

## MatBA®-MCL Array-CGH Assay

### Overview

Mantle cell lymphoma (MCL) is an aggressive subtype of B-cell non-Hodgkin lymphoma (B-NHL) that is particularly challenging to treat with a median overall survival of 3-4 years. Initial diagnosis is largely based on cell morphology (four variants are evident), immunophenotyping, and presenting clinical features. The chromosomal translocation t(11;14)(q13;q32) involving the *CCND1* and *IGH* genes occurs in 95% of cases. A blastic variant with leukemic presentation is particularly aggressive and is often associated with complex chromosomal abnormalities.

Routine prognostication in MCL currently relies on clinical characteristics represented within the MCL International Prognostic Index (MIPI). Still, considerable clinical heterogeneity exists within identical risk groups and more accurate prognostication is required to identify patients most likely to relapse after standard immuno-chemotherapy.

Other genomic alterations are present in MCL including gain and loss of genomic loci that are associated with morphological variants and clinical outcome. Gains of 3q and 12q and loss of 8p, 9p (*CDKN2A*), 9q, 13q and 17p (*TP53*) have consistently been reported to be associated with unfavorable outcome of MCL patients. The loss of 8p and gain of 8q (*MYC*) are associated with leukemic presentation/progression and within this MCL subtype, loss of 6q is associated with shorter overall survival.

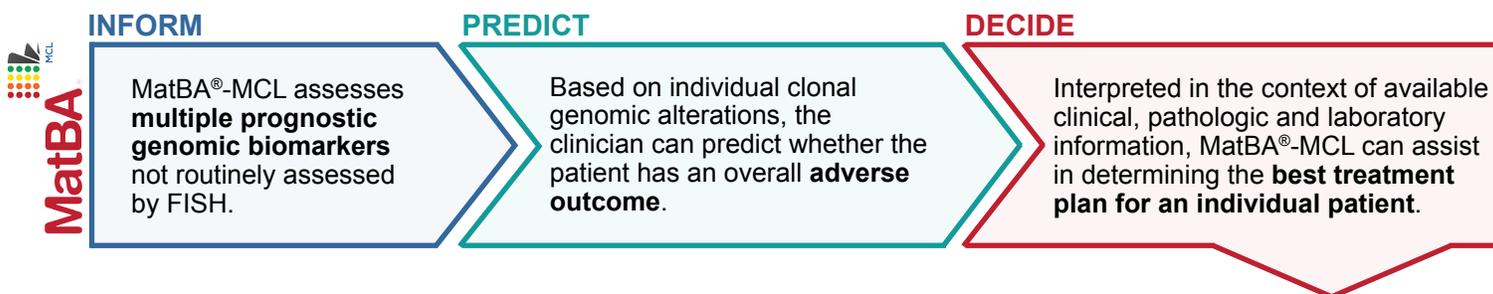
In order to assist in the prognosis of MCL, CGI has developed the mature B-cell neoplasms array (MatBA®) array-based comparative genomic hybridization (MatBA®-MCL Array-CGH). In a single assay, MatBA®-MCL Array-CGH assesses the gain/loss of nine genomic regions.

### Clinical Indications

MatBA®-MCL may assist in the prognosis of patient with newly-diagnosed MCL or suspected leukemic MCL.

### Methodology and Interpretation

DNA is extracted and fluorescently labeled by enzymatic procedures. Genomic gains and losses in the labeled DNA are detected by hybridization to a custom oligonucleotide array in the presence of labeled normal DNA. Quantitative PCR is used to confirm the detected genomic gains and losses. Results are reported as positive or negative for the gain or loss of each respective alteration.



### Assay Specifications

#### Sensitivity

Formalin-fixed paraffin-embedded (FFPE) specimens: 60-70%

Fresh-frozen specimens: 50-60%

Peripheral blood specimens: 30-40%

#### Reporting

Results are reported as positive or negative for the gain or loss of each respective alteration. Results of the assay should be interpreted in the context of available clinical, pathologic, and laboratory information. Identification of genomic gain/loss should not be used alone for the prognosis of MCL.

**TAT:** 10-14 days

**CPT Code:** 81479

#### Specimen Requirements

- FFPE block: containing ≥ 60% tumor. Minimum size: 2 mm x 2 mm tumor area, shipped at room temperature.
- Fresh-Frozen tissue: 0.2 cm<sup>3</sup> minimum (in OCT is acceptable) containing ≥50% tumor. Stored at -80°C /-20°C, shipped on dry ice.
- Peripheral blood: Minimum 3-5 ml, shipped at room temperature.

#### CGI Laboratory Licensure

CAP (Laboratory #: 7191582, AU-ID: 1434060), CLIA (Certificate #: 31D1038733), New Jersey (CLIS ID #: 0002299), New York State (PFI: 8192), Pennsylvania (031978), Florida (800018142), Maryland (1395).



Patient Name:
Sex: Male Female
Date of Birth:
Specimen:
Collected:
Received:
Reported:
Clinical Hx:

Accession Number:
CGI ID No:
Ordering Physician:
Client:
Client Account No:
Client ID No:
Client Address:
Telephone:

MatBA®-MCL Array-CGH Sample Report

Results:

Table with 2 columns: Genomic Aberrations, Result for Aberration. Rows include Loss of 6q21 (POSITIVE), Loss of 8p23.3-p21.3 (NEGATIVE), Loss of 9p21 (CDKN2A) (NEGATIVE), Loss of 9q22 (NEGATIVE), Loss of 13q14 (NEGATIVE), Loss of 17p13 (TP53) (NEGATIVE), Gain of 3q22-q27 (NEGATIVE), Gain of 8q24 (MYC) (POSITIVE), Gain of 12q13.13-q14.1 (NEGATIVE).

Interpretation: Positive for loss of 6q21 and gain of 8q24 (MYC).

Description:

The translocation t(11;14)(q13;q32) involving CCND1 at 11q13 and IGH at 14q32 is a characteristic chromosomal abnormality in mantle cell lymphoma (MCL), but gain and loss of other genomic loci are considered to have prognostic value. Array-CGH, CGH, and FISH studies have revealed the association of loss of 8p, 9p (CDKN2A), 9q, 13q, and 17p (TP53) and gain of 3q and 12q with shorter overall survival in MCL patients. Loss of 8p and gain of 8q (MYC) are associated with leukemic presentation/progression and in this setting, loss of 6q correlates with poor outcome.(1-5)

This assay utilizes microarray-based comparative genomic hybridization (array-CGH) to simultaneously detect the gain and loss of multiple loci in specimen DNA. The sensitivity of the assay is 60-70% for formalin-fixed paraffin-embedded, 50-60% for fresh frozen, and 30-40% for peripheral blood specimens. Samples in which the monoclonal B-cells are present at less than the assay sensitivity, aberrations may not be detected and will be reported as no genomic copy number alterations detected. The test results should not be used solely for prognostication and should be interpreted in the context of other clinical and laboratory findings.

References:

- 1. Viswanatha DS, et al: Blastic mantle cell leukemia: an unusual presentation of blastic mantle cell lymphoma. Mod Pathol 2000, 13:825-33
2. Parry-Jones N, et al: Cytogenetic abnormalities additional to t(11;14) correlate with clinical features in leukaemic presentation of mantle cell lymphoma, and may influence prognosis: a study of 60 cases by FISH. Br J Haematol 2007, 137:117-24
3. Salaverria I, et al: Specific secondary genetic alterations in mantle cell lymphoma provide prognostic information independent of the gene expression-based proliferation signature. J Clin Oncol 2007, 25:1216-22
4. Espinet B, Salaverria I, Bea S, et al: Incidence and prognostic impact of secondary cytogenetic aberrations in a series of 145 patients with mantle cell lymphoma. Genes Chromosomes Cancer 2010, 49:439-51
5. Royo C, et al: The complex landscape of genetic alterations in mantle cell lymphoma. Semin Cancer Biol 2011, 21:322-34

End of Report