IDH1 EXON 4 AND IDH2 EXON 4 MUTATION DETECTION

BACKGROUND:
Acute myeloid leukemia (AML) may be categorized in high, intermediate or favorable risk prognostic categories based upon cytogenetic findings. AML patients with intermediate risk cytogenetics, principally those in whom the karyotype of their leukemic cells is normal, have been further risk stratified by the presence or absence of specific gene mutations. These include internal tandem mutations in fms-related tyrosine kinase 3 (FLT3), tetranucleotide duplications in exon 12 of nucleophosmin (nucleolar phosphoprotein B23, numatrin) (NPM1), and biallelic mutations in CCAAT/enhancer binding protein (C/EBP), alpha (CEBPA).

Mutations in exon 4 of isocitrate dehydrogenase 1 (IDH1) and isocitrate dehydrogenase 2 (IDH2) have recently been identified in AML. IDH1 and IDH2 mutations are most commonly found in cytogenetically normal AML, in which they may have adverse prognostic significance, and appear to be associated with NPM1 mutations. Mutations most frequently occur in IDH1 codon 132 and in IDH2 codons 140 and 172.

REASONS FOR REFERRAL:
Risk stratification of patients with AML.

METHOD:
IDH1 and/or IDH2 mutations are detected and characterized by PCR amplification, and direct sequencing of the coding and junctional regions of exon 4.

LIMITATIONS:
The lower limit of detection of the assay is approximately 20%. The assay is expected to detect >99% of variants within IDH1 exon 4 and IDH2 exon 4 that are present at an allele burden of ~ 20% or greater.

REFERENCE INTERVAL:
Somatic mutations are reported as mutation detected or mutation not detected. Germline mutations are reported as heterozygous or not detected. All sequence variations are reported using standard nomenclature.

PO Box 2178
Milwaukee, WI 53201-2178
Location/Sample Deliveries:
638 N. 18th St. Milwaukee, WI 53233-2121
p800-245-3117 | f414-937-6202 | www.bcw.edu

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: 5-10 days

CPT CODES:
IDH1 Exon 4 Mutation Detection: 81403
IDH2 Exon 4 Mutation Detection: 81403
IDH1 & IDH2 Exon 4 Mutation Detection: 81403 x 2

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

REFERENCES:
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2. Boissel N, Nibourel O, Renneville A, et al. Prognostic impact of isocitrate dehydrogenase enzyme isoforms 1 and 2 mutations in acute myeloid leukemia: A study by the Acute Leukemia French Association Group. J Clin Oncol 2010;28:3717-23.
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6. Marcucci G, Maharry K, Wu YZ et al. IDH1 and IDH2 gene mutations identify novel molecular subsets within de novo cytogenetically normal acute myeloid leukemia: a Cancer and Leukemia Group B study. J Clin Oncol 2010;28:2348-55.
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11. Ward PS, Patel J, Wise DR, et al. The Common Feature of Leukemia-Associated IDH1 and IDH2 Mutations Is a Neomorphic Enzyme Activity Converting α-Ketoglutarate to 2-Hydroxyglutarate. Cancer Cell 2010;17:225-34.

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