MAYO CLINIC LABORATORIES

# Test Definition: NPMFM

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)

### 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 | Ambient | 72 hours | |
| | Refrigerated (preferred) | 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 minimal 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.

The continued presence of *NPM1* mutant transcripts is associated with a higher chance of relapse than those with non-detectable *NPM1* mutant transcripts. Minimal residual disease (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

Jacksonville

## Fees & Codes

## 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 | Final Diagnosis: | 59465-5 |
| 620707 | Signing Pathologist | 19139-5 |