year.

diagnosis

The diagnosis of AML requires examination of peripheral blood and bone marrow samples. Workup should comprise morphological examination, cytochemistry, immunophenotyping, cytogenetics and molecular genetics.

risk assessment

Risk assessment in AML includes the patient's age, the initial leukocyte count, the AML subtype, karyotype data and selected molecular markers. AML with the chromosomal translocations t(15;17) (acute promyelocytic leukemia; APL), t(8;21) and t(16;16) (including acute myelomonocytic leukemia with preponderance of eosinophil granulocytes) are considered as favorable, as are AML with mutations in the C/EBPα gene, and the nucleophosmin gene [II, A]. An antecedent or concomitant myelodysplastic syndrome or a complex aberrant karyotype, alterations of the FLT3 gene are adverse prognostic factors. Preexisting medical conditions such as diabetes or coronary heart disease may affect the feasibility of intensive chemotherapy. Patients beyond the age of 60 years are more susceptible to treatment complications but also have an adverse prognosis due to more frequent unfavorable cytogenetics.

If an infection is suspected, a thoracic CT scan, and an abdominal ultrasound or CT scan may be carried out to assess lung, liver, spleen, lymph nodes and kidneys for possible pathological alterations. Cardiac examination including echocardiography is recommended for patients with cardiac risk factors or a history of heart disease [A].

In addition to hematological and chemistry tests coagulation screening is to be carried out before the insertion of central venous lines, and to detect leukemia-related coagulopathy (particularly if morphology suggests a diagnosis of APL). HLA typing of patients and their family members is carried out in patients who are candidates for allogeneic bone marrow or stem-cell transplantation [A].

treatment plan

Treatment is divided into induction and consolidation chemotherapy. Whenever possible it should be planned with a curative intent. Candidates for allogeneic stem-cell transplantation should be identified early during induction. Patients with poor performance status and considerable co-morbidity, as well as elderly patients not eligible for curative treatment, should receive supportive care. Whenever possible AML treatment should be carried out within clinical trials and in centers offering a multidisciplinary approach. Such centers should provide an adequate infrastructure including a full hematology and medical oncology service, close collaboration with a bone marrow transplant unit, as well as an infectious disease expert and adequate transfusion and psycho-oncology services.

induction chemotherapy

Chemotherapy should be postponed until all material satisfactory for diagnostic tests has been harvested. Patients with excessive leukocytosis at presentation may require emergency leukapheresis before induction chemotherapy.

Induction chemotherapy should include an anthracycline and cytosine arabinoside [II, A]. Patients failing to respond to one or two cycles of such treatment are considered refractory. APL induction chemotherapy should be complemented with all-trans retinoic acid (ATRA) [II, A]. Hematopoietic growth factors are an optional adjunct to intensive chemotherapy, and their role in priming leukemic cells during chemotherapy remains to be confirmed.

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consolidation therapy

Patients entering clinical and hematological remission should receive one to several cycles of post-remission therapy [II, A]. There is no consensus on a single 'best' post remission treatment strategy

Patients with good risk features as defined above should receive chemotherapy only, preferably with high-dose cytarabine.

All other patients with an HLA-identical sibling are candidates for allogeneic stem-cell transplantation in first remission [III, A]. Recently, regimens with dose-reduced conditioning are increasingly applied especially in patients >40–45 years. Patients with particular poor risk features and no donor in the family may qualify for an allogeneic transplant with an unrelated matched donor [III, A]. In the situation of a KIR mismatch, haplo-identical transplants may be considered.

Patients not entering complete remission after induction therapy are at high risk for failure of treatment and should be considered candidates for allogeneic transplantation.

The role of high-dose consolidation chemotherapy with autologous peripheral stem-cell support in AML is controversial. Maintenance chemotherapy and ATRA are beneficial in APL only [III, A].

therapy of relapsed or refractory patients

Patients in second or subsequent remission may qualify for allogeneic transplantation with an unrelated HLA-matched donor. In relapsed APL arsenic trioxide can induce remission even if patients have become refractory to ATRA [III, B].

response evaluation

Response to induction is monitored through clinical examination, serial peripheral blood counts and bone marrow aspirates. During induction-induced aplasia a bone marrow aspirate should be obtained to monitor for early marrow response or leukemic blast persistence. The usual requirements of AML remission are a normal cellularity of the bone marrow, blast levels <5 % in bone marrow smears and morphologically normal hematopoiesis [B].

follow-up

Patients are followed clinically and with hematological examinations to detect early relapse. Serial bone marrow examination is of uncertain value in remission patients without any clinical or hematological evidence of relapse.

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 expert authors and the ESMO faculty.

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