

Nucleophosmin (NPM1) Mutation Analysis, Bone Marrow

# Overview

#### **Useful For**

Detection of nucleophosmin (*NPM1*) mutation provides information for prognosis in patients with newly diagnosed acute myeloid leukemia. *NPM1* mutation with absence of FLT3-ITD (FMS-like tyrosine kinase-3 internal tandem duplication) is associated with a better prognosis. This RNA based quantitative test detects about 95% of *NPM1* mutations and can be used for 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)



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# **Specimen Minimum Volume**

1 mL

# Reject Due To

Gross	Reject
hemolysis	
Moderately to	Reject
severely	
clotted	

# 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

Nucleophosmin (*NPM1*) 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 the type A, B, and D mutations and provides a useful target for measurable residual disease (MRD) monitoring.



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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). Bone marrow sample is processed, added to an individual sample cartridge, and loaded onto the GeneXpert machine. It quantifies mutant *NPM1* 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 <u>Test Prices</u> for detailed fee information.
- Clients without access to Test Prices can contact <u>Customer Service</u> 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<sup>®</sup> Information

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

Result ID	Test Result Name	Result LOINC <sup>®</sup> Value
620655	Final Diagnosis:	59465-5
620707	Signing Pathologist	19139-5