NGS for Myeloid Neoplasm (MNGS)

Warde Medical Laboratory
300 W Textile Rd
Ann Arbor, MI 48109

Powered By Pierian

PATIENT	DOB	DISEASE	MRN	REPORT DATE	REPORT STATUS
Test Patient2	01/02/2000	Myeloid neoplasm	0000111		Final

REPORT SUMMARY

Executive Summary

No mutations of potential clinical importance are detected.

Reviewed by Kajal Sitwala, MD Ph.D.

Genomic Findings

IA	IB	IIC	IID
No variants reported.	No variants reported.	No variants reported.	No variants reported.

CLINICALLY RELEVANT RESULTS

Tier I - Strong Clinical Significance

No variants were reported for this classification tier.

Tier II - Potential Clinical Significance

No variants were reported for this classification tier.

FREE TEXT

TIER III - VARIANTS OF UNCERTAIN SIGNIFICANCE

No variants were reported for this classification tier.

PATIENT	DOB	DISEASE	MRN	REPORT DATE	REPORT STATUS
Test Patient2	01/02/2000	Myeloid neoplasm	0000111		Final

CLASSIFICATION AND LEVELS OF EVIDENCE

The variant classification system used in this report is based on joint consensus recommendations of the Association for Molecular Pathology, American Society of Clinical Oncology, and the College of American Pathologists (J Mol Diagn 2017, 19:4-23). Tiers IA, IB, IIC, IID, III and IV describe variant categories of descending clinical significance in the patient. Variants in Tier IV are not reported in accordance with the consensus recommendations.

IA	IB	IIC	IID
Variant of strong clinical significance, Level A evidence (FDA approved therapy or practice guideline in patient's tumor type)	Variant of strong clinical significance, Level B Evidence (consensus in the field based on well-powered studies in patient's tumor type)	Variant of potential clinical significance, Level C evidence (FDA approved therapy or practice guideline in other tumor type(s), evidence from multiple small published studies, or based on availability of investigational therapies)	Variant of potential clinical significance, Level D evidence (case reports or preclinical studies)

III	Variant of uncertain clinical significance

IV	Benign or likely benign variant

TEST DETAILS

REPORTED GENES

ABL1, *ANKRD26*, *ASXL1*, *ATRX*, *BCOR*, *BCORL1*, *BRAF*, *BTK*, *CALR*, *CBL*, *CBLB*, *CBLC*, *CCND2*, *CDC25C*, *CDKN2A*, *CEBPA*, *CSF3R*, *CUX1*, *CXCR4*, *DCK*, *DDX41*, *DHX15*, *DNMT3A*, *ETNK1*, *ETV6*, *EZH2*, *FBXW7*, *FLT3*, *GATA1*, *GATA2*, *GNAS*, *HRAS*, *IDH1*, *IDH2*, *IKZF1*, *JAK2*, *JAK3*, *KDM6A*, *KIT*, *KMT2A*, *KRAS*, *LUC7L2*, *MAP2K1*, *MPL*, *MYC*, *MYD88*, *NF1*, *NOTCH1*, *NPM1*, *NRAS*, *PDGFRA*, *PHF6*, *PPM1D*, *PTEN*, *PTPN11*, *RAD21*, *RBBP6*, *RPS14*, *RUNX1*, *SETBP1*, *SF3B1*, *SH2B3*, *SLC29A1*, *SMC1A*, *SMC3*, *SRSF2*, *STAG2*, *STAT3*, *TET2*, *TP53*, *U2AF1*, *U2AF2*, *WT1*, *XPO1*, *ZRSR2*

CGW VERSION

CGW_v6.26

DATABASE DETAILS

The versions, releases, builds, dates of the following databases were used to generate this report.

- Genomic Build: GRCh37.p13
- Genomic Annotation Sources: NCBI RefSeq v105
- dbSNP: 149
- COSMIC: v98
- gnomAD: r2.1
- dbNSFP: 4.3c
- NHLBI ESP: v.0.0.30
- dbscSNV: v1.1
- ClinVar: 20230403
- ExAC: v1.0

PATIENT	DOB	DISEASE	MRN	REPORT DATE	REPORT STATUS
Test Patient2	01/02/2000	Myeloid neoplasm	0000111		Final

CODING EXON COVERAGE METRICS

Level 2: 200x coverage for > 95% of positions was not achieved for the targeted exon regions listed below:

Gene Transcript ID (Exon/Intron('))					
ABL1 NM_005157.4 (7)	*BRAF* NM_004333.4 (15)	*DHX15* NM_001358.2 (3)	*DNMT3A* NM_022552.4 (6)	*EZH2* NM_004456.4 (6)	*EZH2* NM_004456.4 (10)
EZH2 NM_004456.4 (14)	*IDH1* NM_005896.2 (3)	*KMT2A* NM_005933.3 (15)	*KRAS* NM_004985.3 (4)	*NF1* NM_000267.3 (4)	*PTPN11* NM_002834.3 (7)
SF3B1 NM_012433.2 (17)	*STAG2* NM_006603.4 (24)	*TP53* NM_000546.5 (10)	*U2AF1* NM_006758.2 (2)		

METHODOLOGY

Assay Methods: Warde Medical Laboratory's MNGS test is a targeted next-generation sequencing (NGS) assay designed to identify genomic alterations in whole blood and bone marrow samples. The MNGS test uses Anchored-Multiplex PCR enrichment chemistry (Integrated DNA Technology) and is designed to detect multiple classes of variants including single nucleotide variants (SNVs), small insertions/deletions (indels), internal tandem duplications (ITDs), and certain copy number variations (CNVs) in selected genes relevant to Myeloid Neoplasms.

DNA specimens are extracted from a whole blood or bone marrow. Preparation of sequencing libraries includes end repair of enzymatically fragmented DNA, annealing of universal adaptors with sample indices and molecular barcodes, and target enrichment with VariantPlex gene-specific primers. Denatured library pools are sequenced using Illumina v2 or v3 reagents on a MiSeq with a minimum target depth of 3 million reads per sample.

Bioinformatic Analysis Methods: Sequencing files are uploaded to Archer Analysis Unlimited (AAU) Platform v7.1 for identification of genomic alterations according to the human genome reference build GRCh37 (hg19). Variant classification files are then uploaded to Clinical Genomic Workspace (Velsera) for variant classification and report generation. Variants are reported according to HGVS nomenclature (hgvs-nomenclature.org) and classified according to the AMP classification system into tiers IA, IB, IIC, IID, III and IV. These tiers are stratified by clinical utility ('actionability' for clinical decision-making as to diagnosis, prognosis, treatment options, and carrier status) and previously reported data in the medical literature. Variations found in gnomAD (https://gnomad.broadinstitute.org/) that have 1% minor allele frequency (except those that are also in Clinvar denoted as clinically relevant, used in a clinical diagnostic assays, or reported as a mutation in a publication) are classified as tier IV benign variants. Tier IV variants are not included in the report.

Test Performance: Single base substitutions, small indels, and small duplications (up to 100 bp): accuracy >99%; reproducibility >99%; sensitivity ≥5% variant allele fraction (VAF) with coverage ≥200x. Larger indels (101 bp to 1 kb) will be reported if observed with a VAF ≥5% and coverage ≥200x. Events larger than 1 kb such as gene-level copy number variants (CNVs) may be identified and gain/loss will be reported when detected at coverage ≥200x.

Additional Notes:

- Copy Number Variation (CNV) is assessed using a group of CNV-normal control samples as a baseline.
- This assay is clinically validated for the detection of somatic variants in samples of myeloid-origin malignancies.

PATIENT	DOB	DISEASE	MRN	REPORT DATE	REPORT STATUS
Test Patient2	01/02/2000	Myeloid neoplasm	0000111		Final

• It is possible that pathogenic variants may not be reported by one or more of the tools because of the parameters used. However, tool parameters were optimized to maximize specificity and sensitivity.

DISCLAIMER

This Report was generated using the materials and methods described above, which required the use of various reagents, protocols, instruments, software, databases, and other items, some of which were provided or made accessible by third parties. A defect or malfunction in any such reagents, protocols, instruments, software, databases, and/or other items may compromise the quality or accuracy of the Report.

The Report has been created based on, or incorporates references to, various scientific manuscripts, references, and other sources of information, including without limitation manuscripts, references, and other sources of information that were prepared by third parties that describe correlations between certain genetic mutations and particular diseases (and/or certain therapeutics that may be useful in ameliorating the effects of such diseases). Such information and correlations are subject to change over time in response to future scientific and medical findings. **Warde Medical Laboratory** makes every effort to monitor the information used to generate a report and will issue a corrected report when information changes.

The Report must always be interpreted within the clinical context. A physician should always consider the Report along with all other pertinent information and data prior to providing a diagnosis to a patient or developing and implementing a plan of care for a patient. The Report should never be considered or relied upon alone in making any diagnosis or prognosis. The manifestation of many diseases are caused by more than one gene variant, a single gene variant may be relevant to more than one disease, and certain relevant gene variants may not have been considered in the Report. In addition, many diseases are caused or influenced by modifier genes, epigenetic factors, environmental factors, and other variables that are not addressed by the Report (or that are otherwise unknown). This Report is based on an NGS assay which does not distinguish between somatic and germline variants. As such, the relevance of the Report should be interpreted in the context of a patient's clinical manifestations.

The test performance characteristics were determined by **Warde Medical Laboratory**. The Report was generated by the **Warde Medical Laboratory** as required by the CLIA 1988 regulations. The Report, and the tests used to generate the Report, have not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary. The test results have been shown to be clinically useful. This laboratory is CLIA certified to perform high complexity testing.

REFERENCES

PATIENT AND ORDER DETAILS

PATIENT	PHYSICIAN	SPECIMEN	CASE
DATE OF BIRTH 01/02/2000 SEX	FACILITY Warde Lab ORDERING PHYSICIAN Kajal Sitwala	SPECIMEN TYPE Blood specimen EXT. SPECIMEN ID DATE COLLECTED 02/12/2024 DATE RECEIVED 02/12/2024	DATE REPORTED