Overview
Mutations in TP53 (Tumor Protein) are found in an estimated 10% of Chronic Lymphocytic Leukemia (CLL) patients at diagnosis. The majority of patients carry TP53 mutations with 17p13 deletion. However, ~5% of CLL patients harbor TP53 mutation in the absence of 17p13 deletion. The presence of TP53 mutation with or without 17p13 deletion has been associated with significantly poorer overall response rates to conventional DNA-damaging chemotherapy, shorter progression-free survival and overall survival. The most frequent TP53 mutations occur at codon 175, 179, 209, 248, 273 and 281. These mutations disrupt the DNA-binding and the transactivation activity of the protein. The assay covers any mutations in the Exon 5-9 and the adjacent splice junctions sequence.

Clinical Indications
Chronic Lymphocytic Leukemia.

Clinical Utility
TP53 mutation assay for patients at diagnosis or with progressive disease before having first-line treatment. Assists in CLL patient prognosis, clinical management and distinguishes patient populations that are unlikely to respond to the treatment with alkylating agents and purine analogues.

Methodology and Interpretation
Genomic DNA is extracted and amplified by PCR using primer sets flanking exons 5-9 of TP53. Amplification products are sequenced bi-directionally.

Assay Specifications

Sensitivity
Analytical sensitivity of this assay is 25%.

Specimen Requirements
• 2-3 ml peripheral blood or bone marrow in an EDTA tube (Lavender-top).
• Specimen should be stored, transported at room temperature or 2-8°C, and received within 48 hours of collection.

Reporting
Results are reported as positive or negative for the detection of a mutation in exons 5-9 of TP53. A negative result for TP53 mutation cannot entirely exclude the presence of a mutation outside Exons 5-9, or other loci involved in CLLs.

TAT
7-10 days

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)

CPT Codes
81404
TP53 MUTATION ASSAY SAMPLE REPORT

Results:

<table>
<thead>
<tr>
<th>Exon</th>
<th>Nucleotide Change</th>
<th>Amino Acid Change</th>
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<tbody>
<tr>
<td>5-6</td>
<td>17601C&gt;T</td>
<td>p.R196X</td>
</tr>
<tr>
<td>7-9</td>
<td>None Detected</td>
<td>None Detected</td>
</tr>
</tbody>
</table>

Interpretation: **Positive for TP53 mutation.**

Description:

TP53 (Tumor Protein 53) is located at chromosome 17p13 and encodes for a transcription factor that responds to diverse cellular stresses to regulate target genes that induce cell cycle arrest, apoptosis, senescence, DNA repair, or changes in metabolism. Somatic TP53 gene alterations are frequent in most human cancers and include mutations and deletions.

Mutations in TP53 are found in about 10% of untreated chronic lymphocytic leukemia (CLL) patients. More than 90% of mutations in CLL have been detected in Exons 5-9. Mutations are mostly detected in CLL patients also exhibiting 17p13 deletion. About 5% of CLL patients carry TP53 mutation in absence of 17p13 deletion. (1, 2, 3). The presence of TP53 mutations in CLL has been associated with shorter progression-free survival, overall survival as well as poorer response rates to the chemotherapy (4).

Genomic DNA is extracted and amplified by PCR using two pairs of primers flanking Exons 5-9 of TP53. Amplification products are sequenced bi-directionally. Results are reported as positive or negative for the detection of a mutation. Analytical sensitivity of this assay is 25% of mutant in a background of wild-type genomic DNA. A negative result cannot entirely exclude the presence of TP53 mutations in the specimen. Mutation results should be interpreted in conjunction with other clinical information and laboratory test results such as IGHV mutation status and FISH (5).

References:


End of Report