

KIT Exon 8 and 17 Mutations in Acute Myeloid Leukemia

DETECTS KIT EXON 8 AND EXON 17 MUTATIONS IN CORE BINDING FACTOR IN ACUTE MYELOID LEUKEMIA

Clinical Background

- The *KIT* gene encodes a receptor tyrosine kinase and may be mutated in certain sarcomas and myeloid hematologic malignancies, such as systemic mastocytosis and acute myeloid leukemia (AML).
- In AML, *KIT* mutations deregulate kinase activity and appear to preferentially occur in 20–40 percent of adult and pediatric core-binding factor-related leukemias with t(8;21)/*AML1-ETO* or inv(16)/*CBFA-MYH11* and confer a poor prognosis.¹⁻⁴
- The mutations are clustered in the kinase domain (point mutations at codons 816 and 822 in exon 17) and the extracellular domain (insertion/deletion mutations around codon 419 in exon 8).^{1,5}

Indications for Ordering

The principal use for this test is to determine the risk group for newly diagnosed AML patients with inv(16) or t(8;21).

Limitations

- Results of this test must always be interpreted in the context of morphologic and other relevant data, and should not be used alone for a diagnosis of malignancy.
- Samples that do not show a *KIT* mutation may still harbor mutations that exist in too few AML cells to be detected by this test.
- Rare *KIT* exon 8 mutations that do not cause a net insertion or deletion are not detected by this test.

Methodology

- Genomic DNA is extracted and fragments harboring *KIT* exons 8 and 17 are amplified by PCR.

- Exon 8 fragments are analyzed by capillary electrophoresis for insertion/deletion mutations; exon 17 fragments are sequenced.
- This test can detect *KIT* mutations in exon 8 in samples with as low as 5 percent mutated cells and in exon 17 in samples with as low as 30 percent mutated cells.

Interpretation

- Not detected: No mutations in *KIT* exons 8 or 17 were detected.
- Positive: A mutation in *KIT* exon 8 or 17 was detected.

References

- Paschka P, et al. Adverse prognostic significance of *KIT* mutations in adult acute myeloid leukemia with inv(16) and t(8;21): a cancer and leukemia group B study. *J Clin Oncol* 2006;24:3904–11.
- Care RS, et al. Incidence and prognosis of *KIT* and *FLT3* mutations in core binding factor (CBF) acute myeloid leukemias. *Br J Hematol* 2003;121:775–7.
- Goemans BF, et al. Mutations in *KIT* and *RAS* are frequent events in pediatric core-binding factor acute myeloid leukemia. *Leukemia* 2005;19:1536–42.
- Shimada A, et al. *KIT* mutations, and not *FLT3* internal tandem duplication, are strongly associated with a poor prognosis in pediatric acute myeloid leukemia with t(8;21): a study of the Japanese childhood AML cooperative study group. *Blood* 2006;107:1806–9.
- Kohl TM, et al. *KIT* exon 8 mutations associated with core-binding factor (CBF)-acute myeloid leukemia (AML) cause hyperactivation of the receptor in response to stem cell factor. *Blood* 2005; 105:3319–21.

Test Information

2002437

KIT Mutations in AML by Fragment Analysis and Sequencing

For specific collection, transport, and testing information, refer to the ARUP Web site at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.