

BCR-ABL1 T315I Mutation

DETECTS AND QUANTITATES T315I-POSITIVE BCR-ABL1 TRANSCRIPTS IN CHRONIC MYELOGENOUS LEUKEMIA

Clinical Background

- Chronic myelogenous leukemia (CML) is characterized by the *BCR-ABL1* fusion oncogene. Patients with CML typically respond very favorably to treatment with tyrosine-kinase inhibitors (TKIs) such as imatinib.¹ However, a subset of patients will eventually acquire secondary ABL1 kinase-domain mutations that promote TKI resistance.²
- A subset of patients who develop TKI resistance do so because of the presence of the T315I point mutation in the ABL1 kinase domain.³
- Detection and quantitation of the T315I point mutation is clinically useful in managing those patients who fail current front-line CML therapies.

Indications for Ordering

The *BCR-ABL1* T315I mutation has been associated with resistance to TKIs used to treat CML patients. Patients with a T315I mutation may benefit from alternative therapies.

Interpretation

- Not detected: The T315I mutation was not detected.
- Detected: The T315I mutation was detected (percent of mutant allele).

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 demonstrate the T315I mutation by this test may still have the mutation, but in quantities below the test's limit of detection.
- This test may not accurately detect mutations if present in fewer than 5 percent of CML cells.

Methodology

- Total RNA is extracted, reverse-transcribed into cDNA, and amplified across the *BCR-ABL1* fusion breakpoint.
- Amplicons are subjected to a second PCR reaction targeting ABL exon 6 and subsequently pyrosequenced. The percent of mutant allele is reported.

References

1. Druker BJ, et al. Efficacy and safety of a specific inhibitor of the BCR-ABL tyrosine kinase in chronic myeloid leukemia. *N Engl J Med* 2001;344:1031–7.
2. Jabbour E, et al. Long-term outcome of patients with chronic myeloid leukemia treated with second-generation tyrosine kinase inhibitors after imatinib failure is predicted by the in vitro sensitivity of BCR-ABL kinase domain mutations. *Blood* 2009;114:2037–43.
3. Jabbour E, et al. Characteristics and outcomes of patients with chronic myeloid leukemia and T315I mutation following failure of imatinib mesylate therapy. *Blood* 2008;112:53–5.

Test Information

2004924 *BCR-ABL1*, T315I Mutation Detection, Quantitative

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

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

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