BACKGROUND:
Acute myeloid leukemia with mutated NPM1, in the absence of a coexisting internal tandem duplication in the FMS-like tyrosine kinase 3 gene (FLT3 ITD), is associated with a favorable prognosis in patients with normal cytogenetics and other intermediate risk karyotypes.\(^1\)\(^4\) The NPM1 gene is located at chromosome 5q35 and contains 12 exons. NPM1 encodes for nucleophosmin, a 37 kDa nucleolar chaperone protein that shuttles between the nucleus and cytoplasm. Somatic heterozygous length mutations in NPM1 exon 12 are present in approximately 35% of adult AML cases, including up to 60% of those with normal cytogenetics, but are found in only 8% of childhood AML.\(^5\)\(^6\) NPM1 exon 12 mutations produce C-terminus changes that result in abnormal cytoplasmic localization of nucleophosmin. These mutations are associated with FLT3 ITD in approximately 40% of cases.\(^5\)

In adults, NPM1-mutated AML is strongly associated with acute myelomonocytic and acute monocytic leukemias. Approximately 80 – 90% of acute monocytic leukemias have NPM1 length mutations.\(^1\)

REASONS FOR REFERRAL:
Risk stratification in patients with cytogenetically normal AML.

METHOD:
NPM1 exon 12 mutations are detected by PCR amplification with fluorescently labeled primers and capillary electrophoresis-based fragment analysis.

LIMITATIONS:
This assay will only detect known length mutations in NPM1 exon 12. Rare mutations in other exons will not be detected. The lower limit of detection of the assay is approximately 5%. This assay is expected to detect >99% of NPM1 exon 12 length mutations that are present at a level of 5% or greater at >99% specificity.

REFERENCE INTERVAL:
No mutation detected.
Sequence variations are reported using standard nomenclature.

SPECIMEN REQUIREMENTS:
3-5 ml EDTA (lavender top) whole blood or 2-5 ml EDTA bone marrow or DNA, high quality, ≥ 500ng at 25ng/ul.
SHIPPING REQUIREMENTS:
Place the room temperature specimen and requisition in plastic bags, seal and insert in a Styrofoam container. Seal the Styrofoam container, place in a sturdy cardboard box and tape securely. Ship the package in compliance with your overnight carrier guidelines. Address package to:

Client Services/Molecular Oncology Laboratory  
BloodCenter of Wisconsin  
638 N. 18th Street  
Milwaukee, WI 53233  
800-245-3117, ext. 6250

TURNAROUND TIME: 3-6 days

CPT CODES: 81310

PANEL ORDERING:
AML post-FLT3 Comprehensive Mutation Panel Turnaround Time: 7-10 days
- NPM1 Mutation Analysis CPT Codes: 81310
- CEBPA Mutation Analysis CPT Codes: 81403
- DNMT3A Exon 23 Sequence Analysis CPT Codes: 81403
- IDH1 Exon 4 Mutation Detection CPT Codes: 81403
- IDH2 Exon 4 Mutation Detection CPT Codes: 81403
AML Mutation Panel Turnaround Time: 7-10 days
- FLT3 Mutation Analysis CPT Codes: 81245, 81246
- NPM1 Mutation Analysis CPT Codes: 81310
- CEBPA Mutation Analysis CPT Codes: 81403

REFLEX ORDERING:
AML Mutation Panel - Reflex
- FLT3 Mutation Analysis CPT Codes: 81245, 81246 Turnaround Time: 7-10 days
- NPM1 Mutation Analysis (if indicated) CPT Codes: 81310 Turnaround Time: add 3-6 days
- CEBPA Mutation Analysis (if indicated) CPT Codes: 81403 Turnaround Time: add 5-10 days

NPM1 Mutation Analysis with Reflex to CEBPA
- NPM1 Mutation Analysis CPT Codes: 81310 Turnaround Time: 3-6 days
- CEBPA Mutation Analysis (if indicated) CPT Codes: 81403 Turnaround Time: add 5-10 days

REFERENCES:

ADDITIONAL REFERENCES: