Overview

Useful For

Aiding in the diagnosis of new cases of multiple myeloma or other plasma cell proliferative disorders as a part of a profile

Identifying prognostic markers based on the anomalies found

Testing Algorithm

This test is designed for diagnostic specimens from patients with multiple myeloma or other plasma cell proliferative disorders. If a request for testing has been submitted within 12 months of a complete and informative plasma cell proliferative disorder fluorescence in situ hybridization (FISH) study, the current test request will be cancelled.

For **diagnostic** samples, all probes in the initial panel will be evaluated if sufficient plasma cells are identified. The initial panel includes testing for the following the probes listed:

17p-, TP53/D17Z1

1q gain, TP73/1q22

14q32 rearrangement, IGH break-apart

8q24.1 rearrangement, MYC break-apart

-13/13q-, RB1/LAMP1

Based on the results from the initial panel, reflex testing may be performed to identify the following abnormalities using the probes listed:

t(11;14)(q13;q32), CCND1/IGH fusion

t(14;16)(q32;q23) IGH/MAF fusion

t(4;14)(p16.3;q32) FGFR3/IGH fusion

t(14;20)(q32;q12) IGH/MAFB fusion

t(6;14)(p21;q32) CCND3/IGH fusion

Hyperdiploidy will be evaluated and reported by flow cytometry as part of this evaluation and incorporated into the final interpretation. For samples with an unsuccessful flow evaluation for hyperdiploidy and with sufficient plasma cells, FISH testing for the following abnormalities will be performed using the probes listed:

+3/+7, D3Z1/D7Z1

+9/+15, D9Z1/D15Z4

For **follow-up** samples, the following probes will be evaluated if sufficient plasma cells are identified:

17p-, TP53/D17Z1

1q gain, TP73/1q22

8q24.1 rearrangement, MYC break-apart

If a diagnostic sample was uninformative for a probe set due to an insufficient number of plasma cells, attempts may be made to achieve results for the missing probe on a subsequent sample (if sufficient plasma cells are identified).

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
MPCDB	Probe, Each Additional (MPCDS)	No	No

Method Name

Only orderable as part of a profile. For more information see MSMRT / Mayo Algorithmic Approach for Stratification of

Myeloma and Risk-Adapted Therapy Report, Bone Marrow.
Fluorescence In Situ Hybridization (FISH)

NY State Available
Yes

Specimen

Specimen Type
Bone Marrow

Specimen Required
Only orderable as part of a profile. For more information see MSMRT / Mayo Algorithmic Approach for Stratification of Myeloma and Risk-Adapted Therapy Report, Bone Marrow.

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

Specimen Minimum Volume
2 mL

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information
Multiple myeloma is a hematologic neoplasm that generally originates in the bone marrow and develops from malignant plasma cells. There are 4 main categories of plasma cell proliferative disorders : monoclonal gammopathy of undetermined significance (MGUS), monoclonal immunoglobulin deposition diseases (amyloidosis), plasmacytoma, and multiple myeloma. MGUS, which occurs in 3% to 4% of individuals over age 50 years, represents the identification of an asymptomatic monoclonal protein, yet approximately 1% per year will progress to multiple myeloma. Amyloidosis represents a rare group of deposition disorders including primary amyloidosis vs. light chain and heavy chain disease. Plasmacytomas represent isolated collections of bone or extramedullary plasma cells with a risk for development of multiple myeloma. Generalized bone pain, anemia, limb numbness or weakness, symptoms of hypercalcemia, and recurrent infections are all symptoms that may indicate multiple myeloma.
As myeloma progresses, the malignant plasma cells interfere with normal blood product formation in the bone marrow resulting in anemia and leukopenia. Myeloma also causes an overstimulation of osteoclasts, causing excessive breakdown of bone tissue without the normal corresponding bone formation. These bone lesions are seen in approximately 66% of myeloma patients. In advanced disease, bone loss may reach a degree where the patient suffers fractures easily.

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. Patients with more aggressive multiple myeloma experience suboptimal responses to some therapeutic approaches; therefore, identifying these patients is critically important for selecting appropriate treatment options.

Reference Values

Only orderable as part of a profile. For more information see MSMRT / Mayo Algorithmic Approach for Stratification of Myeloma and Risk-Adapted Therapy Report, Bone Marrow.
An interpretive report will be provided.

Interpretation

A neoplastic clone is detected when the percent of cells with an abnormality exceeds the normal reference range for any given probe.
The absence of an abnormal clone does not rule out the presence of neoplastic disorder.

Cautions

This test is not approved by the US Food and Drug Administration, and it is best used as an adjunct to existing clinical and pathologic information.

Supportive Data

Each probe was independently tested and verified on unstimulated peripheral blood and bone marrow specimens. Normal cutoffs were calculated based on the results of 25 normal specimens. Each probe set was evaluated to confirm the probe set detected the abnormality it was designed to detect.

Clinical Reference

1. Swerdlow SH, Campo E, Harris NL, et al, eds: WHO Classification of Tumour of Haematopoietic and Lymphoid Tissues. 4th ed. IARC Press; 2017
2. 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
3. Rajkumar SV, Landgren O, Mateos MV: Smoldering multiple myeloma. Blood. 2015 May 14;125(20):3069-75. doi: 10.1182/blood-2014-09-568899
4. Muchtar E, Dispenzieri A, Kumar S, et al: Interphase fluorescence in situ hybridization in untreated AL amyloidosis has an independent prognostic impact by abnormality type and treatment category. Leukemia. 2017 Jul;31(7);1562-1569 doi: 10.1038/leu.2016.369
5. Lakshman A, Paul S, Rajkumar SV, et al: Prognostic significance of interphase FISH in monoclonal gammopathy of undetermined significance. Leukemia. 2018 Aug;32(8);1811-1815 doi: 10.1038/s41375-018-0030-3
6. Bochtler T, Hegenbart U, Kunz C, et al: Prognostic impact of cytogenetic aberrations in AL amyloidosis patients after high-dose melphalan: a long-term follow-up study. Blood. 2016 Jul 28;128(4):594-602 doi: 10.1182/blood-2015-10-676361
7. Treatment guidelines: multiple myeloma. mSMART 3.0. Accessed January 16, 2020. Available at www.msmart.org/mm-treatment-guidelines

Performance

Method Description

This test is performed using commercially available and laboratory-developed probes. Deletion or monosomy of chromosome 17, copy number gain of 1q, and additional copies of chromosomes 3, 7, 9, and 15 are detected using enumeration strategy probes. Translocations involving *IGH* are detected using dual-color, dual-fusion fluorescence in situ hybridization 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

Specimen Retention Time
14 days

Performing Laboratory Location
Rochester

Fees & Codes

Test Classification
This test was developed, and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
88271x2, 88274x1, 88291x1–FISH Probe, Analysis, Interpretation; 1 probe set
88271x2, 88274x1–FISH Probe, Analysis; each additional probe set (if appropriate)