Client: ARUP Example Report Only
500 Chipeta Way
Salt Lake City, UT 84108
UNITED STATES

Physician: EXAMPLE, PHYSICIAN

Patient: RAML EU, pos

DOB	
Sex:	Unknown
Patient Identifiers:	56913
Visit Number (FIN):	57302
Collection Date:	2/7/2024 09:02

Rapid Acute Myeloid Leukemia Targeted Therapy Mutation Panel

ARUP test code 3017050

Rapid AML Interp

See Note

Rapid AML Targeted Therapy Mut Panel

Submitted diagnosis or diagnosis under consideration for variant interpretation: Acute myeloid leukemia

Result:

Variants of Known Clinical Significance in Hematologic Malignancies

1. KIT c.1250_1256delinsGAAC, p.Thr417_Asp419delinsArgThr (NM_000222.3)
VAF: 22.4%

2. TP53 c.530C>T, p.Pro177Leu (NM_000546.6)
VAF: 3.4%

Variants of Unknown Clinical Significance in Hematologic Malignancies

None found

This result has been reviewed and approved by [redacted]

Low coverage regions:
Listed below are regions where the average sequencing depth (number of times a particular nucleotide is sequenced) in at least 20% of the region-of-interest is less than our stringent cutoff of 300. Sensitivity for detection of low allelic frequency variants may be reduced in areas with reduced depth of coverage.
None

BACKGROUND INFORMATION: Rapid Acute Myeloid Leukemia Targeted Therapy Mutation Panel

CHARACTERISTICS: Acute myeloid leukemia (AML) is a genetically heterogeneous hematologic malignancy characterized by the clonal expansion of myeloid blasts (e.g., undifferentiated myeloid precursors) in the peripheral blood, bone marrow, and/or other tissues, which results in impaired hematopoiesis and bone marrow failure. AML is the most common acute leukemia in adults (approximately 80 percent of leukemia cases) and accounts for the largest number of annual deaths from leukemia in the United States. The median age at diagnosis is 67 years, and 54 percent of patients are diagnosed at 65 years or older. Advances in the

treatment of AML have led to significant improvement in outcomes for younger patients; however, prognosis in the elderly, in whom the majority of new cases occur, remains poor. Recent studies have identified recurrently mutated genes with diagnostic and/or prognostic impact in AML. The presence of certain mutations may inform clinical management. This test has a fast turnaround time, which is critical in the timely identification of prognostic markers and advantageous in immediate patient management. Furthermore, it is more cost effective than the use of multiple single gene tests and can be used to complement the morphologic and cytogenetic workup of AML.

GENES TESTED: The following regions are targeted to detect clinically relevant hotspot mutations, unless otherwise indicated: CEBPA* (NM_004364) exon 1; FLT3 (NM_004119) exons 14, 15, 16, 20; IDH1 (NM_005896) exon 4; IDH2 (NM_002168) exon 4; KIT (NM_000222) exons 8, 9, 10, 11, 17; KRAS (NM_004985) exons 2, 3, 4; NPM1 (NM_002520) exon 11; NRAS (NM_002524) exons 2, 3, 4; TP53* (NM_000546) all coding exons
*CEBPA and TP53 are fully covered; any clinically relevant or potentially relevant variants will be reported. More information about the targeted regions of this test is included in the Additional Technical Information available in the Laboratory Test Directory.

METHODOLOGY: Genomic DNA was isolated from peripheral blood or bone marrow and then enriched for the targeted exonic regions of the tested genes. The variant status was determined by massively parallel sequencing. The hg19 (GRCh37) human genome assembly was used as a reference for identifying genetic variants. Clinically relevant hotspot variants are reported.

LIMITATIONS: Variants outside the targeted regions or below the limit of detection are not identified. Variants other than hotspot mutations may not be reported. Variants in regions that are not included in the targeted coding exons of the preferred transcript for the targeted genes are not detected. Variants at exon-intron boundaries may not be detected. In some cases, variants may not be identified due to technical limitations in the presence of pseudogenes, GC-rich, repetitive or homologous regions, or regions overlapping with primers designed for target enrichment. It is also possible large insertion/deletion variants may not be identified. RNA variants, gene fusions, copy number variants, translocations, and other structural variants are not detected by this test. Variant allele frequency (VAF) is not reported for FLT3-ITD mutations and FLT3-ITD mutations larger than 126 base pairs (bp) or in regions overlapping with primers may not be detected. Interpretation of this test result may be impacted if this patient has had an undisclosed allogeneic bone marrow transplant or stem cell transplant. This test does not distinguish between somatic and germline variants.

LIMIT OF DETECTION (LOD): 5 percent variant allele frequency (VAF) for single nucleotide variants (SNV) and small variants less than 25 bp; 10 percent VAF for FLT3-ITDs (3-126 bp). Variants greater than 25 bp may be detected at LOD, but the analytical sensitivity may be reduced.

ANALYTICAL SENSITIVITY: The positive percent agreement (PPA) estimates for the respective variant classes (with 95 percent credibility region) are listed below.
Single nucleotide variants (SNVs): 98.9 percent (95.2-99.8 percent)
Insertions/deletions/multiple nucleotide variants (1-25bp): >99 percent (96.2-99.9 percent)
FLT3-ITDs: 97.7 percent (90.1-99.8 percent)

CLINICAL DISCLAIMER: Results of this test must always be interpreted within the context of clinical findings and other relevant data and should not be used alone for a diagnosis or

management of malignancy. This test is not intended to detect minimal residual disease.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the U.S. Food and Drug Administration. This test was performed in a CLIA-certified laboratory and is intended for clinical purposes.

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Rapid AML Interp	24-038-101756	2/7/2024 9:02:00 AM	2/7/2024 9:02:27 AM	2/8/2024 2:15:00 PM

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