

# ESMO Minimum Clinical Recommendations for diagnosis, treatment and follow-up of acute myeloblastic leukaemia (AML) in adult patients

## Incidence

- The crude incidence of acute myeloblastic leukaemia (AML) in adults in Europe is 5–8 cases/100000/year. The mortality is ~4–6 cases/100000/year.

## Diagnosis

- The diagnosis of AML requires examination of peripheral blood samples and bone marrow aspirates. Work-up should comprise morphological examination, cytochemistry, immuno-phenotyping and cytogenetic analysis.

## Risk assessment

- Risk assessment in AML includes the patient's age, the initial leucocyte count, the AML subtype, karyotype data and medical conditions in the patient's history that may affect the feasibility of intensive chemotherapy. Elderly patients (>60 years) have an adverse prognosis and are more susceptible to treatment complications. AML with the chromosomal translocations t(15;17) (acute promyelocytic leukaemia; APL), t(8;21) and t(16;16) (including acute myelomonocytic leukaemia with preponderance of eosinophil granulocytes) are considered as favourable [II, A]. An antecedent or concomitant myelodysplastic syndrome or complex aberrant karyotype are adverse prognostic factors.
- If fungal infection is suspected a thoracic CT scan and an abdominal ultrasound or a CT scan may be performed to assess liver, spleen, lymph nodes and kidneys for possible pathological alterations. Cardiac examination including echocardiography is recommended for patients with risk factors or a history of heart disease [A].
- In addition to haematological and chemistry tests a coagulation screening is to be performed prior to the insertion of central venous lines. Human leucocyte antigen (HLA) typing should be performed on patients who are candidates for an allogeneic bone marrow or stem cell transplant, and should include their family members [A].

## Treatment plan

- Treatment is divided into induction and consolidation chemotherapy. Whenever possible treatment should be planned with a curative intent. Candidates for allogeneic stem cell transplanta-

tion 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 in clinical trials and in centres offering a multidisciplinary approach. Such centres should provide an adequate infrastructure including a full haematology and medical oncology service, close collaboration with a bone marrow transplant unit as well as an infectious disease unit and an adequate transfusion service.

## Induction chemotherapy

- Chemotherapy should be postponed until satisfactory material for all diagnostic tests has been harvested. Patients with excessive leucocytosis at presentation may require emergency leucapheresis prior to induction chemotherapy.
- Induction chemotherapy should include an anthracycline and cytosine arabinoside [II, A]. Patients failing to respond to one to two cycles of such treatment are considered refractory. In addition, APL induction chemotherapy should include all-*trans* retinoic acid (ATRA) [III, A].

## Consolidation therapy

- Patients entering clinical and haematological remission should receive one to several cycles of post-remission therapy [III, A]. There is no consensus on a single preferred post-remission treatment strategy. Patients with good risk features as defined above should receive chemotherapy only, preferably including high-dose cytarabine. 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 their family may qualify for allogeneic transplant with an unrelated matched donor [III, A]. 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 [III, A].

## Therapy of relapsed or refractory patients

- Patients in second or subsequent remission may qualify for allogeneic transplantation with an unrelated 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 leukaemic blast persistence. The usual requirements of AML remission are a normal cellularity of the bone marrow, morphologically normal haematopoiesis and blast levels <5% at evaluation of bone marrow smears [B].

## Follow-up

- Patients are followed clinically with haematological examination to detect early relapse. Serial bone marrow examination is of uncertain value in remission patients without any clinical or haematological 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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4. Zittoun RA, Mandelli F, Willemze R et al. Autologous or allogeneic bone marrow transplantation compared with intensive chemotherapy in acute myelogenous leukemia. *N Engl J Med* 1995; 332: 217–223.

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