

BACKGROUND:

Core binding factor acute myeloid leukemias (CBF-AMLs) are defined by the presence of the recurrent translocations $t(8;21)(q22;q22)$ or $inv(16)(p13.1;q22)/t(16;16)(p13.1;q22)$, and account for approximately 15% of adult cases of de novo AML.^{1,2} Although CBF-AMLs are classified as having favorable prognoses, only about 50% of patients can be cured of their disease.²

The differences in outcomes within the CBF-AML category are believed to relate to genetic heterogeneity among individual patients' malignancies. KIT (C-Kit) encodes for a type III receptor tyrosine kinase. Activating mutations in KIT are found in approximately 30% of CBF-AML, with the most frequently reported variants clustering in exons 8 and 17.³ KIT mutations appear to be associated with adverse outcomes, particularly those in exon 17.

In addition to their prognostic significance, preclinical (in vitro) studies suggest that KIT mutations may predict responsiveness to tyrosine kinase inhibitor therapy in a mutation selective manner.⁴ Tyrosine kinase inhibitors are not FDA approved for the treatment of core binding factor leukemias.

KIT MUTATION ANALYSIS:

Mutation analysis of KIT exons 8 and 17 is ordered as a single test for patients with core binding factor leukemias.

REASONS FOR REFERRAL:

- Risk stratification of patients with core binding factor AML.

METHOD:

KIT mutations in AML cells are detected and characterized by a combination of PCR amplification, fragment analysis, and direct sequencing of the coding and junctional regions of the KIT gene.

LIMITATIONS:

The lower limit of detection of the assay is approximately 20% (allele proportion). The assay is expected to detect >99% of KIT variants present in the coding and junctional regions at a level of approximately 20% or greater. Specificity is expected to be >99%.

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.

SHIPPING REQUIREMENTS:

Place the room temperature specimen and requisition in plastic bags, seal and insert in an insulated container. Seal the container, place in a sturdy cardboard box and tape securely. Ship the package in compliance with your overnight carrier guidelines. Address the package to:

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

TURNAROUND TIME:

10-14 days

CPT AND ORDER CODES:

CPT Codes: 83891 x 1, 83892 x 2, 83898 x 3, 83904 x 2, 83909 x 1, 83912 x 1

Order Code: 4638

REFERENCES:

1. Arber DA, Brunning RD, Le Beau MM, et al. Acute myeloid leukaemia with recurrent genetic abnormalities. In: Swerdlow SH, Campo E, Harris NL et al., eds. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th ed. Lyon, France: WHO Press, 2008:110-23.
2. Paschka P. Core Binding Factor Acute Myeloid Leukemia. Semin Oncol 2008;35:410-17.
3. Dohner K, Dohner H. Molecular characterization of acute myeloid leukemia. Haematologica 2008;93:976-982.
4. Mrozek K, Marcucci G, Paschka P, Bloomfield C. Advances in molecular genetics and treatment of core-binding factor acute myeloid leukemia. Curr Opin Oncol 2008;20:711-18.

March 2011

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