

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  | No                   | No               |
|         | Sorting, BM              |                      |                  |
| MPCDB   | Probe, Each Additional   | No, (Bill Only)      | No               |
|         | (MPCDS)                  |                      |                  |
| 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** 



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## **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 <u>Hematopathology/Cytogenetics Test Request</u> (T726) with the specimen.

# **Specimen Minimum Volume**

3 mL

## Reject Due To

| Gross         | Reject |
|---------------|--------|
| hemolysis     |        |
| Fully clotted | Reject |

### 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.



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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



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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 both commercially available and laboratory developed probes. Deletion or monosomy of chromosomes 13 and 17 and copy number gain of 1q are detected using enumeration strategy probes. Centromere probes are used to detect chromosomal gain of chromosomes 3, 7, 9, and 15. Translocations involving *IGH* with *FGFR3*, *CCND1*, *CCND3*, *MAF*, and *MAFB* are detected using dual-color, dual-fusion (D-FISH) strategy probes. Rearrangement of *IGH* and *MYC* are detected using a break-apart strategy probe. 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



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## **Specimen Retention Time**

14 days

## **Performing Laboratory Location**

Mayo Clinic Laboratories - Rochester Main Campus

## **Fees & Codes**

#### **Fees**

- Authorized users can sign in to <u>Test Prices</u> for detailed fee information.
- Clients without access to Test Prices can contact <u>Customer Service</u> 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact <u>Customer Service</u>.

#### **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             |