MAYO CLINIC LABORATORIES

Test Definition: MRDMM

Multiple Myeloma Measurable Residual Disease (MRD), Flow Cytometry, Bone Marrow

Overview

Useful For
Detecting low level (measurable residual disease) myeloma cells after therapy

Highlights
This is a high-sensitivity flow cytometry test for detection of measurable (also known as minimal) residual myeloma cells, post treatment.

It uses adopted EuroFlow guidelines and Cytognos analysis software.

It has a sensitivity of 10(-5) or better, depending on the antigenic profile of abnormal plasma cells

Method Name
Immunophenotyping for Measurable Residual Disease (MRD)

NY State Available
Yes

Specimen

Specimen Type
Bone Marrow

Ordering Guidance
This test should be ordered on patients treated for multiple myeloma to confirm remission has been achieved, annual follow-up of those in remission, or in uncertain remission.

This test **should not be ordered** on known relapsing patients or at diagnosis. For these situations or if fluorescence in situ hybridization is requested, order either PCPRO / Plasma Cell DNA Content and Proliferation, Bone Marrow or MSMRT / Mayo Algorithmic Approach for Stratification of Myeloma and Risk-Adapted Therapy Report, Bone Marrow.

Shipping Instructions
It is recommended that specimens arrive within 2 days of collection. Collect and package specimen as close to shipping time as possible.

Necessary Information
1. Include patient's disease state (untreated, treated, monoclonal gammopathy of undetermined significance, stable).
2. Provide Immunofix information if available.

Specimen Required

Specimen Type: Redirected bone marrow
Container/Tube:
Preferred: Yellow top (ACD solution A or B)
Acceptable: Lavender top (EDTA)
Specimen Volume: 4 mL

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

Specimen Minimum Volume
2 mL

Reject Due To
All specimens will be evaluated at Mayo Clinic Laboratories for test suitability

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Bone Marrow	Ambient (preferred)	72 hours	
	Refrigerated	72 hours	

Clinical & Interpretive

Clinical Information
Multiple myeloma is an incurable malignant neoplasm of plasma cells. One of the best prognostic factors in multiple myeloma is the level of measurable (also known as minimal) residual disease post chemotherapy or autologous stem cell transplantation. The greater depth of the response (less malignant cells present), the longer time to progression and overall survival.(1)

Reference Values
An interpretive report will be provided.

Interpretation
The interpretation of the test is done by evaluating automated and manually gated populations to isolate abnormal plasma cells. If there is an abnormal plasma cell population (cluster of 20 cells or more), then the result is measurable residual disease (MRD)-positive, with the percentage of abnormal plasma cells out of total analyzed events. If no abnormal population is found, then the result will be interpreted as MRD-negative.

This test will be processed as a laboratory consultation. An interpretation of the immunophenotypic findings and correlation with the previous patient history will be provided by a hematopathologist for every case.

Cautions
There are situations in which current gating strategies are insufficient to identify abnormal plasma cells. This can occur if

the abnormal plasma cells do not phenotypically differ from normal plasma cells. In addition, in patients who have undergone therapeutic antibody treatment (anti-CD38, for example), decreased antigen expression on plasma cells may interfere with the gating strategy.

Clinical Reference

1. Martinez-Lopez J, Lahuerta JJ, Pepin F, et al. Prognostic value of deep sequencing method for minimal residual disease detection in multiple myeloma. Blood. 2014;123(20):3073-3079
2. Rawstron AC, Child JA, de Tute RM, et al. Minimal residual disease assessed by multiparameter flow cytometry in multiple myeloma: impact on outcome in the medical research council myeloma IX Study. J Clin Oncol. 2013;31(20):2540-2547
3. Roschewski M, Stetler-Stevenson M, Yuan C, et al. Minimal residual disease: What are the minimum requirements? J Clin Oncol. 2014;32(5):475-476
4. Stetler-Stevenson M, Paiva B, Stoolman L, et al. Consensus guidelines for myeloma minimal residual disease sample staining and data acquisition. Cytometry B Clin Cytom. 2016;90(1):26-30. doi:10.1002/cyto.b.21249
5. Callander NS, Baljevic M, Adekola K, et al. NCCN Guidelines Insights: Multiple Myeloma, Version 3.2022. J Natl Compr Canc Netw. 2022;20(1):8-19. doi:10.6004/jnccn.2022.0002

Performance

Method Description

Flow cytometric immunophenotyping for measurable residual disease (MRD) of bone marrow is performed using the following antibodies:
Tube 1: CD138, CD27, CD38, CD56, CD45, CD19, CD117, and CD81.
Tube 2: CD138, CD27, CD38, CD56, CD45, CD19, cyKappa, and cyLambda.
Abnormal plasma cell populations are detected through demonstrating CD38 (multiepitope) and CD138 positivity along with immunoglobulin light chain restriction (ie, the presence of either predominately kappa or lambda immunoglobulin light chains) and abnormality of CD56, CD117, CD27, CD81, CD19 and/or CD45 expression.

The sensitivity of this assay is conservatively estimated to be 0.001% (1 x 10[-5]) with a minimum number of 2 x 10(-6) total events collected, and an abnormal plasma cell immunophenotype detected in a cluster of at least 20 cells and can be as high as 0.0002% (2 x 10[-6]). The sensitivity of the assay will be lower in samples with less than 2 x 10(-6) total events acquired. The validated limit of detection (sensitivity) meets current National Comprehensive Cancer Network, International Myeloma Working Group, and EuroFlow guidelines for MRD assessment by flow cytometry in multiple myeloma. The percentage of clonal plasma cells estimated by flow cytometry is affected by specimen processing and antigen loss with specimen aging. MRD reporting is affected by sample volume and cellularity.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Preanalytical processing: Monday through Saturday
Results reported: Monday through Friday

Report Available
2 to 4 days

Specimen Retention Time
14 days

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
88184-Flow Cytometry; first cell surface, cytoplasmic or nuclear marker
88185 x 9-Flow Cytometry; additional cell surface, cytoplasmic or nuclear marker
88188-Flow Cytometry Interpretation, 9 to 15 Markers

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MRDMM	Multiple Myeloma MRD by Flow, BM	93022-2

Result ID	Test Result Name	Result LOINC® Value
CK146	% Minimal Residual Disease (MRD)	93021-4
CK147	% Normal Plasma Cells (of total PC)	93020-6
CK148	Non-Aggregate Events	38257-2
CK149	Total Plasma Cell Events	93019-8
CK150	Poly PC Events	93018-0
CK151	Abnormal PC Events	93017-2
CK152	Final Diagnosis	74226-2
615796	% B-cell Precursors	101131-1
615797	% Mast Cells	101130-3
616082	Validated Assay Sensitivity	101129-5
616083	Lower Limit of Quantitation (LLOQ)	87706-8

615798	Patient / Sample Theoretical LOQ	101128-7