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# ACUTE MYELOID LEUKEMIA

## *Epidemiology and pathogenesis*

Acute myeloid leukemia is a haematologicalneoplasm caused by the proliferation of immature cells, called blasts, in the bone marrow. These cells can be detected also in the peripheral blood, they can either infiltrate organs and tissues such as liver (epatomegaly), spleen (splenomegaly), lymphnodes (lymphoadenopathy), skin (purplish skin nodules) and the central nervous system (confusion, headache, neurological disorders). This leukemia is rare and accounts for approximately 3% of all malignancies and 25% of all forms of leukemia. It is more common in the older people, usually in the sixth decade of life. The onset is "acute", it occurs within a few days or weeks with symptoms such as fever, infections, fatigue or bleeding events.

## *Signs and Symptoms*

In acute myeloid leukemia, blasts proliferate and accumulate in the bone marrow, thus preventing the normal maturation of other cells: white and red blood cells and platelets. The white blood cells' decrease (leukopenia), characterized by neutrophils' decrease (neutropenia) is responsible for infections (eg. pharyngitis, cystitis, pneumonia and other). The red blood cells and hemoglobindecrease (anemia) causes paleness, fatigue and shortness of breath. Finally, the plateletdecrease (thrombocytopenia) is associated to an increased risk of bleeding, and variable manifestations at the skin (petechiae), mucous membranes (gingivorrhagia, epistaxis), urinary tract (hematuria), genitals (metrorrhagia), and at the bowel (melena).

## *Diagnosis*

The World Health Organizationclassification of myeloid malignancies (2016) listed different type of acute myeloid leukemia. The classification considers the following clinical parameters: the presence of ≥20% of blasts and DNA alterationsto diagnose disease.Large portions of genetic material can be altered, and which can be identified with cytogenetic analyses. In other case, smaller proportion of genetic alterations can be identified with molecular analyses. Indeed,it is typical to detect DNA damage in this neoplasm. These DNA alterations are extremely important because they allow to classify acute myeloid leukemia with different prognosis and then choose the most appropriate treatment for individual patient. At diagnosis, therefore bone marrow morphology, cytogenetic and molecular analysis (PCR or FISH) is performed. In Varese, some patients are also studied with massive sequencing by applying Next Genaration Sequencing (NGS) techniques.

## *Prognosis*

The acute myeloid leukemiaprognosis depends on patient-related factors (e.g age, comorbidities, ..)and disease-related factors (e.gde novo or secondary to other hematological diseases, previous chemotherapy or radiotherapy, …) and on the presence of specific cytogenetic and molecular mutations.

*Treatment*

Treatment choices are personalized and based on multiple factors. Patients fitting to an intensive treatmentcan be initiated to chemotherapy course including one induction cycle followed by consolidation cycles. The aim of induction cycle is to reset the blasts in the bone marrow, the purpose of the following cycles is to “consolidate” the response and todelete the minimal residual disease. All chemotherapy cycles include an inpatient hospitalization. Transfusion support is added in case of severe anemia or thrombocytopenia, furthermore anti-infective therapy (bacterial or fungal) is crucial.

In specific cases, this induction and consolidation chemotherapy can be associated with a non-chemotherapy treatment with molecular target (target) therapies. These therapies are directed against the altered functions, which have been triggered by molecular abnormalities or a therapy with monoclonal antibody.

If the patient with acute myeloid leukemia has higher risk diagnosis, allogenic hematopoietic stem cell transplantation is carried out after the achievement of complete morphological and genetic remission. The stem cell donor can be a brother/sister, or a donor registered in the international bone marrow donor register.

Some patients, however, cannot fit to an intensive chemotherapy. In those cases, the use of a non-intensive chemotherapy is appropriate: this is mostly subcutaneous hypomethylating drugs in combination with oral bcl2-inhibitor. These treatments are mostly managed in the outpatients clinic.

The choice about treatment course in leukemia patients is in agreement with the most recently published national (Italian Society of Hematology – SIE and Italian Bone Marrow Transplant Group - GITMO) and international guidelines (European Leukemia Net - ELN 2017; European Society for Medical Oncology - ESMO 2020; American Society of Hematology 2020; The National Comprehensive Cancer Network - NCCN 2021). Especially in recent years, research has made it possible to make many advances in the treatment of acute myeloid leukemia and several studies with experimental drugs are currently underway. For more information about the hematologic trials available in Varese, please visit the section “Trial Unit” of the Institutional website (https://www.asst-settelaghi.it/ematologia).