Meridian Molecular Diagnostics

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MYELOID NEOPLASM NEXT-GENERATION SEQUENCING PANEL (54-GENE) — FINAL REPORT

PATIENT	SPECIMEN	REQUESTED BY
DOE, JONATHAN R. MRN MRN-4471902 | DOB 1967-09-14 58 y / Male	Reference accession MMD-26-NGS-22150 Client accession S26-BM-01187 Bone marrow aspirate, EDTA Collected 2026-04-22	Riverbend Regional Medical Center A. Patel, MD Received 2026-04-25 Reported 2026-05-04

CLINICAL HISTORY (PROVIDED BY ORDERING SITE)

58-year-old man with three weeks of progressive fatigue, dyspnea on exertion, gingival bleeding, and scattered lower-extremity ecchymoses. CBC on admission: WBC 38.4 x10^9/L, hemoglobin 7.9 g/dL, platelets 31 x10^9/L. Peripheral smear with 41% circulating blasts, some with folded nuclei and abundant cytoplasm. No prior hematologic history, no prior chemotherapy or radiation. Bone marrow performed to evaluate for acute leukemia.

RESULT SUMMARY

POSITIVE — Clinically significant variants detected. **NPM1** (Tier I), **FLT3** internal tandem duplication (Tier I), and **DNMT3A** (Tier II) identified. See variant table and interpretation.

DETECTED VARIANTS

Gene	Variant (HGVS)	Consequence	VAF	Tier
NPM1	`NM_002520.7:c.860_863dup` `p.(Trp288CysfsTer12)`	Frameshift insertion (type A, 4-bp TCTG duplication)	**39%**	**I**
FLT3	`Internal tandem duplication, exon 14 (~36 bp insertion)`	In-frame ITD; ITD/WT allelic ratio 0.62	**31%**	**I**
DNMT3A	`NM_022552.5:c.2645G>A` `p.(Arg882His)`	Missense, R882 hotspot	**44%**	**II**

Tier I: variants of strong clinical significance. Tier II: variants of potential clinical significance. VAF = variant allele frequency. FLT3-ITD allelic ratio estimated by fragment analysis run in parallel.

SELECTED GENES WITH NO REPORTABLE VARIANT

No reportable variant detected in: CEBPA, RUNX1, TP53, ASXL1, IDH1, IDH2, NRAS, KRAS, KIT, TET2, SRSF2, U2AF1, SF3B1, EZH2, BCOR, STAG2, PTPN11, WT1, PHF6, ZRSR2, JAK2, CALR, MPL, SETBP1, CSF3R, NF1, RAD21, GATA2, ETV6, CBL. (Full 54-gene list and coverage metrics in appendix retained by the laboratory.)

INTERPRETATION

This myeloid NGS panel identifies a **mutated NPM1** variant (type A frameshift insertion, VAF 39%) together with a **FLT3 internal tandem duplication** (VAF 31%, ITD/WT allelic ratio 0.62) and a **DNMT3A** R882H missense variant (VAF 44%). In the context of an acute myeloid leukemia established by the morphology and flow cytometry studies, mutated NPM1 is a World Health Organization and ICC disease-defining genetic abnormality; the diagnosis is therefore **acute myeloid leukemia with mutated NPM1**, and a blast threshold of 20% is not required for this entity. The concurrent FLT3-ITD is prognostically adverse and is a target for FLT3 inhibitor therapy; the allelic ratio is reported to support treatment decisions. The DNMT3A R882H variant is commonly co-mutated with NPM1 and FLT3-ITD and is frequently a clonal hematopoiesis founder event; it does not by itself define or change the WHO/ICC disease category, and is reported here for completeness and potential prognostic relevance. Correlation with morphology, flow cytometry, and cytogenetics is recommended; this report is one component of the integrated diagnostic workup.

METHODOLOGY & LIMITATIONS

Hybrid-capture targeted NGS of 54 myeloid-associated genes performed on genomic DNA from bone marrow. Mean target coverage 1,150x; minimum 250x. Analytical sensitivity approximately 5% VAF for single-nucleotide variants and small indels; FLT3-ITD detection supplemented by capillary fragment analysis. The assay does not reliably detect large structural rearrangements, copy-number changes, or variants in regions of low coverage or high homology. A negative result does not exclude a mutation below the limit of detection. This laboratory-developed test was validated by Meridian Molecular Diagnostics; it has not been cleared or approved by the FDA.

Electronically signed: Okafor, Daniel U., MD, PhD, Laboratory Director, and Lucia M. Fernandez, PhD, Variant Scientist — 2026-05-04. Results released to ordering institution for integration into the combined hematopathology report.