

## Overview

### Useful For

Evaluation of known or suspected hematologic neoplasms, specifically of myeloid origin (eg, acute myeloid leukemia, myelodysplastic syndrome, myeloproliferative neoplasm, myelodysplastic/myeloproliferative neoplasm, unexplained cytopenias) at the time of diagnosis or possibly disease relapse

Aiding in determining diagnostic classification

Providing prognostic or therapeutic information for helping guide clinical management

Evaluating patients with suspected VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome

Determining the presence of new clinically important gene mutation changes at relapse

### Genetics Test Information

This test includes next-generation sequencing to evaluate for the following 47 genes and select intronic regions:

*ANKRD26, ASXL1, BCOR, BCORL1, BRAF, CALR, CBL, CEBPA, CSF3R, DDX41, DNMT3A, ELANE, ETNK1, ETV6, EZH2, FLT3, GATA1, GATA2, IDH1, IDH2, JAK2, KDM6A, KIT, KRAS, MPL, NF1, NPM1, NRAS, PHF6, PPM1D, PTPN11, RAD21, RUNX1, SETBP1, SH2B3, SF3B1, SMC3, SRSF2, STAG2, STAT3, TERT, TET2, TP53, U2AF1, UBA1, WT1, and ZRSR2.*

For a list of genes and exons targeted by this test see [Targeted Genes Interrogated by Myeloid Neoplasms, Comprehensive OncoHeme Next-Generation Sequencing](#).

### Testing Algorithm

For more information see:

- [Acute Leukemias of Ambiguous Lineage Testing Algorithm](#)
- [Acute Myeloid Leukemia: Testing Algorithm](#)
- [Acute Myeloid Leukemia: Relapsed with Previous Remission Algorithm](#)
- [Myeloproliferative Neoplasm: A Diagnostic Approach to Bone Marrow Evaluation](#)
- [Mast Cell Disorder: Diagnostic Algorithm, Bone Marrow](#)

### Special Instructions

- [Myeloproliferative Neoplasm: A Diagnostic Approach to Bone Marrow Evaluation](#)
- [Hematopathology Patient Information](#)
- [Acute Leukemias of Ambiguous Lineage Testing Algorithm](#)
- [Acute Myeloid Leukemia: Testing Algorithm](#)
- [Acute Myeloid Leukemia: Relapsed with Previous Remission Algorithm](#)
- [Mast Cell Disorder: Diagnostic Algorithm, Bone Marrow](#)
- [Targeted Genes Interrogated by Myeloid Neoplasms, Comprehensive OncoHeme Next-Generation Sequencing](#)

**Highlights**

Next-generation sequencing detection of somatic gene mutations, including type, pattern, and distribution, has diagnostic, prognostic, and potential therapeutic implications for patients with hematologic cancers of myeloid origin.

**Method Name**

Next-Generation Sequencing (NGS)

**NY State Available**

Yes

**Specimen****Specimen Type**

Varies

**Shipping Instructions**

**Bone marrow and whole blood specimens must arrive within 14 days of collection.**

**Necessary Information**

**The following information is required:**

1. Clinical diagnosis
2. Pertinent clinical history, including disease phase (diagnostic, remission, relapse/refractory) and therapy status (especially if patient has received a hematopoietic stem cell transplant).
3. Clinical or morphologic suspicion
4. Date of collection
5. Specimen source

**Specimen Required**

**Submit only 1 of the following specimens:**

**Preferred**

**Specimen Type:** Bone marrow aspirate

**Container/Tube:**

**Preferred:** Lavender top (EDTA) or yellow top (ACD)

**Acceptable:** Green top (sodium heparin)

**Specimen Volume:** 2 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.

**Specimen Stability Information:** Ambient (preferred) 14 days/Refrigerate 14 days

**Additional Information:** To ensure minimum volume and concentration of DNA is met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.

**Acceptable:**

**Specimen Type:** Whole blood

**Container/Tube:**

**Preferred:** Lavender top (EDTA) or yellow top (ACD)

**Acceptable:** Green top (sodium heparin)

**Specimen Volume:** 3 mL

**Collection Instructions:**

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

**Specimen Stability Information:** Ambient (preferred) 14 days/Refrigerate 14 days

**Additional Information:** To ensure minimum volume and concentration of DNA is met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.

**Specimen Type:** Extracted DNA from blood or bone marrow

**Container/Tube:** 1.5- to 2-mL tube

**Specimen Volume:** Entire specimen

**Collection Instructions:**

1. DNA must be extracted within 14 days after collection.
2. Label specimen as extracted DNA and source of specimen.
3. Provide volume and concentration of the DNA.

**Specimen Stability Information:** Frozen (preferred)/Refrigerate/Ambient

**Additional Information:** DNA must be extracted in a CLIA-certified laboratory or equivalent and must be extracted from a specimen type listed as acceptable for this test (including applicable anticoagulants). We cannot guarantee that all extraction methods are compatible with this test. If testing fails, one repeat will be attempted, and if unsuccessful, the test will be reported as failed and a charge will be applied.

**Forms**

1. [Hematopathology Patient Information](#) (T676)
2. If not ordering electronically, complete, print, and send a [Hematopathology/Cytogenetics Test Request](#) (T726) with the specimen.

**Specimen Minimum Volume**

Blood, Bone marrow: 1 mL

Extracted DNA: 100 mcL at 20 ng/mcL concentration

**Reject Due To**

Gross hemolysis	Reject
Gross lipemia	OK
Bone marrow biopsies Slides Paraffin shavings or frozen tissues Paraffin-embedded tissues Paraffin-embedded bone marrow aspirates Moderately to severely clotted	Reject

### Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies	14 days	

### Clinical & Interpretive

#### Clinical Information

Next-generation sequencing is a comprehensive molecular diagnostic methodology that can interrogate multiple regions of genomic tumor DNA in a single assay. Many hematologic neoplasms are characterized by morphologic or phenotypic similarities but can have characteristic somatic mutations in many genes that enable more specific categorization. In addition, many myeloid neoplasms lack a clonal cytogenetic finding at diagnosis (normal karyotype) but can be diagnosed or confirmed and classified according to the gene mutation profile. Patients with unexplained cytopenias may harbor acquired genetic alterations in hematopoietic cells (clonal cytopenias of uncertain significance), which may carry risk of developing overt myeloid malignancies. The presence and pattern of gene mutations in known or suspected myeloid neoplasm can provide critical diagnostic, prognostic, and therapeutic information to help guide management for the patient's physician. Patients presenting with severe inflammatory features, often with cytopenias, may have VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome and can be identified by the presence of somatic *UBA1* gene mutation.

#### Reference Values

An interpretive report will be provided.

**Interpretation**

Detailed variant assessment and interpretive comments will be provided for all reportable genetic alterations.

If this test is ordered in the setting of erythrocytosis and suspicion of polycythemia vera, interpretation requires correlation with a concurrent or recent prior bone marrow evaluation.

**Cautions**

This test is a targeted next-generation sequencing (NGS) assay that encompasses 47 genes with variable full exon, partial region (including select intronic or noncoding regions), or hot spot coverage (depending on specific locus). Therefore, this test will not detect other genetic abnormalities in genes or regions outside the specified target areas. The test detects single base substitutions (ie, point mutations) as well as small insertion or deletion type events, but it does not detect gene rearrangements (ie, translocations), gene fusions, copy number alterations, or large scale (segmental chromosome region) deletions and complex changes.

This assay does not distinguish between somatic and germline alterations in analyzed gene regions, particularly with variant allele frequencies near 50% or 100%. If nucleotide alterations in genes associated with germline variant syndromes are present and there is a strong clinical suspicion or family history of malignant disease predisposition, additional genetic testing and appropriate counseling may be indicated. A low incidence of gene mutations associated with myeloid neoplasms can be detected in nonmalignant hematopoietic cells in individuals with advancing age (clonal hematopoiesis of indeterminate potential), and these may not be clearly distinguishable from tumor-associated mutations. Some apparent mutations classified as variants of uncertain significance may represent rare or low-frequency polymorphisms.

Prior treatment for hematologic malignancy could affect the results obtained in this assay. In particular, a prior allogeneic hematopoietic stem cell transplant may cause difficulties in resolving somatic or polymorphic alterations or in assigning variant calls correctly to donor and recipient fractions, if pertinent clinical or laboratory information (eg, chimerism engraftment status) is not provided.

Correlation with clinical, histopathologic, and additional laboratory findings is required for final interpretation of NGS results and is the responsibility of the managing physician.

**Clinical Reference**

1. National Comprehensive Cancer Network (NCCN). NCCN Guidelines: Acute Myeloid Leukemia. NCCN; Version 3.2024. Accessed November 27, 2024. Available at [www.nccn.org/guidelines/guidelines-detail?category=1&id=1411](http://www.nccn.org/guidelines/guidelines-detail?category=1&id=1411)
2. National Comprehensive Cancer Network (NCCN). NCCN Guidelines: Myeloproliferative Neoplasms. NCCN; Version 2.2024. Accessed November 27, 2024. Available at [www.nccn.org/guidelines/guidelines-detail?category=1&id=1477](http://www.nccn.org/guidelines/guidelines-detail?category=1&id=1477)
3. National Comprehensive Cancer Network (NCCN). NCCN Guidelines: Myelodysplastic Syndromes. NCCN; Version 1.2025. Accessed November 27, 2024. Available at [www.nccn.org/guidelines/guidelines-detail?category=1&id=1446](http://www.nccn.org/guidelines/guidelines-detail?category=1&id=1446)
4. He R, Chiou J, ChiouA, et al. Molecular markers demonstrate diagnostic and prognostic value in the evaluation of myelodysplastic syndromes in cytopenia patients. *Blood Cancer J.* 2022;12(1):12. doi:10.1038/s41408-022-00612-w
5. Malcovati L, Galli A, Travaglino E, et al. Clinical significance of somatic mutation in unexplained blood cytopenia. *Blood.* 2017;129(25):3371-3378. doi:10.1182/blood-2017-01-763425

6. DiNardo CD, Stein EM, de Botton S, et al. Durable remissions with ivosidenib in IDH1-mutated relapsed or refractory AML. *N Engl J Med.* 2018;378(25):2386-2398. doi:10.1056/NEJMoa1716984
7. Stein EM, DiNardo CD, Fathi AT, et al. Molecular remission and response patterns in patients with mutant-IDH2 acute myeloid leukemia treated with enasidenib. *Blood.* 2019;133(7):676-687. doi:10.1182/blood-2018-08-869008
8. Dohner H, Estey E, Grimwade D, et al. Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. *Blood.* 2017;129(4):424-447. doi:10.1182/blood-2016-08-733196
9. Smith CC. The growing landscape of FLT3 inhibition in AML. *Hematology Am Soc Hematol Educ Program.* 2019;2019(1):539-547. doi:10.1182/hematology.2019000058
10. Kennedy JA, Ebert BL. Clinical implications of genetic mutations in myelodysplastic syndrome. *J Clin Oncol.* 2017;35(9):968-974. doi:10.1200/JCO.2016.71.0806
11. Dauer N, Schlenk RF, Russell NH, Levis MJ. Targeting FLT3 mutations in AML: review of current knowledge and evidence. *Leukemia.* 2019;33(2):299-312. doi:10.1038/s41375-018-0357-9
12. Swerdlow SH, Campo E, Harris NL, et al. WHO Classification of Tumours of Hematopoietic and Lymphoid Tissues. 4th ed. IARC Press; 2017. Who Classification of Tumours. Vol 2
13. Beck DB, Ferrada KA, Sikora AK, et al. Somatic mutations in UBA1 and severe adult-onset autoinflammatory disease. *N Engl J Med.* 2020;383:2628-2638. doi:10.1056/NEJMoa2026834
14. Obiorah IE, Patel BA, Groarke EM, et al. Benign and malignant hematologic manifestations in patients with VEXAS syndrome due to somatic mutations in UBA1. *Blood Adv.* 2021;5:3203-3215. doi:10.1182/bloodadvances.2021004976

## Performance

### Method Description

Next-generation sequencing is performed for the presence of a mutation in targeted regions of 47 genes. For details regarding the targeted gene regions identified in this test see [Targeted Genes Interrogated by Myeloid Neoplasms, Comprehensive OncoHeme Next-Generation Sequencing](#). Extracted DNA from the clinical specimen is fragmented, adapter ligated, and a sequence library of fragments is prepared using a custom capture hybridization method. Individual patient samples are indexed ("bar-coded") for identification, and the library is sequenced on an Illumina platform. Sequence data are processed through a bioinformatics pipeline, and a variant call file is generated for final analysis and reporting.(Unpublished Mayo method)

Genes analyzed: ANKRD26, ASXL1, BCOR, BCORL1, BRAF, CALR, CBL, CEBPA, CSF3R, DDX41, DNMT3A, ELANE, ETNK1, ETV6, EZH2, FLT3, GATA1, GATA2, IDH1, IDH2, JAK2, KDM6A, KIT, KRAS, MPL, NF1, NPM1, NRAS, PHF6, PPM1D, PTPN11, RAD21, RUNX1, SETBP1, SH2B3, SF3B1, SMC3, SRSF2, STAG2, STAT3, TERT, TET2, TP53, U2AF1, UBA1, WT1, and ZRSR2

### PDF Report

No

### Day(s) Performed

Monday through Friday

### Report Available

---

16 to 21 days

**Specimen Retention Time**

Whole blood, bone marrow: 2 weeks; Extracted DNA: 3 months

**Performing Laboratory Location**

Mayo Clinic Laboratories - Rochester Main Campus

**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**

81450

**LOINC® Information**

Test ID	Test Order Name	Order LOINC® Value
NGSHM	Myeloid Neoplasms, NGS, V	99961-5

Result ID	Test Result Name	Result LOINC® Value
MP024	Specimen Type	31208-2
NGSD	Indication for Test	42349-1
37276	Pathogenic Mutations Detected	82939-0
37282	Clinical Trials	82786-5
37277	Variants of Unknown Significance	93367-1
37278	Additional Notes	48767-8
37279	Method Summary	85069-3
37420	Disclaimer	62364-5
37280	OncoHeme Panel Gene list	36908-2
37287	Reviewed By:	18771-6
37283	Interpretation	69047-9
601696	NGSHM Result	No LOINC Needed