Overview

Useful For
Evaluation of multiple myeloma at the time of diagnosis, for prognostic and potential therapeutic indications

Identification of the presence of new, clinically important, gene alteration changes at relapse

Genetics Test Information
This test includes next-generation sequencing to evaluate for the following 61 genes and intronic regions: AKT1, AKT2, AKT3, AKT3-G, ATM, B2M, BIRC2, BIRC3, BRAF, CCND1, CD38, CDK4, CDK7, CDKN1B, CDKN2A, CDKN2A-G, CRBN, CUL4A, CUL4B, CXCR4, DIS3, DIS3-G, EGFR, FAM46C, FGFR3, FGFR3-G, GRB2, IDH1, IDH2, IDH3A, IFNGR2, IGF1R, IKZF1, IKZF3, IL6, IL6R, IRF4, JAK2, KDM6A, KDM6A-G, KRAS, MYC, MYD88, NFKB2, NR3C1, NRAS, NSD2, PIK3CA, PIK3CG, PIK3R1, PIK3R1-G, PIK3R2, PIM1, PIM2, PIM3, PSMA1, PSMB5, PSMB5-G, PSMD1, PSMG2, PTPN11, RB1, STAT3, TGFBR2, TLR4, TP53, TRAF3, and XBP1.

Highlights
Next-generation sequencing detection of somatic gene variations in multiple myeloma may have prognostic and potential therapeutic implications.

This test is appropriate for diagnosis and disease relapse.

Additional Tests

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
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<tbody>
<tr>
<td>CSNMM</td>
<td>NGSMM Pre-Analysis Cell Sorting, BM</td>
<td>No</td>
<td>Yes</td>
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Testing Algorithm
See Targeted Genes Interrogated by Multiple Myeloma Next-Generation Sequencing in Special Instructions for a list of the genes and exons targeted by this assay.

Special Instructions
- Hematopathology Patient Information
- Targeted Genes Interrogated by Multiple Myeloma Next-Generation Sequencing

Method Name
Next-Generation Sequencing (NGS)

NY State Available
Yes

Specimen

Specimen Type
Bone Marrow

Shipping Instructions
Ship samples Monday through Friday

**Necessary Information**

The following information is required:

1. Clinical diagnosis
2. Pertinent clinical history
3. Clinical or morphologic suspicion
4. Date of collection
5. Specimen source

**Specimen Required**

**Specimen Type:** Bone marrow aspirate

**Container/Tube:** Lavender top (EDTA) or yellow top (ACD)

**Specimen Volume:** 2 mL

**Collection Instructions:**

1. Invert several times to mix bone marrow.
2. Send specimen in original tube.
3. Label specimen as bone marrow.

4. **Fresh specimen is required for this test,** as testing is performed on sorted cells.

**Forms**

1. **Hematopathology Patient Information** (T676) in Special Instructions

2. If not ordering electronically, complete, print, and send a **Hematopathology/Cytogenetics Test Request** (T726) with the specimen.

**Specimen Minimum Volume**

1 mL

**Reject Due To**

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<tbody>
<tr>
<td>Gross hemolysis</td>
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<tr>
<td>Gross lipemia</td>
<td>OK</td>
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<tr>
<td>Other</td>
<td>Bone marrow biopsies Slides Paraffin shavings Frozen tissues Paraffin-embedded tissues Paraffin-embedded bone marrow aspirates Extracted DNA Bone marrow aspirate samples with &lt;15% plasma cells by cytologic differential count</td>
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Test Definition: NGSMM
NGS Multiple Myeloma

Specimen Stability Information

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<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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<tbody>
<tr>
<td>Bone Marrow</td>
<td>Ambient</td>
<td>4 days</td>
<td>PURPLE OR PINK TOP/EDTA</td>
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Clinical and Interpretive

Clinical Information

Multiple myeloma (MM) is a malignancy of bone marrow plasma cells with an annual incidence of 200,000 per annum. Comprehensive clinical, radiologic, and laboratory evaluation can initially stratify patients by disease phase and burden. Cytogenetic and FISH studies are important to help classify MM into standard, intermediate, and high risk groups. Advances in nontargeted therapies, including autologous bone marrow transplantation, have significantly improved the outcome of many patients; however, most patients with myeloma suffer relapse after initial treatment. Clinical next-generation sequencing (NGS) technology has enabled a deeper and more detailed evaluation of MM genetics. Testing allows for further risk categorization of the disease through the identification of additional abnormalities of prognostic and potentially therapeutic value. Application of targeted NGS-based analysis is a useful adjunct to the standard evaluation of MM patients at diagnosis and relapse. This test comprises a DNA-based multigene panel that includes preanalytic plasma cell enrichment, NGS, and detailed analysis resulted in a clinical report.

Reference Values

An interpretive report will be provided.

Interpretation

An interpretive report will be provided that includes the gene alterations identified, if present.

Cautions

This test is a targeted next-generation sequencing (NGS) panel assay that encompasses 61 genes and gene regions with variable full exon, partial region, or hot spot coverage (depending on specific locus). This test will, therefore, 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. It does not detect gene rearrangements (ie, translocations), gene fusions, copy number variants, or large scale (segmental chromosome region) deletions and complex changes.

This assay does not distinguish between somatic and germ line alterations in analyzed gene regions, particularly with variant allele frequencies (VAF) near 50% or 100%. If nucleotide alterations in genes associated with germ line 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. Variant calls detected between 5% and 10% VAF may indicate low-level (ie, subclonal) tumor populations, although the clinical significance of these findings may not be evident. Some apparent alterations classified as variants of undetermined significance (VUS) may represent rare or low frequency polymorphisms.

Prior treatment for hematologic malignancy could affect the results obtained in this assay. In particular, prior allogeneic hematopoietic stem cell transplant (HSCT) 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.
NGS analysis should not be attempted if the plasma cell percentage is below approximately 15% by cytologic differential count, as the risk of insufficient target cell population enrichment is more likely, leading to assay failure.

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

Clinical Reference


Performance

Method Description
See Targeted Genes Interrogated by Multiple Myeloma Next-Generation Sequencing in Special Instructions for details regarding the targeted gene regions identified by this test. Plasma cells are enriched by fluorescence activated cell sorting. 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 for identification and the library is sequenced on an Illumina platform. Sequence data is processed through a bioinformatics pipeline and a variant call file is generated for final analysis and reporting.(Unpublished Mayo method)

PDF Report
No

Day(s) and Time(s) Test Performed
Monday

Analytic Time
14 days

Maximum Laboratory Time
21 days

Specimen Retention Time
DNA 3 months

Performing Laboratory Location
Rochester

Fees and Codes
Test Definition: NGSMM
NGS Multiple Myeloma

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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
81455-Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA and RNA analysis when performed, 51 or greater genes (e.g., ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, RLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed.

LOINC® Information

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