Test Definition: MSMRT

Mayo Algorithmic Approach for Stratification of Myeloma and Risk-Adapted Therapy Report, Bone Marrow

Overview

Useful For

Risk stratification of patients with treated multiple myeloma, which can assist in determining treatment and management decisions

Risk stratification of patients with newly diagnosed multiple myeloma

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CSMRT	MPCDS Pre-Analysis Cell Sorting, BM	No	No
MPCDB	Probe, Each Additional (MPCDS)	No, (Bill Only)	No
MPCDS	mSMART Eval, PCPDs, FISH	Yes, (Order PCPDS)	No

Testing Algorithm

Based on the flow cytometric analysis and the presence of greater than or equal to 0.1% monotypic plasma cells, the pre-analysis cell sorting and fluorescence in situ hybridization for plasma cell proliferative disorders may be performed at an additional charge.

For more information see Multiple Myeloma: Laboratory Screening.

Special Instructions

- Multiple Myeloma: Laboratory Screening

Method Name

Flow Cytometry/DNA Content/Cell Cycle Analysis

NY State Available

Yes

Specimen

Specimen Type

Bone Marrow

Ordering Guidance

This test should be ordered at diagnosis or for a known relapsing patient of multiple myeloma.

For follow-up of a plasma cell neoplasm (plasma cell proliferative disorder), order MSMRD / Myeloma Stratification and Risk-Adapted Therapy with Reflex to Measurable/Minimal Residual Disease, Bone Marrow.

Necessary Information

Include patient's disease state (untreated, treated, monoclonal gammopathy of undetermined significance, stable).

Specimen Required

Specimen Type: Redirected bone marrow
Preferred: Yellow top (ACD solution A or B)
Acceptable: Lavender top (EDTA) or green top (heparin)
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

3 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 increasingly recognized as a disease characterized by marked cytogenetic, molecular, and proliferative heterogeneity. This heterogeneity is manifested clinically by varying degrees of disease aggressiveness. Multiple myeloma patients with more aggressive disease experience suboptimal responses to some therapeutic approaches; therefore, identifying these patients is critically important for selecting appropriate treatment options.

The Mayo algorithmic approach for stratification of myeloma and risk-adapted therapy classifies patients into either standard or high-risk categories based on the results of 2 assays: plasma cell proliferation and fluorescence in situ hybridization for specific multiple myeloma-associated abnormalities.

Reference Values

Plasma cell clonality:
Normal bone marrow
No monotypic clonal plasma cells detected

DNA index:
Normal polytypic plasma cells
DNA index (G0/G1 cells): Diploid 0.95-1.05

Interpretation

The interpretation of results includes an overview of the results and the associated diagnostic, prognostic, and therapeutic implications.

Cautions

This test report is best used for newly diagnosed patients with multiple myeloma. It is designed for patients with multiple myeloma and may not be applicable for monoclonal gammopathy of uncertain significance, smoldering myeloma, or amyloidosis.

This stratification system is not meant to replace existing prognostic systems such as the International Staging System.

Clinical Reference

1. Gonsalves WI, Buadi FK, Ailawadhi S, et al. Utilization of hematopoietic stem cell transplantation for the treatment of multiple myeloma: a Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) consensus statement. Bone Marrow Transplant. 2019;54(3):353-367. doi:10.1038/s41409-018-0264-8
2. Kapoor P, Ansell SM, Fonseca R, et al. Diagnosis and management of waldenstrom macroglobulinemia: Mayo Stratification of Macroglobulinemia and Risk-Adapted Therapy (mSMART) guidelines 2016. JAMA Oncol. 2017;3(9):1257-1265. doi:10.1001/jamaoncol.2016.5763
3. Mikhael JR, Dingli D, Roy V, et al. Management of newly diagnosed symptomatic multiple myeloma: updated Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) consensus guidelines 2013. Mayo Clin Proc. 2013;88(4):360-376. doi:10.1016/j.mayocp.2013.01.019
4. Swerdlow S, Campo E, Harris NL, et al. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th ed. IARC Press; 2017. WHO Classification of Tumours, Vol. 2
5. Kumar SK, Rajkumar SV. The multiple myelomas-current concepts in cytogenetic classification and therapy. Nat Rev Clin Oncol. 2018;15(7):409-421 doi:10.1038/s41571-018-0018-y
6. Rajkumar SV, Landgren O, Mateos MV. Smoldering multiple myeloma. Blood. 2015;125(20):3069-3075. doi:10.1182/blood-2014-09-568899
7. Aljama MA, Sidiqi MH, Lakshman A, et al. Plasma cell proliferative index is an independent predictor of progression in smoldering multiple myeloma. Blood Adv. 2018;2(22):3149-3154
8. Mellors PW, Binder M, Ketterling RP, et al. Metaphase cytogenetics and plasma cell proliferation index for risk stratification in newly diagnosed multiple myeloma. Blood Adv. 2020 May 26;4(10):2236-2244
9. Sidana S, Jevremovic D, Ketterling RP, et al: Rapid assessment of hyperdiploidy in plasma cell disorders using a novel multi-parametric flow cytometry method. Am J Hematol. 2019;94(4):424-430
10. Ghosh T, Gonsalves WI, Jevremovic D, et al. The prognostic significance of polyclonal bone marrow plasma cells in

patients with relapsing multiple myeloma. Am J Hematol. 2017;92(9):E507-E512

Performance

Method Description

Flow cytometric immunophenotyping of bone marrow is performed using the following antibodies: CD19, CD38, CD45, CD138, cytoplasmic kappa and lambda immunoglobulin, and DAPI (4',6-diamidino-2-phenylindole). Plasma cell clonality is detected through demonstrating CD38 and CD138 positivity along with immunoglobulin light chain restriction (ie, the presence of either predominately kappa or lambda immunoglobulin light chains) and abnormality of CD19 and/or CD45 expression. DNA index of clonal plasma cells and their proliferation activity is determined through staining of double-stranded DNA using DAPI.

Plasma cells (monoclonal/monotypic and polyclonal/polytypic) are detected by immunoglobulin light chain restriction, surface immunophenotype, and DNA content. If present, the light chain expressed by the monotypic plasma cells is indicated. The percentage of clonal plasma cells estimated by flow cytometry is affected by specimen processing and antigen loss with specimen aging. Manual differential counting remains the accepted standard for determining the bone marrow plasma cell percentage. The percentage of monotypic plasma cells in S-phase of the cell cycle is determined by quantitative DNA analysis. The DNA index is a calculated value. The presence of more than 1 value indicates the presence of cell populations with differing DNA contents within the monotypic plasma cells. (Dispenzieri A, Buadi F, Kumar SK, et al. Treatment of immunoglobulin light chain amyloidosis: Mayo Stratification of Myeloma and Risk-Adapted Therapy [mSMART] Consensus Statement. Mayo Clin Proc. 2015;90[8]:1054-1081. doi:10.1016/j.mayocp.2015.06.009)

Plasma Cell Proliferation:
This test is performed using commercially available and laboratory-developed probes on sorted plasma cells. Deletion of the *TP53* locus from chromosome 17 or monosomy 17 and deletion of the *CDKN2C* locus or gain of the 1q22 locus are detected using enumeration strategy probe sets. If necessary, hyperdiploidy will be assessed using enumeration strategy probe sets for chromosomes 3, 7, 9, and 15. Rearrangements involving *IGH* and *MYC* are detected using dual-color break-apart strategy probe sets. Dual-color, dual-fusion fluorescence in situ hybridization strategy probe sets are used when a rearrangement of the *IGH* gene is detected. For each probe set, 50 plasma cells (if possible) are scored and the result for each probe is reported.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Saturday

Report Available

1 to 11 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

88182-Flow cytometry, cell cycle or DNA analysis
88184-Flow cytometry; first cell surface, cytoplasmic or nuclear marker
88185 x 5-Flow cytometry; additional cell surface, cytoplasmic or nuclear marker (each)
88187-Flow cytometry interpretation, 2 to 8 Markers

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MSMRT	mSMART Algorithmic Testing, BM	93363-0

Result ID	Test Result Name	Result LOINC® Value
CK056	Monotypic Plasma Cells:	93362-2
CK057	Monotypic PC per Total Events	93021-4
CK058	Monotypic Plasma Cells S-phase	93361-4
CK059	Monotypic Plasma Cells DNA Index	93360-6
CK060	Monotypic Plasma Cells DNA Ploidy	93359-8
CK061	Polytypic PC per Total Events	93358-0
CK062	Polytypic PC per All Plasma Cells	93020-6
CK134	Final Diagnosis	22637-3