NCCN and ESMO guidelines For the diagnosis and management of AML

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Both the NCCN and ESMO guidelines recommend including the following tests in the diagnostic work-up for AML:

- Complete blood count (CBC) with manual differential and routine chemistry profile (including liver function tests, serum creatinine, lactate dehydrogenase [LDH], and uric acid).
- Coagulation profile – Prothrombin time (PT), partial thromboplastin time (PTT), fibrinogen).
- Bone marrow aspiration and biopsy, including classical cytogenetics, Immunophenotyping, and molecular testing for c-KIT, FLT3-ITD, NPM1, and CEBPA.
- HLA typing of patient and family.
- Assessment of cardiac risk factors (by echocardiogram or multi-gated acquisition [MUGA] scan).

ESMO guidelines include the following additional tests to the diagnostic workup for all patients:

- Imaging studies, including dental survey and computed tomography (CT) scan of the chest and abdomen, or chest x-ray and abdominal ultrasound.
- Sperm preservation in men (if desired by patient).
- Pregnancy test in women.

The NCCN further recommends the following tests if neurologic symptoms are present:

- CT of brain without contrast, if CNS hemorrhage suspected.
- Brain magnetic resonance imaging (MRI) with contrast, if leukemic meningitis suspected
- Positron emission tomography (PET)/CT, if clinical suspicion for extramedullary disease
- Lumbar puncture

Risk stratification of AML

Risk	Cyto	Molecular
Favorable	T (8,21) t (15;17) t (16;16) inv (16)	CN AML with NPM1 positive while FLT3 ITD negative Isolated biallelic CEBPA mutation
Intermediate	CN(i.e.: Normal karyotype "NK") +8 alone t(9;11) Other non-defined as favorable or unfavorable	By ELN further classification into int I and int II
Unfavorable	Complex (≥3) Monosomal karyotype (the presence of ≥2 autosomal monosomies or a single autosomal monosomy associated with at least one structural abnormality.) t(9;22) 11q23 rather than t(9;11) t(6;9) Inv3, t(3;3) 5q, 7q	CN AML with FLT3 ITD

Both the NCCN and the ESMO guidelines are in agreement with the following general recommendations for treatment:

- Treatment should be given only in specialized medical centers.
- Possible curative treatments include induction chemotherapy (incorporating an anthracycline and cytarabine); post-remission (consolidation) therapy; and, in intermediate to high-risk patients, possible allogeneic stem cell transplantation
- All-trans retinoic acid (ATRA) should be started immediately if APL is suspected, and combined with anthracycline-based chemotherapy once the diagnosis of APL is confirmed
- Among the NCCN guidelines recommendations is that patients with poor performance status, significant comorbities, and/or advanced age (i.e. some patients ≥ 60 years old and most patients ≥ 70 years old) should receive low-intensity therapy or supportive care if a clinical trial is not available.

Supportive Care

The NCCN guidelines recommend that all patients receive supportive care that includes the following:

- Use of leukodepleted, irradiated blood products
- Tumor lysis prophylaxis — not all AML patients are at high risk for tumor lysis syndrome (TLS).
- Growth factors for post-remission therapy.
- Use and choice of antibiotics for prophylaxis.

For individuals receiving treatment for APL, the supportive care recommendations also include the following:

- Aggressive transfusion support with platelets, fresh frozen plasma (FFP), and cryoprecipitate.
- Close monitoring for possible APL differentiation syndrome.
- Prophylaxis with prednisone for individuals receiving ATRA plus arsenic trioxide
- In patients receiving arsenic trioxide, monitoring with serial electrocardiograms.

The NCCN recommends that the following not be used in APL patients:

- Leukapheresis, except in life-threatening cases with leukostasis that is unresponsive to other treatment
- Myeloid growth factors