Acute Myeloid Leukemia Molecular Genetic Testing

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Acute myeloid leukemias (AMLs) are a heterogeneous group of disorders characterized by the clonal expansion of myeloid precursors in the peripheral blood, bone marrow, and/or other tissues, which results in impaired hematopoiesis and bone marrow failure.[1,2,3,4] AML is the most common acute leukemia in adults (~80% of leukemia cases) and accounts for the largest number of annual deaths from leukemia in the United States.[2,4] Gene alterations, along with translocations and inversions, carry prognostic importance in AML. In addition to large chromosomal rearrangements, molecular changes have also been implicated in the development of AML. A comprehensive evaluation of several molecular markers, including *FLT3*, *NPM1*, *IDH1*, and *IDH2*, is important for risk assessment and prognostication in certain patients with AML, and may guide treatment decisions.[2]

For more information on ARUP's massively parallel sequencing (also referred to as next generation sequencing) testing for AML, refer to the Acute Myeloid Leukemia Mutation Panel by Next Generation Sequencing and Rapid Acute Myeloid Leukemia Targeted Therapy Mutation Panel Test Fact Sheets.

Testing Strategy

At diagnosis, the minimum AML workup includes a bone marrow aspirate for morphology, flow cytometric immunophenotyping, cytogenetics (eg, karyotyping and fluorescence in situ hybridization [FISH]), and appropriate molecular genetic testing.[1,2,3]

Disease Overview

Incidence

>20,0000 cases/year in the U.S.[4]

Age of Onset

Median is 67 years[2]

Symptoms

- Symptoms resulting from thrombocytopenia, neutropenia, and anemia due to the accumulation of blasts in the marrow[2]
- Morphologic hallmark: excessive accumulation of blasts (typically >20%) and other defined immature cells which affect one or more myeloid lineage[2]

Test Interpretation

For more detailed information on the prognostic significance of molecular markers in AML, see the ARUP Consult Acute Myeloid Leukemia topic.

Featured ARUP Testing

Detect and quantitate gene alterations/translocations/ inversions. Use for minimal residual disease (MRD) and relapse risk monitoring.

CBFB-MYH11 inv(16) Detection, Quantitative 2011114

Method: Quantitative Reverse Transcription Polymerase Chain Reaction

NPM1 Mutation Detection by RT-PCR, Quantitative 3000066

Method: Quantitative Reverse Transcription Polymerase Chain Reaction

PML-RARA Detection by RT-PCR, Quantitative (Test on Referral as of 1/17/2023) 2002871

Method: Reverse Transcription Polymerase Chain Reaction

RUNX1-RUNX1T1 (AML1-ETO) t(8;21) Detection, Quantitative 2010138

Method: Reverse Transcription Polymerase Chain Reaction

Use for diagnosis, prognosis, and management. Not intended for MRD monitoring.

FLT3 ITD and TKD Mutation Detection 3001161

Method: Capillary Electrophoresis

IDH1 and IDH2 Mutation Analysis, exon 4 2006444

Method: Polymerase Chain Reaction/Sequencing

Sensitivity/Specificity

Gene	Methodology	Analytical Sensitivity	Analytical Specificity (%)
FLT3 ITD and TKD	PCR/CE	Signal ratio of 0.05 for ITD and 0.05 for TKD D835	100
IDH1 and *IDH2*	PCR/sequencing	40% mutated cells	100
NPM1	Quantitative reverse transcription PCR	1:100,000	100
CBFB-MYH11[a]	Quantitative reverse transcription PCR	1:10,000	100
PML-RARA[a]	Quantitative reverse transcription PCR	1:10,000	85
RUNX1-RUNX1T1[a]	Quantitative reverse transcription PCR	1:100,000	100

[a]These fusions can initially be screened by FISH but are also useful in monitoring for MRD.

CE, capillary electrophoresis; PCR, polymerase chain reaction

Limitations

- Variants outside the targeted regions or below the limit of detection will not be identified.
- Results must always be interpreted within the patient's clinical context and in conjunction with other relevant data and should not be used alone for a diagnosis of malignancy.

References

1. Arber DA, Borowitz MJ, Cessna M, et al. Initial diagnostic workup of acute leukemia: guideline from the College of American Pathologists and the American Society of Hematology. *Arch Pathol Lab Med*. 2017;141(10):1342-1393.

2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Acute myeloid leukemia. Version 3.2020. Last update Dec 2019; accessed Sep 2020.

3. Weinberg OK, Sohani AR, Bhargava P, et al. Diagnostic work-up of acute myeloid leukemia. *Am J Hematol*. 2017;92(3):317-321.

4. De Kouchkovsky I, Abdul-Hay M. Acute myeloid leukemia: a comprehensive review and 2016 update. *Blood Cancer J*. 2016;6(7):e441.

5. Swerdlow S, Campo E, Jaffe E, et al. *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues.* 4th ed. International Agency for Research on Cancer; 2017.

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