Multiple Myeloma by FISH

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. Fluorescence in situ hybridization (FISH) testing for relevant markers should be performed upon diagnosis and in low-risk individuals at time of relapse to aid in risk stratification.

Test Description

Plasma cells are isolated from a bone marrow (BM) aspirate using CD138+ microbeads. CD138+ cells (plasma cells) are then analyzed by FISH using specific probes for the following:

- \( \text{CCND1/IGH} \) fusion t(11;14)
- \( \text{CKS1B} \) (1q gain)
- \( \text{IGH} \) rearrangement (14q32)
- \( \text{ASS1} \) (+9)
- \( \text{PML} \) (+15)
- \( \text{TP53} \) (17p deletion)

If \( \text{IGH} \) rearrangement detected does not involve \( \text{CCND1} \), additional probes are added:

- \( \text{FGFR3/IGH} \) fusion t(4;14)
- \( \text{MAF/IGH} \) fusion t(14;16)

Disease Overview

Incidence

1.8% of all cancers in the U.S.\(^2\)

Age of Onset

Most frequently diagnosed between ages 65 and 74 years (median age 69 years)\(^2\)

Symptoms

Presenting clinical features include symptoms of\(^2\):

- Hypercalcemia
- Impaired renal function
- Anemia
- Bone disease (lesions)
FISH Testing and Prognostic Issues

Abnormalities are detected by conventional cytogenetics in ~30% of MMs. FISH testing increases this number to >90%. Cytogenetic abnormalities affect the prognosis of patients with MM. Because most genetic subtypes in MM are primary, ploidy state, *IGH* translocation, and genetic status need only be assessed once at diagnosis. However, repeat testing is justified in cases of gain/amplification of *CKS1B* (1q21) and deletion of *TP53* (17p13), as these markers occur in disease progression and confer a worse prognosis.

<table>
<thead>
<tr>
<th>Genetic Markers and Resulting Prognostic Issues</th>
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<tr>
<td><strong>Markers</strong></td>
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<td><strong>Characteristics and Prognostic Value</strong></td>
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<tr>
<td><strong>Primary Cytogenetic Abnormalities</strong></td>
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<tr>
<td>Hyperdiploidy</td>
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<td>(3, 5, 7, 9, 11, 15, 19, 21)</td>
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<td>14q32 (<em>IGH</em>) rearrangement</td>
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<td>7 major oncogenes involved: 11q13 [<em>CCND1</em>], 16q23 [<em>MAF</em>], 4p16 [<em>FGFR3/MMSET</em>], 6p21 [<em>CCND3</em>], 20q11 [<em>MAFB</em>], 8q24 [<em>MAFA</em>], 12p13 [<em>CCND2</em>]</td>
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<tr>
<td>t(4;14)(p16;q32) <em>IGH-FGFR3/MMSET</em></td>
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<td>High to intermediate risk</td>
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<tr>
<td>Detectable only by FISH (cytogenetically cryptic)</td>
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<tr>
<td>t(11;14)(q13;q32) <em>IGH-CCND1</em></td>
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<tr>
<td>Standard risk</td>
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<tr>
<td>t(14;16)(q32;q23) <em>IGH-MAF</em></td>
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<tr>
<td>High risk</td>
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**Secondary Cytogenetic Abnormalities**
<table>
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<tr>
<th>Markers</th>
<th>Characteristics and Prognostic Value</th>
<th>Recurrent Testing</th>
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</table>
| Gain/amplification of 1q21 (*CKS1B*) | Presence: 30-70% of MM ⁴,⁵  
Presence higher in disease progression  
High risk  
May be observed in hypodiploid, hyperdiploid, and IGH translocation-positive MM  
Confers a poor prognosis in all subtypes | Repeat testing justified |
| Deletion 17p (*TP53*)                 | Presence: 5-10% of MM  
Presence higher in disease progression  
High risk ⁴  
May be observed in hypodiploid, hyperdiploid, and IGH translocation-positive MM  
Confers a poor prognosis in all subtypes | Repeat testing justified |

**Test Interpretation**

**Analytical Sensitivity/Specificity**

>95%

**Results**

- Abnormal: gain/loss/rearrangement/translocation detected; percentage of cells affected (out of 200) reported
- Normal: no evidence of gains, deletions, rearrangements, or translocations of loci tested

**Limitations**

Only detects aberrations specific to probes used

**References**


2. NCCN Clinical Practice Guidelines in Oncology, Multiple Myeloma. 2.202 National Comprehensive Cancer Network [Accessed: Jan 2020]


Related Information

Plasma Cell Dyscrasias
Plasma Cell Dyscrasias Testing Algorithm

Related Tests

Chromosome FISH, Multiple Myeloma Panel Process and Hold 2006270
Method: Cell culture/Fluorescence in situ Hybridization

Chromosome Analysis, Bone Marrow 2002292
Method: Giemsa Band

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