

Overview

Useful For

Evaluating multiple myeloma at the time of diagnosis and at disease relapse or when changing clinical management to provide prognostic information and determine potential therapeutic implications

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CSPMM	NGPCM Pre-Analysis Cell Sorting, BM	No	No

Genetics Test Information

This test includes next-generation sequencing to evaluate the following 26 genes and select intronic regions: *BIRC3*, *BRAF*, *CCND1*, *CDKN2A*, *CRBN*, *CUL4A*, *CUL4B*, *CXCR4*, *DIS3*, *EGFR*, *IDH1*, *IDH2*, *IKZF1*, *IKZF3*, *KRAS*, *MYC*, *MYD88*, *NRAS*, *NSD2*, *PIK3CA*, *PIM1*, *STAT3*, *TENT5C*, *TP53*, *TRAF3*, and *XBP1*.

Testing Algorithm

See [Targeted Genes Interrogated by MayoComplete Plasma Cell Myeloma Next-Generation Sequencing](#) for a list of the genes and exons targeted by this assay.

Special Instructions

- [Hematopathology Patient Information](#)
- [Targeted Genes Interrogated by MayoComplete Plasma Cell Myeloma Next-Generation Sequencing](#)

Highlights

Next-generation sequencing detection of somatic gene variations in plasma cell myeloma may have prognostic and potential therapeutic implications. This test is appropriate for diagnosis and disease relapse.

Method Name

Next-Generation Sequencing (NGS)

NY State Available

Yes

Specimen

Specimen Type

Varies

Shipping Instructions

Bone marrow aspirate samples must arrive within 4 days of collection.

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Bone marrow aspirate

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

Specimen Volume: 2 mL

Collection Instructions:

1. Minimum plasma cell percentage is 5%.
2. Invert several times to mix bone marrow.
3. Send bone marrow specimen in original tube. **Do not aliquot.**
4. Label specimen as bone marrow.
5. **Fresh specimen is required for this test**, as testing is performed on sorted cells.

Specimen Stability Information: Ambient (preferred) 4 days/Refrigerate

Specimen Type: Paraffin-embedded bone marrow clot

Container/Tube: Paraffin block

Collection Instructions:

1. Send 1 slide stained with hematoxylin and eosin.
2. Minimum plasma cell percentage is 20%.
3. Required amount of tissue area is at least 25mm(2).
4. Tissue should be fixed in 10% neutral-buffered formalin. Other fixatives are not acceptable.
5. Decalcified specimens (eg, bone marrow core biopsies) are not acceptable.

Specimen Stability Information: Ambient

Specimen Type: Tissue slide; bone marrow clot

Slides: 10 unstained slides

Container/ Tube: Transport in plastic slide holders.

Collection Instructions:

1. Send 10 unstained, nonbaked slides with 5-micron thick sections of tissue and 1 slide stained with hematoxylin and eosin
2. Minimum amount of plasma cells is 20%
3. Required amount of tissue area is at least 25mm(2).
4. Tissue should be fixed in 10% neutral-buffered formalin. Other fixatives are not acceptable.
5. Decalcified specimens (eg, bone marrow core biopsies) are not acceptable.

Specimen Stability Information: Ambient

Forms

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

Specimen Minimum Volume

Bone marrow aspirate: 1 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK
Specimens that have been decalcified (all methods) Bone marrow core biopsies Paraffin shavings Frozen tissue Extracted DNA Moderately to severely clotted bone marrow aspirate	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical & Interpretive

Clinical Information

Multiple myeloma (MM) is a malignancy of bone marrow plasma cells with an annual global incidence of nearly 200,000. Comprehensive clinical, radiologic, and laboratory evaluation can initially stratify patients by disease phase and burden. Cytogenetic and fluorescence in situ hybridization 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 genetic 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, resulting in a clinical report.

Reference Values

An interpretive report will be provided.

Interpretation

Genomic variants detected by this test will be documented in a detailed laboratory-issued report. This report will contain information regarding the detected alterations and their associations with prognosis or possible therapeutic implications in plasma cell myeloma. The information in the clinical report may be used by the patient's clinician to help guide decisions concerning management. Final interpretation of next-generation sequencing results requires correlation with all relevant clinical, pathologic, and laboratory findings and is the responsibility of the managing clinician.

Cautions

This test is a targeted next-generation sequencing (NGS) panel assay that encompasses 26 genes with variable full exon, partial region (including select intronic or noncoding regions), or hot spot coverage (depending on specific genetic 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. This test is not configured to detect structural genomic rearrangements (ie, translocations), gene fusions, copy number alterations, or large-scale (segmental chromosome region) deletions and other complex genomic changes.

This assay does not distinguish between somatic and germline alterations in analyzed gene regions, particularly with variant allele frequencies near approximately 50% or 100%. If nucleotide alterations in genes associated with germline mutation 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. Some apparent mutations classified as variants of undetermined significance may represent rare or low population frequency polymorphisms.

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

NGS testing should not be pursued if the initial plasma cell percentage is below approximately 5% by cytologic differential count in the bone marrow aspirate, as the ability to obtain a sufficiently enriched target plasma cell population for evaluation is significantly less likely. Inadequate samples (eg, insufficient DNA quantity or quality) will preclude further testing and will be noted in the interpretive report.

Clinical Reference

1. Swerdlow S, Campo E, Harris NL, et al, eds: WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th ed. IARC Press; 2017. WHO Classification of Tumours, Vol 2
2. Onaindia A, Medeiros LJ, Patel KP. Clinical utility of recently identified diagnostic, prognostic, and predictive molecular biomarkers in mature B-cell neoplasms. *Mod Pathol*. 2017 Oct;30(10):1338-1366. doi: 10.1038/modpathol.2017.58
3. Walker BA, Mavrommatis K, Wardell CP, et al: Identification of novel mutational drivers reveals oncogene dependencies in multiple myeloma. *Blood*. 2018 Aug 9;132(6):587-597. doi: 10.1182/blood-2018-03-840132
4. Walker BA, Boyle EM, Wardell CP, et al: Mutational spectrum, copy number changes, and outcome: Results of a sequencing study of patients with newly diagnosed myeloma. *J Clin Oncol*. 2015 Nov 20;33(33):3911-20. doi: 10.1200/JCO.2014.59.1503
5. Kortuem KM, Braggio E, Bruins L, et al: Panel sequencing for clinically oriented variant screening and copy number detection in 142 untreated multiple myeloma patients. *Blood Cancer J*. 2016 Feb 26;6(2):e397. doi: 10.1038/bcj.2016.1
6. Jimenez C, Jara-Acevedo M, Corchete LA, et al: A next-generation sequencing strategy for evaluating the most

common genetic abnormalities in multiple myeloma. J Mol Diagn. 2017 Jan;19(1):99-106

7. Yellapantula V, Hultcrantz M, Rustad EH, et al: Comprehensive detection of recurring genomic abnormalities: a targeted sequencing approach for multiple myeloma. Blood Cancer J. 2019 Dec 11;9(12):101. doi: 10.1038/s41408-019-0264-y

8. Cutler SD, Knopf P, Campbell CJV, et al: DMG26 A targeted sequencing panel for mutation profiling to address gaps in the prognostication of multiple myeloma. J Mol Diagn. 2021 Dec;23(12):1699-1714

Performance

Method Description

This is a laboratory-developed target enriched next generation sequencing (NGS) panel. DNA is extracted from validated specimen sources including bone marrow aspirate and formalin-fixed paraffin embedded tissues (eg, bone marrow clot). Bone marrow aspirate specimens are enriched for plasma cells sorted by a flow cytometric cell selection method prior to DNA extraction. Library preparation for NGS is performed followed by probe hybridization and capture. Sequencing of the final sample library is performed on a NGS instrument. Following bioinformatic processing of the sequencing data, the sequencing results are interpreted to provide a final clinical report. Genomic alterations are called according to human genome reference build GRCh37 (hg19).(Unpublished Mayo method).

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

16 to 21 days

Specimen Retention Time

Bone marrow aspirate: 2 weeks; DNA: 3 months; FFPE tissue block: Unused portions of blocks will be returned to the client; Unstained slides: Not retained

Performing Laboratory Location

Rochester

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
NGPCM	Plasma Cell Myeloma, NGS, V	104241-5

Result ID	Test Result Name	Result LOINC® Value
MP074	Specimen Type	31208-2
MP075	Indication for Test	42349-1
618515	NGPCM Result	No LOINC Needed
618516	Pathogenic Mutations Detected	82939-0
618517	Interpretation	69047-9
618519	Variants of Unknown Significance	93367-1
618520	Additional Information	48767-8
618518	Clinical Trials	82786-5
618521	Method Summary	85069-3
618522	Disclaimer	62364-5
618523	Panel Gene List	36908-2
618524	Reviewed By	18771-6