

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

### incidence

The crude 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. Work-up should comprise morphological examination, cytochemistry, immunophenotyping, cytogenetic and selected molecular analysis.

### 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 [II, A]. An antecedent or concomitant myelodysplastic syndrome or complex aberrant karyotypes are adverse prognostic factors. Preexisting medical conditions such as diabetes or coronary heart disease may affect the feasibility of intensive chemotherapy. Elderly patients have an adverse prognosis and are more susceptible to treatment complications.

If an infection is suspected, a thoracic computed tomography (CT) scan and an abdominal ultrasound or a CT scan may be performed 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, a coagulation screening is to be performed before the insertion of central venous lines. Human leukocyte antigen (HLA) typing of patients and their family members identifies patients who are candidates for an allogeneic bone marrow or stem-cell transplants [A].

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### 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 comorbidity, as well as elderly patients not eligible for curative treatment, should receive supportive care. Whenever possible AML treatment should be in clinical trials and in centers offering a multidisciplinary approach. Such centers should provide an adequate infrastructure including a full hematology and medical oncology service, a close collaboration with a bone marrow transplant unit, as well as an infectious disease service and an adequate transfusion service.

### 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. Especially in these patients with high leukocyte counts, adequate measures should be taken to avoid tumor lysis syndrome during the first days of treatment (including a prephase if appropriate).

Induction chemotherapy should include an anthracycline and cytarabine [II, A]. Patients failing to respond to one to 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.

### consolidation therapy

Patients entering clinical and hematological remission should receive one to several cycles of postremission therapy [II, A]. There is no consensus on a single 'best' postremission 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]. 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]. The role of prolonged monthly maintenance or high-dose consolidation

chemotherapy with autologous peripheral stem-cell support in AML is controversial. Maintenance chemotherapy and ATRA are beneficial in APL [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.

### literature

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