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

Physician: TEST,

Patient: MYE NGS, Positive Example

DOB	4/1/1961
Gender:	Male
Patient Identifiers:	29122
Visit Number (FIN):	29427
Collection Date:	4/1/2021 12:18

Myeloid Malignancies Mutation Panel by Next Generation Sequencing

ARUP test code 2011117

Myeloid Malignancy Proposed Diagnosis	AML unspec
Myeloid Malignancies Panel Specimen	Whole Blood
Myeloid Malignancies Panel Interp	See Note Myeloid Malignancies Mutation Panel NGS Submitted diagnosis or diagnosis under consideration for variant interpretation: Acute myeloid leukemia, unspecified (AML unspec) TIER 1: Variants of Known Clinical Significance in Hematologic Malignancies 1. KIT c.2447A>T, p.Asp816Val (NM_000222.2) VAF: 40.3% KIT encodes a receptor tyrosine kinase that is involved in signaling associated with cell survival, proliferation, and differentiation (7). Somatic mutations of KIT are found in 4-6% of acute myeloid leukemia (AML) patients, with the highest incidence (17-41%) in AML patients with t(8;21) or inv(16) abnormalities (known as core binding factor AML) (3) (1) (8) (10) (15) (16) (19), and in approximately 2% of MDS patients (12). In AML patients with t(8;21) or inv(16), KIT activating mutations occur most frequently in exon 17, most commonly affecting codon Asp816 (as seen here) (13). In AML patients with t(8;21), KIT mutations correlate with a higher risk of relapse and shorter overall survival (3) (4) (13) (14) (15) (18). In AML patients with inv(16), one study found that mutated KIT correlates with poor prognosis (14), while other studies found no prognostic impact associated with KIT mutations (3) (13) (15). Another study also showed that KIT mutations present at a variant allele frequency of 25% or greater are associated with a higher risk of relapse in patients with core binding factor AML (2). In AML patients with normal karyotype, KIT codon Asp816 mutations did not correlate with clinical outcomes (18). 2. PTPN11 c.179G>T, p.Gly60Val (NM_002834.3) VAF: 43.8% PTPN11 encodes SHP-2, a non-receptor protein tyrosine phosphatase that relays signals from activated growth factor receptors to RAS and other signaling molecules (11). PTPN11 mutations are found in approximately 5-7% of

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patients with AML (1) (5) (9) (20). Germline PTPN11 mutations are also found in approximately 50% of individuals with Noonan syndrome, and these individuals are at an increased risk for development of a myeloid neoplasm (17). This particular missense mutation occurs in the N-terminal SH2 domain and has been reported in myeloid malignancies (6). In AML patients, PTPN11 mutations are associated with mutated NPM1 (9). PTPN11 mutations do not correlate with survival in adult AML patients overall or AML patients with NPM1 mutations but do correlate with poor outcome in the subgroup of AML patients without NPM1 mutations in one study with a very small number of patients (9).

TIER 2: Variants of Unknown Clinical Significance in Hematologic Malignancies

None found

References

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This result has been reviewed and approved by [redacted]

Low coverage regions:
This list contains regions where the average sequencing depth (number of times a particular position is sequenced) for 20% or more of the region is below our stringent cutoff of 300. Sensitivity for detection of low allelic frequency mutations may be reduced in areas with low depth of coverage. The sequencing reads from these regions were manually reviewed. If high quality variants are detected in these regions they will be listed above in Tier 1 or Tier 2.

None

BACKGROUND INFORMATION: Myeloid Malignancies Panel Interp

CHARACTERISTICS: Myeloid malignancies are clonal disorders of hematopoietic stem and progenitor cells that include myelodysplastic syndromes (MDS), myeloproliferative neoplasms (MPN), myelodysplastic/myeloproliferative neoplasms (MDS/MPN), and acute myeloid leukemia (AML). Recent studies have identified recurrently mutated genes with diagnostic and/or prognostic impact in myeloid malignancies. The presence of certain mutations may inform clinical management. This multi-gene 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 myeloid malignancies.
GENES TESTED: ANKRD26, ASXL1, ASXL2, BCOR, BCORL1, BRAF, CALR, CBL, CBLB, CEBPA, CSF3R, CUX1*, DDX41, DNMT1*, DNMT3A, ELANE, ETNK1, ETV6, EZH2, FBXW7, FLT3, GATA1, GATA2, GNAS, HNRNPK, IDH1, IDH2, IL7R, JAK1, JAK2, JAK3, KDM6A*, KIT, KMT2A, KRAS, LUC7L2, MPL, NOTCH1, NPM1*, NRAS, NSD1, PHF6, PIGA, PRPF40B, PRPF8, PTPN11, RAD21, RUNX1, SETBP1, SF3B1, SH2B3, SMC1A, SMC3, SRSF2, STAG2, STAT3, STAT5B*, SUZ12*, TET2, TP53, U2AF1, U2AF2, WT1, ZRSR2.
* - One or more exons of the preferred transcript were not covered by sequencing for the indicated gene; see limitations section below.
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 of the targeted genes was determined by massively parallel sequencing. The hg19 (GRCh37) human genome assembly was used as a reference for identifying genetic variants.
LIMITATIONS: Variants outside the targeted regions or below the limit of detection are not identified. Variants in regions that are not included in the preferred transcript for the targeted

genes are not detected. In some cases, variants may not be identified due to technical limitations in the presence of pseudogenes or in repetitive or homologous regions. It is also possible some insertion/deletion variants may not be identified. The following regions were not sequenced due to technical limitations of the assay:
CUX1 (NM_181552) exon 24
DNMT1 (NM_001130823) exon 5
KDM6A (NM_001291415) exon 13
NPM1 (NM_002520) exon 1
STAT5B (NM_012448) exons 6-9
SUZ12 (NM_015355) exons 1-9
LIMIT OF DETECTION (LOD): 5 percent variant allele fraction (VAF) for single nucleotide variants (SNV) and small variants less than 24 base pairs (bp). Variants greater than 24bp may be detected at LOD, but the analytical sensitivity may be reduced.
ANALYTICAL SENSITIVITY: The positive percent agreement (PPA) estimate for the respective variant classes (with 95 percent credibility region) are listed below. Genes included on this test are a subset of a larger methods-based validation from which the PPA values are derived.
Single nucleotide variants (SNVs): 96.9 percent (95.1 - 98.1 percent)
Insertions/Duplications (1-24bp): 98.1 percent (95.5 - 99.3 percent)
Insertions/Duplications (greater than 24bp): > 99 percent (92.9 - 100.0 percent)
Deletions (1-24bp): 96.7 percent (92.8 - 98.7 percent)
Deletions (greater than 24bp): 90 percent (79.5 - 96.1 percent)
Multi-nucleotide variants (MNVs): 97 percent (93.0 - 99.0 percent)
FLT3 ITDs: Greater than 99 percent (97.1 - 100.0 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 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 US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.

EER Myeloid Malignancies Panel by NGS

See Note

Access ARUP Enhanced Report using the link below:

-Direct access: [redacted]

H=High, L=Low, *=Abnormal, C=Critical

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Myeloid Malignancy Proposed Diagnosis	21-091-110484	4/1/2021 12:18:00 PM	4/1/2021 12:18:00 PM	4/7/2021 10:48:00 AM
Myeloid Malignancies Panel Specimen	21-091-110484	4/1/2021 12:18:00 PM	4/1/2021 12:18:00 PM	4/7/2021 10:48:00 AM
Myeloid Malignancies Panel Interp	21-091-110484	4/1/2021 12:18:00 PM	4/1/2021 12:18:00 PM	4/7/2021 10:48:00 AM
EER Myeloid Malignancies Panel by NGS	21-091-110484	4/1/2021 12:18:00 PM	4/1/2021 12:18:00 PM	4/7/2021 10:48:00 AM

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