Chronic Lymphocytic Leukemia Mutation Panel by Next Generation Sequencing

Last Literature Review: December 2019 Last Update: July 2023

Chronic lymphocytic leukemia (CLL) is a hematopoietic disorder characterized by chronic monoclonal B-cell proliferation. Recent studies have identified recurrently mutated genes with diagnostic and/or prognostic impact in CLL and other lymphoid malignancies. The presence of certain mutations may inform clinical management. This multigene panel by massively parallel sequencing (next generation sequencing) is a more cost-effective approach when compared to the cost of multiple single gene tests. This test can be used to complement the morphologic and cytogenetic workup of CLL and other lymphoid malignancies.

Featured ARUP Testing

Chronic Lymphocytic Leukemia Mutation Panel by Next Generation Sequencing 3001858

Method: Massively Parallel Sequencing

For more information on the testing strategy for CLL, refer to ARUP Consult's Chronic Lymphocytic Leukemia topic.

Disease Overview

Diagnostic Issues

- Genetic targets contained in the panel are relevant in CLL and other lymphoid malignancies
- Identification of one or more clonal genetic abnormalities may aid in establishing the diagnosis of a neoplasm, but results must be interpreted within the context of other clinical and hematologic findings
- Identification of certain variants or patterns of variants may aid in prognostication of patients with CLL

Prognostic and Treatment Issues

- Certain variants or patterns of variants may have prognostic significance
- Certain variants may be sensitive to or provide resistance to targeted therapies

Genetics

Genes Tested

ATM, *BCL2*, *BIRC3*, *BRAF*, *BTG1*, *BTK*, *CARD11*, *CD79B*, *CXCR4*, *DDX3X*, *FBXW7*, *IKZF3*, *KRAS*, *MAP2K1*, *MED12*, *MGA*, *MYD88*, *NOTCH1*, *NRAS*, *PLCG2*, *POT1*, *RNASEH2A*, *RNASEH2B*, *RPS15*, *SAMHD1*, *SF3B1*, *TP53*, *XPO1*, *ZMYM3*

For some genes, one or more exons of the preferred transcript are not covered by sequencing for the indicated gene. See the Genes Tested table below for full list of targeted regions and exclusions.

Test Interpretation

Results

- Positive: a somatic variant in one of the tested genes was detected
  - Clinical relevance will be described, if known
- Negative: no variants were detected in the sequenced genes

Limitations

- A negative result does not exclude a diagnosis of CLL
- Not intended to detect minimal residual disease (MRD)
- This test does not determine *IGHV* mutation status
- Variants may be present below the limit of detection (LOD) of 5% allele frequency
- Variants greater than 24 base pairs may be detected at LOD, but the analytical sensitivity may be reduced
- Variants may not be identified due to technical limitations in the presence of pseudogenes or in repetitive or homologous regions

- Variants in regions that are not included in the preferred transcript for the targeted genes will not be detected; see Genes Tested table below for full list of targeted regions and exclusions
- Interpretation of this test result may be impacted if this patient has had an undisclosed allogenic bone marrow transplant or stem cell transplant
- Does not detect translocations, gene rearrangements, copy number alterations, or microsatellite instability
- Does not distinguish between somatic and germline variants

Analytic Sensitivity

Variant Class	Analytic Sensitivity (PPA)[a] Estimate (%)	Analytic Sensitivity (PPA) 95% Credibility Region[a] (%)
SNVs	96.9	95.1-98.1
Insertions/duplications (1-24bp)	98.1	95.5-99.3
Insertions/duplications (>24bp)	>99	92.9-100.0
Deletions (1-24bp)	96.7	92.8-98.7
Deletions (>24bp)	90	79.5-96.1
MNVs	97	93.0-99.0

[a]Genes included on this test are a subset of a larger methods-based validation from which the PPA values are derived.

bp, base pairs; MNVs, multinucleotide variants; PPA, positive percent agreement; SNVs, single nucleotide variants

Genes Tested

Gene	Preferred Transcript[a, b]
ATM	NM_000051
BCL2	NM_000633
BIRC3	NM_001165 (exon 5 excluded)
BRAF	NM_004333
BTG1	NM_001731
BTK	NM_000061
CARD11	NM_032415
CD79B	NM_000626
CXCR4	NM_003467
DDX3X	NM_001193416
FBXW7	NM_033632

[a]This is the transcript number used for analyzing and reporting variants. The transcript version number may change periodically and thus is not listed here. The transcript with version number will be included on the patient's report if a variant is detected in the gene.

[b]Noncoding exons are not analyzed, except for regions containing known clinically relevant variants in the NOTCH1 3'UTR. In addition, coding exons noted here as excluded are not sequenced due to technical limitations of the assay.

Gene	Preferred Transcript[a, b]
IKZF3	NM_012481
KRAS	NM_004985
MAP2K1	NM_002755
MED12	NM_005120
MGA	NM_001164273
MYD88	NM_002468
NOTCH1	NM_017617
NRAS	NM_002524
PLCG2	NM_002661
POT1	NM_015450
RNASEH2A	NM_006397
RNASEH2B	NM_024570
RPS15	NM_001018 (exon 3 excluded)
SAMHD1	NM_015474
SF3B1	NM_012433
TP53	NM_000546
XPO1	NM_003400
ZMYM3	NM_201599

[a]This is the transcript number used for analyzing and reporting variants. The transcript version number may change periodically and thus is not listed here. The transcript with version number will be included on the patient's report if a variant is detected in the gene.

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Related Information

Chronic Lymphocytic Leukemia - CLL