BACKGROUND:
Somatic mutations in the ASXL1 gene have been described in all types of myeloid malignancies including acute myeloid leukemia (AML)\(^1\), myeloproliferative neoplasms (MPN)\(^4\), myelodysplastic syndromes (MDS)\(^5\), chronic myelomonocytic leukemia (CMML)\(^7\), and rarely in juvenile myelomonocytic leukemia (JMML)\(^8\). Most ASXL1 mutations occur in exon 13 (referred to as exon 12 in many publications) and are frequently frameshift or nonsense mutations that result in C-terminal truncation of the protein upstream of the plant homeodomain finger region.

Around 6.5% of de novo and ~30% of secondary AML contain ASXL1 mutations\(^1\). ASXL1 mutations have been reported to have prognostic value in certain subgroups of AML patients: Among patients with intermediate-risk karyotypes, ASXL1 mutations have been associated with shorter overall and event free survival\(^9\); among patients with normal karyotypes, ASXL1 mutations have been associated with inferior survival in European LeukemiaNet (ELN) “favorable” patients (mutated CEBPA and/or mutated NPM1 without FLT3-ITD) but not in ELN Intermediate-I patients\(^2\). ASXL1 mutations are more frequent in males, elderly patients, and patients with a history of MDS\(^9\).

ASXL1 mutations occur in ~16% of MDS cases, 34.5% of primary myelofibrosis cases, and ~45% of CMML cases while being rare in polycythemia vera and essential thrombocytocemia\(^1,4,5-7\).

ASXL1 mutations are associated with poor prognosis typified by aggressive disease, shorter overall survival\(^1,4,9\), elevated International Prognostic Scoring System risk group\(^6\), and transformation to AML\(^5,7\).

REASONS FOR REFERRAL:
Risk stratification and possible treatment decisions in patients with myeloid malignancies.

METHOD:
The assay is performed by PCR amplification and bidirectional sequencing of the coding regions and intron-exon junctions of exon 13 (also referred to as exon 12 in many publications) of the ASXL1 gene. If needed, fragment analysis is performed to confirm length mutations.
LIMITATIONS:
The lower limit of detection of the assay is approximately 20% (allele proportion).

REFERENCE INTERVAL:
Mutations are reported as mutation detected or mutation not detected using standard nomenclature. Polymorphisms are not reported but are available upon request.

SPECIMEN REQUIREMENTS:
3-5 ml EDTA (lavender top) whole blood or 2-5 ml EDTA bone marrow.

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: 5-10 days

CPT CODES: 81479

REFERENCES: