MAYO CLINIC LABORATORIES

Test Definition: NPMFM

Nucleophosmin (NPM1) Mutation Analysis, Bone Marrow

Overview

Useful For

Providing information for prognosis in patients with newly diagnosed acute myeloid leukemia using bone marrow specimens

Monitoring measurable residual disease.

Method Name

Quantitative Reverse Transcription-Polymerase Chain Reaction (RT-PCR)

NY State Available

No

Specimen

Specimen Type

Bone Marrow

Shipping Instructions

Specimen must arrive within 72 hours of collection. Collect and package specimen as close to shipping time as possible. Specimens greater than 3 days old at the time of receipt will be considered unacceptable.

Necessary Information

The following information is required:

1. Pertinent clinical history including if the patient has a diagnosis of chronic myeloid leukemia or other *BCR*::*ABL*1-positive neoplasm
2. Date of collection

Specimen Required

Container/Tube:

Preferred: Lavender top (EDTA)

Specimen Volume: 3 mL

Collection Instructions:

1. Invert several times to mix bone marrow.
2. Send bone marrow specimen in original tube. **Do not aliquot.**
3. Label specimen as bone marrow.

Forms

Hematopathology Patient Information (T676)

Specimen Minimum Volume

1 mL

Reject Due To

Gross hemolysis	Reject
Moderately to severely clotted	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Bone Marrow	Refrigerated (preferred)	72 hours	
	Ambient	72 hours	

Clinical & Interpretive

Clinical Information

Acute myeloid leukemia (AML) is a heterogeneous disease of the blood and bone marrow, characterized by clonal expansion of hematopoietic stem and progenitor cells with impaired differentiation capacity, leading to bone marrow failure. Nucleophosmin *(NPM1)*-mutated AML represents a distinct entity in the World Health Organization classification. *NPM1* mutation occurs in 20% to 30% of AML cases. Most of these patients have a normal karyotype. Detection of an *NPM1* mutation without coexisting *FLT3*-ITD (FMS-like tyrosine kinase-3 internal tandem duplication) suggests a more favorable prognosis. More than 50 different heterozygous mutations have been identified in *NPM1* in exon 12. Three mutation types, A, B, and D, account for about 95% of the *NPM1* mutations. *NPM1* mutation detection has been utilized in monitoring measurable residual disease.

Reference Values

An interpretive report will be provided.

Interpretation

A nucleophosmin *(NPM1)* gene mutation occurs in 20% to 30% of acute myeloid leukemia (AML) cases. AML with *NPM1* mutation is a subtype of AML classification. Detection of an *NPM1* mutation with absence of *FLT3*-ITD (FMS-like tyrosine kinase-3 internal tandem duplication) is associated with better outcomes, increased complete remission, and improved overall survival in AML. Concurrent *NPM1* and *FLT3*-ITD mutations confer intermediate risk in AML.

Three mutation types, A, B, and D, account for about 95% of the *NPM1* mutations in AML. This RNA-based quantitative test detects the transcripts of type A, B, and D mutations and provides a useful target for measurable residual disease (MRD) monitoring.

The continued presence of *NPM1* mutant transcripts is associated with a higher chance of relapse than those with non-detectable *NPM1* mutant transcripts. MRD status prior to allogeneic hematopoietic stem cell transplant has been shown to be a good predictor of outcome.

Cautions

Because of the design of this assay, a very small number of *NPM1* alterations at diagnosis may not be detected by the more targeted quantitative polymerase chain reaction component.

Clinical Reference

1. Heath EM, Chan SM, Minden MD, Murphy T, Shlush LI, Schimmer AD. Biological and clinical consequences of *NPM1* mutations in AML. Leukemia. 2017;31(4):798-807
2. Falini B, Sciabolacci S, Falini L, Brunetti L, Martelli MP. Diagnostic and therapeutic pitfalls in NPM1-mutated AML: notes from the field. Leukemia. 2021;35(11):3113-3126
3. Hindley A, Catherwood MA, McMullin MF, Mills KI. Significance of NPM1 Gene Mutations in AML. Int J Mol Sci. 2021;22(18):10040
4. Khoury JD, Solary E, Abla O, et al. The 5th edition of the World Health Organization classification of haematolymphoid tumours: myeloid and histiocytic/dendritic neoplasms. Leukemia. 2022;36(7):1703-1719

Performance

Method Description

The assay is performed using an automated platform, GeneXpert (Cepheid). The bone marrow sample is processed, added to an individual sample cartridge, and loaded onto the GeneXpert machine. It quantifies mutant *NPM1* messenger RNA (mRNA) transcript types A, B, and D in exon 12 and reports the percent ratio of mutant *NPM1* to *ABL1* endogenous control mRNA transcript.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

1 to 8 days

Specimen Retention Time

2 weeks

Performing Laboratory Location

Mayo Clinic Jacksonville Clinical Lab

Fees & Codes

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Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

81310

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
NPMFM	NPM1 Mutation Analysis, BM	75034-9

Result ID	Test Result Name	Result LOINC® Value
620655	Interpretation	59465-5
620707	Signing Pathologist	19139-5
623218	Indication for Testing	42349-1
623219	Specimen	31208-2
623281	Source	31208-2
623220	Sample ID	80398-1
623221	Result	82939-0
623222	Method Summary	85069-3
623223	Disclaimer	62364-5