

Overview

Useful For

Evaluating 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

As an aid in determining diagnostic classification using bone marrow specimens

Providing prognostic or therapeutic information for guiding clinical management

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 45 genes for mutation detection: *ABL1*, *ASXL1*, *ANKRD26*, *BRAF*, *CBL*, *CSF3R*, *DDX41*, *DNMT3A*, *FLT3*, *GATA2*, *HRAS*, *IDH1*, *IDH2*, *JAK2*, *KIT*, *KRAS*, *WT1*, *MPL*, *MYD88*, *NPM1*, *NRAS*, *PPM1D*, *PTPN11*, *SETBP1*, *SF3B1*, *SMC1A*, *SMC3*, *SRSF2*, *U2AF1*, *BCOR*, *CALR*, *CEBPA*, *ETV6*, *EZH2*, *IKZF1*, *NF1*, *PHF6*, *PRPF8*, *RB1*, *RUNX1*, *SH2B3*, *STAG2*, *TET2*, *TP53*, and *ZRSR2*.

Additionally, 35 fusion driver genes are evaluated, allowing sequencing of over 700 unique fusion transcripts: *ABL1*, *ABL2*, *BCL2*, *BRAF*, *CCND1*, *CREBBP*, *EGFR*, *ETV6*, *FGFR1*, *FGFR2*, *FUS*, *HMGA2*, *JAK2*, *KAT6A (MOZ)*, *KAT6B*, *KMT2A*, *KMT2A PTDs*, *MECOM*, *MET*, *MLLT10*, *MRTFA (MKL1)*, *MYBL1*, *MYH11*, *NTRK2*, *NTRK3*, *NUP214*, *NUP98*, *PAX5*, *PDGFRA*, *PDGFRB*, *RARA*, *RUNX1*, *TCF3*, *TFE3*, and *NZF384*

Method Name

Next-Generation Sequencing (NGS)

NY State Available

No

Specimen

Specimen Type

Bone Marrow

Necessary Information

A reason for testing and a bone marrow pathology report are requested with each specimen. The laboratory will not reject testing if this information is not provided; however, appropriate testing and/or interpretation may be compromised or delayed in some instances. If not provided, an appropriate indication for testing may be entered by Mayo Clinic Laboratories.

Specimen Required

Container/Tube:

Preferred: Lavender top (EDTA)

Acceptable: Yellow top (ACD-B)

Specimen Volume: 4 mL

Collection Instructions:

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

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

This next-generation sequencing test provides a comprehensive genomic profile, including gene mutations and fusions, for myeloid neoplasms in a single assay. Many hematologic neoplasms are characterized by morphologic or phenotypic similarities but can have characteristic somatic mutations in many genes or a specific gene fusion that enables specific disease classification. In addition, many myeloid neoplasms lack a clonal cytogenetic finding at diagnosis (normal karyotype) but can be diagnosed, 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. Detection of a specific gene fusion or gene mutations in known or suspected myeloid neoplasm can provide critical diagnostic, prognostic, and therapeutic information to help guide management for the patient's health care provider.

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 45 genes with variable full exon, partial region (including select intronic or noncoding regions), or hot spot coverage (depending on specific locus) and 35 targeted fusion driver genes. 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), small insertions or deletions as well as gene fusions, but it does not detect copy number alterations or large scale (segmental chromosome region) deletions and complex changes.

This assay does not distinguish between somatic mutations 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); 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 alterations (ie, 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 29, 2024. Available at 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 29, 2024. Available at 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 29, 2024. Available at www.nccn.org/guidelines/guidelines-detail?category=1&id=1446
4. He R, Chiou J, Chiou A, 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. 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

7. 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
8. 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
9. Daver N, Schlenk RF, Russell NH, Levis MJ. Targeting FLT3 mutations in AML: review of current knowledge and evidence. *Leukemia*. 2019;33(2):299-312
10. Khoury JD, Solary E, Abla O, et al. The 5th ed of the World Health Organization classification of haematolymphoid tumors: myeloid and histiocytic/dendritic neoplasms. *Leukemia*. 2022;36(7):1703-1719

Performance

Method Description

This assay includes DNA-based sequencing for 45 genes, including the hotspots of 28 genes and 17 full genes, and RNA-based sequencing for 35 fusion driver genes, which allows detection of over 700 unique fusions.

DNA and RNA are extracted from bone marrow samples. After library preparation using Ion AmpliSeq technology, the samples are subjected to Ion Torrent next-generation sequencing (NGS) with post-sequencing analysis on an NGS instrument, Genexus. NGS bioinformatics is performed using the software provided by Thermo Fisher. Genomic alterations are called according to the Genome Reference Consortium Human Build 37 (GRCh37), hg19, described using standard nomenclature, and interpreted using the current standards and guidelines recommended by Association of Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.

Test validation has shown greater than 99% accuracy, 100% (intra- and interassay) reproducibility, and a sensitivity of detection of 5% variant allele fraction with a minimum depth coverage of 250X for single base substitutions, deletion-insertion events (including FLT3-ITD), and gene fusions for the targeted gene mutations and fusions included in the validation design. (Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

5 to 14 days

Specimen Retention Time

Bone marrow: 2 weeks; DNA/RNA: 1 year

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

81455

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
NGHMM	Comprehensive NGS Myeloid, BM	99961-5

Result ID	Test Result Name	Result LOINC® Value
620042	Specimen Type	31208-2
620043	Indication for Test	42349-1
620054	Pathogenic Mutations Detected	82939-0
620045	Interpretation	59465-5
620046	Clinical Trials	82786-5
620047	Variants of Unknown Significance	93367-1
620048	Additional Notes	48767-8
620049	Method Summary	85069-3
620050	Disclaimer	62364-5
620055	Panel Gene List	36908-2
620051	Signing Pathologist	18771-6