Overview

Useful For

Aiding in the diagnosis of new cases of multiple myeloma or other plasma cell proliferative disorders

Identifying prognostic markers based on the abnormalities found

This test **should not be used** to track the progression of disease.

Reflex Tests

Test ID	Reporting Name	Available Separately	Always Performed
_PBCT	Probe, +2	No, (Bill Only)	No
_PADD	Probe, +1	No, (Bill Only)	No
_PB02	Probe, +2	No, (Bill Only)	No
_PB03	Probe, +3	No, (Bill Only)	No
_IL25	Interphases,	No, (Bill Only)	No
_I099	Interphases, 25-99	No, (Bill Only)	No
_I300	Interphases, >=100	No, (Bill Only)	No

Additional Tests

Test ID	Reporting Name	Available Separately	Always Performed
CSPCF	PCPDS Pre-Analysis Cell Sorting, BM	No	Yes

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.

This test includes a charge for application of the first probe set (2 FISH probes) and professional interpretation of results. Additional charges will be incurred for all reflex probes performed. Analysis charges will be incurred based on the number of cells analyzed per probe set. If no cells are available for analysis, no analysis charges will be incurred.

When this test is ordered, pre-analysis cell sorting will be performed at an additional charge.

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 abnormalities using the probes listed:

17p-, *TP53*/D17Z1

1q gain, *TP73*/1q22

14q32 rearrangement, *IGH*

t(11;14), *CCND1*/*IGH*

8q24.1 rearrangement, *MYC*

-13/13q-, *RB1*/*LAMP1*

+9/+15, D9Z1/D15Z4

+3/+7, D3Z1/D7Z1

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

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

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

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

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

For follow-up samples, only *TP73*/1q22, *TP53*/D17Z1 and *MYC* probes along with a single probe that was abnormal in a previous study will be tested. If a previous sample was uninformative due to an insufficient number of plasma cells, analysis will begin with the initial panel (if sufficient plasma cells are identified).

Initial screening will be performed to determine if sufficient plasma cells are present within the provided specimen. If the standard algorithm is not desired, indicate which probes should be used.

If specimen is received greater than 96 hours from collection, this test will be canceled and MFCF / Myeloma, FISH, Fixed Cells will be added as the more appropriate test.

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Bone Marrow

Advisory Information

This assay detects abnormalities observed in the bone marrow of patients with a plasma cell disorder.

-For paraffin-embedded tissue specimens, order PLASF / Plasma Cell Proliferative Disorder, FISH, Tissue.

-For fixed cell pellet specimens, order MFCF / Myeloma, FISH, Fixed Cells.

-Testing will be changed to the appropriate test if this test is ordered on either of the previous specimens or if bone marrow specimens are received more than 96 hours from collection.

Shipping Instructions

1. Specimen should arrive within 96 hours of collection.

2. Advise Express Mail or equivalent if not on courier service.

Necessary Information

1. Provide a reason for referral with each specimen. The laboratory will not reject testing if this information is not provided but appropriate testing and interpretation may be compromised or delayed.

2. A pathology and/or flow cytometry report may be requested to optimize testing and aid in interpretation of results.

Specimen Required

Container/Tube:

Preferred: Yellow top (ACD)

Acceptable: Lavender top (EDTA) or green top (heparin)

Specimen Volume: 4 mL

Collection Instructions: Invert several times to mix bone marrow

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)	4 days	
	Refrigerated	4 days	

Clinical and 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 (PCPD): 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. 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.

Reference Values

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.

Cautions

This test is not approved by the FDA and is best used as an adjunct to existing clinical and pathologic information.

Supportive Data

Each probe was independently tested and verified on bone marrow specimens. For each probe set a series of chromosomally abnormal specimens were evaluated to confirm each probe set detected the anomaly it was designed to detect.

Clinical Reference

1. Swerdlow S, Campo E, Harris NL, et al, eds. WHO Classification of Tumours 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):3069-3075. 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.org/10.1182/blood-2015-10-7

7. Treatment guidelines: multiple myeloma. mSMART 3.0, Accessed 01/16/2020. Available at: www.msmart.org/mm-treatment-guidelines

Performance

Method Description

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 fluorescence in situ hybridization (D-FISH) strategy probes. Rearrangements of *IGH* and *MYC* are detected using break-apart strategy (BAP) probes. 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

7 days

Maximum Laboratory Time

10 days

Specimen Retention Time

4 Weeks

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

88271x2, 88291-DNA probe, each (first probe set), Interpretation and report

88271x2-DNA probe, each; each additional probe set (if appropriate)

88271x1-DNA probe, each; coverage for sets containing 3 probes (if appropriate)

88271x2-DNA probe, each; coverage for sets containing 4 probes (if appropriate)

88271x3-DNA probe, each; coverage for sets containing 5 probes (if appropriate)

88274 w/modifier 52-Interphase in situ hybridization, <25 cells, each probe set (if appropriate)

88274-Interphase in situ hybridization, 25 to 99 cells, each probe set (if appropriate)

88275-Interphase in situ hybridization, 100 to 300 cells, each probe set (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
PCPDS	Plasma Cell Prolif, Sort, FISH	In Process

Result ID	Test Result Name	Result LOINC Value
606080	Result Summary	62357-9
606081	Interpretation	69965-2
606082	Result Table	93356-4
606083	Result	62356-1
GC054	Reason for Referral	42349-1
606084	Specimen	31208-2
606085	Source	39111-0
606086	Method	85069-3
606087	Additional Information	48767-8
606088	Disclaimer	62364-5
606089	Released By	18771-6