Multiple Myeloma Panel by FISH

Last Literature Review: April 2024 Last Update: May 2024

Multiple myeloma (MM) is a plasma cell dyscrasia that can evolve from a premalignant monoclonal gammopathy. Prognosis often depends on the presence or absence of particular genetic markers. Bone marrow aspirate and biopsy with fluorescence in situ hybridization (FISH) testing for relevant markers should be performed as clinically indicated, including upon diagnosis and in low-/standard-risk individuals at time of relapse to aid in risk stratification.[1,2]

Featured ARUP Testing

Multiple Myeloma Panel by FISH 3002063

Method: Fluorescence in situ Hybridization (FISH)

Aids in risk stratification of individuals with plasma cell neoplasms (monoclonal gammopathy of unknown significance [MGUS], smoldering multiple myeloma [SMM], multiple myeloma [MM]). Recommended at initial diagnosis and/or at disease progression. Refer to companion test for monitoring.

Companion test:

FISH, Interphase, CD138+ Cells 3002737

Method: Fluorescence in situ Hybridization (FISH)

Use to monitor for a previously identified clone.

Test Description

This test involves the performance of FISH on CD138+ enriched cells (assuming the specimen is sufficient for enrichment) for multiple myeloma prognosis-specific genomic abnormalities:

- 1p (*CDKN2C* loss/deletion)/1q (*CKS1B* gain/amplification)
- 17p (*TP53* loss/deletion)/17q (*NF1*) control
- t(4;14) (*IGH/FGFR3* or *NSD2* [*MMSET*] fusion)
- t(11;14) (*IGH/CCND1* fusion and/or +11)
- t(14;16) (*IGH/MAF* fusion)
- t(14;20) (*IGH/MAFB* fusion)

Disease Overview

Age of Onset

Most frequently diagnosed between ages 65 and 74 years (median age 69 years)[2]

Symptoms

Presenting clinical features include symptoms of[1,2]:

- Hypercalcemia
- Impaired renal function
- Anemia
- Bone disease (lesions)

Clinical Implications of Tested Genomic Abnormalities

Abnormalities are detected by conventional cytogenetics in approximately 30% of MMs. FISH testing increases this number to >90%.[1] Cytogenetic abnormalities affect the prognosis of patients with MM.

Genetic Markers and Clinical Implications: Multiple Myeloma Panel by FISH		
Included Markers	**Clinical Implications**	**Recurrent Testing**
Primary Cytogenetic Abnormalities		
t(4;14) (*IGH/FGFR3* or *NSD2* [*MMSET*] fusion)	Presence: 15% of MM High risk Detectable only by FISH (cytogenetically cryptic)	Test only once

Included Markers	Clinical Implications	Recurrent Testing
Primary Cytogenetic Abnormalities		
t(11;14) (*IGH/CCND1* fusion and/or +11)	Presence: 15-20% of MM Standard risk	Test only once
t(14;16) (*IGH/MAF* fusion)	Presence: 3-5% of MM High risk May be missed by karyotyping	Test only once
t(14;20) (*IGH/MAFB* fusion)	Presence: 1-2% of MM High risk	Test only once
Hyperdiploidy Usually gains (trisomies) of three or more odd-numbered chromosomes (3, 5, 7, 9, 11, 15, 19, 21)	Presence: 50% of MM Standard risk Infrequently occurs with IGH translocations Panel tests the commonly gained chromosome 11	Test only once
Secondary Cytogenetic Abnormalities		
1q (*CKS1B* gain/amplification) • 1q21 gain defined as 3 copies • 1q21 amplification defined as ≥4 copies	Presence: 30-40% of MM Presence higher in disease progression High risk (in the presence of other abnormalities) May co-occur with primary and other secondary cytogenetic abnormalities Confers a poor prognosis in all subtypes	Repeat testing justified
1p (*CDKN2C* loss/deletion)	Presence: 8-12% of MM Presence higher in disease progression High risk May co-occur with primary and other secondary cytogenetic abnormalities Confers a poor prognosis in all subtypes	Repeat testing justified
17p (*TP53* loss/deletion)	Presence: 7-10% of MM Presence higher in disease progression High risk May co-occur with primary and other secondary cytogenetic abnormalities Confers a poor prognosis in all subtypes	Repeat testing justified

Sources: NCCN 2024[2]; Hagen 2022[3]; Rajkumar, 2022[4]; Rajan, 2015[5]

Test Interpretation

Analytic Sensitivity/Specificity

>95%

Results

Results Interpretation: Multiple Myeloma Panel by FISH		
Result Reported	**Genomic Abnormalities Detected**	**Interpretation and Clinical Implications**

Result Reported	Genomic Abnormalities Detected	Interpretation and Clinical Implications
Normal FISH result	None	No evidence of any of the tested abnormalities Other abnormalities (for which this test does not include probes) are not excluded
Abnormal FISH result (specific abnormalities will be reported)	One or more	Results suggest a clonal population of cells with clinical significance in MGUS, MM, and/or SMM Results should be correlated with clinical and other laboratory findings Use companion test 3002737 to monitor for positive results by FISH in future studies

Limitations

- This test only detects genomic abnormalities specific to the probes used.
- When this test is ordered in conjunction with chromosome analysis (karyotype) and/or genomic microarray on low cellularity samples, this test will be prioritized due to the need for CD138+ cell enrichment prior to FISH.
  - Microarray will be prioritized after FISH, followed by karyotype.
  - This may impact the completion of lower priority tests.
- If enrichment fails yield to sufficient CD138+ cells, testing will be performed using unenriched cells if available.

References

1. Swerdlow S, Campo E, Jaffe E, et al. *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues.* 4th ed. International Agency for Research on Cancer; 2017.

2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: multiple myeloma. Version 4.2024. Accessed May 2024.

3. Hagen P, Zhang J, Barton K. High-risk disease in newly diagnosed multiple myeloma: beyond the R-ISS and IMWG definitions. *Blood Cancer J*. 2022;12(5):83.

4. Rajkumar SV. Multiple myeloma: 2022 update on diagnosis, risk stratification, and management. *Am J Hematol*. 2022;97(8):1086-1107.

5. Rajan AM, Rajkumar SV. Interpretation of cytogenetic results in multiple myeloma for clinical practice. *Blood Cancer J*. 2015;5(10):e365.