MAYO CLINIC LABORATORIES

FREQUENTLY ASKED QUESTIONS

IGH SOMATIC HYPERMUTATION IN B-CLL

Q Can slides and blocks from previous studies be used for IGHV testing?

A For this testing a fresh blood or bone marrow aspirate sample is required.

Q When should I order IGHV mutation status testing for my CLL patients?

A According to the CLL International Prognostic Index (CLL-IPI), IGHV mutational status should be performed along with FISH testing when initially determining prognosis in CLL patients and to help inform treatment decisions. Additionally, IGHV mutation status, along with other prognostic factors, may assist with identification of patients who may benefit from Bruton tyrosine kinase (BTK) inhibitors or other current CLL therapies.

Q Does the IGH FISH probe offered in the prognostic CLL FISH panel cover the IGHV testing needs?

A No these are distinct tests that analyze different genetic prognostic factors. The FISH probes set evaluates for numerical or structural changes at the microscopic level in CLL cells and the IGHV somatic hypermutation assay looks at the clonal immunoglobulin heavy chain gene sequence (nucleotide base level) and determines if the patient-specific CLL IGH sequence is essentially similar to germline sequence (unmutated) or has acquired somatic mutations (mutated). Knowing that we are looking for point mutations at the DNA level, as well as possible targeted chromosomal variants, both FISH and molecular studies are needed to acutely address both types of abnormalities that could be present.

Q I've always ordered flow cytometry markers for CD38, ZAP70, and CD49. These are still important indicators, correct?

A Studies have shown only 70-75% concordance of CD38 and ZAP70 with IGHV mutational status. Thus, the use of these flow cytometry-based markers cannot be used as surrogates for the IGHV mutation status in determining prognosis and in subsequent treatment decisions. Some data suggests that CD49D may offer independent prognostic value, but it is not used as part of the CLL-IPI.

Q How often is repeat IGHV mutation analysis necessary? Is it necessary at all?

A There are always exceptions but, in general, the IGHV mutation status of a patient does not change. Typically, prognosis is established once at the time of diagnosis. However it's always important to pay attention not only to the IGHV mutation status but also the level of mutation % found in the initial IGHV results. If the patient presents at or very close to the 2% cutoff number, re-testing could be considered if there has been no treatment since that initial assessment.

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