MatBA®-CLL/SLL Improves Patient Prognosis Accuracy

Resolves prognostic discrepancy between FISH and molecular analyses

Patient Case 174:
64 year old female.
Clinical History:
Untreated.
Specimen:
Peripheral blood.

Clinical Dilemma

Contradictory prognoses left a key clinical question:
What is this patient’s prognosis?

Clinical Solution

INFORM

- Detected gain of 2p, loss of 13q at 2 loci, loss of 18p.
- Includes biomarkers not assessed by FISH.

PREDICT

- The comprehensive genomic assessment gives data that resolves the initial discrepancy.
- The genomic aberrations detected confirmed the patient’s high risk for a poor outcome.

DECIDE

- Test results were used for proper clinical management selection.
- The genomic aberrations detected are evidence for this patient’s unfavorable prognosis. The clinician may choose to select an aggressive course of treatment.

CLL Risk Stratification Per Prognostic Category

Genomic Aberrations Reported by FISH:
- 12 gain
- 11q22 loss (ATM)
- 13q14 loss
- 17p13 loss (TP53)

FISH Analysis:
Reported a favorable/intermediate outcome (loss of 13q).

Genomic Aberrations Reported by MatBA®-CLL/SLL:
- 2p25.3-p15 gain
- 3q26-q27 gain
- 8p23-p21 loss
- 8q24 gain
- 12 gain
- 11q22 loss (ATM)
- 13q14 loss
- 17p13 loss (TP53)
- [6q21 loss]
- [7q31 loss]
- [17q gain]
- [18q gain]
- [18p loss]
- [19 gain]

MatBA®-CLL/SLL:
38% of cases have a favorable prognosis falling under "watch & wait" approach.
39% of cases have a poor outcome.
23% of cases have an unfavorable prognosis missed by FISH.

Impact on therapy selection & clinical management of CLL patients

Patients stratified into "Favorable/Intermediate" by FISH will benefit from distinction into proper prognostic categories by:
- Preventing the selection of "watch and wait" approach for those who would be stratified as intermediate. These patients with early-stage CLL/SLL may benefit from earlier therapy with a lower tumor burden and prior to clonal evolution.
- Delaying therapy for patients with a favorable prognosis, protecting them from toxicity and possible risk of future drug-resistant disease.
- Selecting the proper treatment for patients that initially are mis-prognosed by FISH into the favorable/intermediate category who in fact have an unfavorable prognosis.

MatBA®-CLL/SLL addresses the need to more accurately determine the prognosis of patients at diagnosis - the greatest opportunity to impact the clinical management of CLL patients.
MatBA® - CLL/SLL Array-CGH Report

Results:

<table>
<thead>
<tr>
<th>Genomic Aberration</th>
<th>Result for Aberration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of 8p (8p23.3-p21.3)</td>
<td>Negative</td>
</tr>
<tr>
<td>Loss of 11q (ATM)</td>
<td>Negative</td>
</tr>
<tr>
<td>Loss of 13q (MIR-15A/16.1)</td>
<td>Positive</td>
</tr>
<tr>
<td>Loss of 13q (RB1)</td>
<td>Positive</td>
</tr>
<tr>
<td>Loss of 17p (TP53)</td>
<td>Negative</td>
</tr>
<tr>
<td>Gain of 2p</td>
<td>Positive</td>
</tr>
<tr>
<td>Gain of 3q</td>
<td>Negative</td>
</tr>
<tr>
<td>Gain of 8q</td>
<td>Negative</td>
</tr>
<tr>
<td>Gain of 12</td>
<td>Negative</td>
</tr>
</tbody>
</table>

Interpretation: Positive for the gain of 2p and loss of 13q at two loci. Gain of 2p in CLL patients is associated with an unfavorable prognosis.

Description: The gain and loss of specific genomic regions in the monoclonal proliferation of B-cells in chronic lymphocytic leukemia (CLL) are considered to have diagnostic and prognostic value. Loss of 13q at one locus (MIR-15A/16.1) or both loci (MIR-15A/16.1 and RB1) is observed in approximately 50% of CLL patients and as the sole abnormality is associated with a longer overall survival. Those patients with loss of 17p (TP53) or 11q (ATM) in general, have a shorter overall survival. Other aberrations are variously observed in CLL patients with suggested prognostic value.

This assay utilizes microarray-based comparative genomic hybridization (Array CGH) to simultaneously detect the gain and loss of multiple loci in specimen DNA. Quantitative PCR is used to confirm the detected genomic gains and losses. The sensitivity of the assay is 30-40%. Samples in which the monoclonal B-cells are present at less than 30-40%, aberrations may not be detected and will be reported as no aberrations detected.

End of Report

The tests utilizing analyte-specific reagents (ASR) were developed and their performance characteristics determined by Cancer Genetics, Inc. as required by CLIA B88 regulations. They have not been cleared or approved for specific uses by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary. These tests are used for clinical purposes. Cancer Genetics, Inc., 201 Route 17 North, Rutherford, NJ 07070. Phone number: (888) 334 - 4988 CLIA#: 31D1038733; CAP LAP#: 7191582

CLL Complete™ is a proprietary program developed by CGI to assist physicians in the diagnosis, prognosis and therapy selection for CLL patients. This one-stop-shop solution includes proprietary tests, such as MatBA®-CLL/SLL Array CGH, and the most relevant tests available for the clinical management of CLL patients.