Overview

Useful For

Risk stratification of patients with 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
MPCDS	mSMART Eval, PCPDs, FISH	No	No

Testing Algorithm

Based on the flow cytometric analysis and presence of greater than or equal to 0.1% monotypic plasma cells, the pre-analysis cell sorting and FISH for plasma cell proliferative disorder will be reflexed and performed at an additional charge.

This test is designed for diagnostic specimens. If a request for testing has been submitted within 12 months of a complete and informative plasma cell proliferative disorder FISH study, the current test request will be cancelled.

See Laboratory Screening Tests for Suspected Multiple Myeloma in Special Instructions.

Special Instructions

- Laboratory Screening Tests for Suspected Multiple Myeloma

Method Name

Flow Cytometry/DNA Content/Cell Cycle Analysis

NY State Available

Yes

Specimen

Specimen Type

Bone Marrow

Advisory Information

This test should be ordered at diagnosis of multiple myeloma and when MPCDS / mSMART, Plasma Cell Proliferative Disorder (PCPD), FISH is warranted based on the Laboratory Screening Tests for Suspected Multiple Myeloma algorithm.

This test is designed for diagnostic specimens. If follow-up testing is ordered within 12 months of a complete and

informative PCPDS / Plasma Cell Proliferative Disorder, FISH, Bone Marrow result, the testing will be cancelled. If follow up testing is ordered within 12 months of an initial partial or insufficient study, the testing will proceed.

Necessary Information

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

2. Indicate if patient is on anti-CD38 therapy.

Specimen Required

Specimen Type: Redirected bone marrow

Preferred: Yellow top (ACD)

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

Gross hemolysis	Reject
Other	Fully clotted

Specimen Stability Information

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

Clinical and 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.

Mayo Algorithmic Approach for Stratification of Myeloma and Risk-Adapted Therapy (MSMRT) classifies patients into either standard or high-risk categories based on the results of 2 assays: plasma cell proliferation and FISH 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

An interpretive report will be provided. Patients are classified as high risk, intermediate, or standard risk.

Cautions

Mayo Algorithmic Approach for Stratification of Myeloma and Risk-Adapted Therapy (MSMRT) 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. Rajkumar SV, Greipp PR: Prognostic factors in multiple myeloma. Hematol Oncol Clin North Am 1999 Dec;13(6):1295-1314

2. Garcia-Sanz R, Gonzalez-Fraile MI, Mateo G, et al: Proliferative activity of plasma cells is the most relevant prognostic factor in elderly multiple myeloma patients. Int J Cancer 2004 Dec 10;112(5):884-889

3. Orfao A, Garcia-Sanz R, Lopez-Berges MC, et al: A new method for the analysis of plasma cell DNA content in multiple myeloma samples using a CD38/propidium iodide double staining technique. Cytometry 1994 Dec 1;17(4):332-339

4. Morice WG, Hanson CA, Kumar S, et al: Novel multi-parameter flow cytometry sensitively detects phenotypically distinct plasma cell subsets in plasma cell proliferative disorders. Leukemia 2007 Sep;21(9):2043-2046

5. 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):353â€“367. doi:10.1038/s41409-018-0264-8

6. 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 Sep 1;3(9):1257â€“1265. doi:10.1001/jamaoncol.2016.5763

7. 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 [published correction appears in Mayo Clin Proc. 2013 Jul;88(7):777. Stewart, Keith [corrected to Stewart, A Keith]]. Mayo Clin Proc. 2013;88(4):360â€“376. doi:10.1016/j.mayocp.2013.01.019

8. Swerdlow S, Campo E, Harris NL, et al: WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. IARC Press: Lyon. 2017

9. 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

10. Rajkumar SV, Landgren O, Mateos MV: Smoldering multiple myeloma. Blood 2015 May 14;125(20):3069-3075 doi:10.1182/blood-2014-09-568899

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. 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 predominately lambda 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):1054â€“1081. doi:10.1016/j.mayocp.2015.06.009)

Plasma Cell Proliferative Disorder (PCPD):

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 (BAP) 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) and Time(s) Test Performed

Specimens are processed Monday through Sunday.

Results reported Monday through Friday 8 a.m.-5 p.m.

Analytic Time

1 day with no reflex testing

Maximum Laboratory Time

11 days if reflex testing performed

Specimen Retention Time

14 days

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. For assistance, contact Customer Service.

Test Classification

This test was developed using an analyte specific reagent. Its performance characteristics were 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

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	93357-2

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