
Chronic Myelogenous Leukemia and Acute Lymphoblastic Leukemia by qRT-PCR

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The BCR-ABL1 fusion gene, characterized by the reciprocal chromosomal translocation t(9;22), is found in virtually all patients with CML and in 25-40% of adult patients with ALL.

The three predominant fusion transcripts are distinguished by breakpoints in the BCR region.

Real-time qRT-PCR can be used for diagnostic confirmation and monitoring of transcript levels in patients with CML and ALL.

Analytical sensitivity is at least 0.001% for b3a2 and b2a2 and at least 0.01% for e1a2.

Comparison of sequential results generated from the same sample type by the same laboratory will provide the most meaningful information for monitoring patients on therapy.

We recommend obtaining a baseline BCR-ABL1 peripheral blood level.

The BCR-ABL1 fusion gene is found in >99% of patients with chronic myelogenous leukemia (CML) and 25-40% of adult patients with acute lymphoblastic leukemia (ALL). The fusion gene is a consequence of the reciprocal chromosomal translocation t(9;22)(q34;q11) and is associated with three predominant fusion transcripts. Major breakpoints within the BCR region produce the RNA transcripts b3a2 and b2a2 and minor breakpoints produce the e1a2 transcript. These transcripts encode the p210 (b3a2, b2a2) and p190 (e1a2) oncoproteins, both of which enhance tyrosine kinase activity and are paramount in the pathogenesis of these leukemias.

Molecular-based testing for the BCR-ABL1 gene rearrangement is an essential tool for diagnostic confirmation of patients suspected of CML or ALL and monitoring for treatment response and disease recurrence in patients with these diagnoses. With the advent of exquisitely sensitive quantitative real-time PCR techniques, quantitative reverse-transcription PCR (qRT-PCR) methodologies are now extensively utilized for these applications.

PAML is now offering a real-time qRT-PCR test for diagnostic confirmation and monitoring of minimal residual disease in CML and ALL. This test is specific for the three major RNA transcripts (b3a2, b2a2, and e1a2) and the

sensitivity is at least 0.001% for b3a2 and b2a2 and at least 0.01% for e1a2. RNA is extracted from leukocytes in whole blood or bone marrow and reverse transcribed to cDNA. Concurrent amplification of control gene transcripts permits the calculation of normalized copy numbers of BCR-ABL1 transcripts.

Current clinical recommendation (Blood 2006;108:1809-1820)

The objective of imatinib therapy is to achieve a major molecular response (MMR) by 18 months. A MMR is defined as a one-log reduction in BCR-ABL1 levels after obtaining a complete cytogenetic response, and corresponds in most cases to a 3-log reduction from pretreatment (baseline) levels.

We recommend obtaining a baseline BCR-ABL1 peripheral blood level at diagnosis, with follow-up levels determined every three months. Re-baselining is recommended upon switching laboratories and/or methodologies after monitoring has been initiated.



TEST UPDATE

FROM YOUR LABORATORY SERVICES PROVIDER

Quick Facts



Test Information

BCR/ABL Translocation, RT-PCR

Real-time qRT-PCR

BCRABL

83891, 83902, 83898 x 2, 83903 x 2, 83912

Specimen Type: Whole blood. Preferred volume is 5mL. Minimum volume is 3mL. Send the unopened, original collection tube. Do not split samples.

Bone marrow: Preferred volume is 1mL. Minimum volume is 0.5mL. Send the unopened original collection tube. Do not split samples. (Exception: if bone marrow sample is also to be used for cytogenetic studies, sample may be shared. However, dilution of sample may be needed due to the PCR-inhibiting effects of heparin).

Specimen Collection: Draw EDTA (lavender top tube) or sodium citrate (blue top tube). Full microcontainers (EDTA) are acceptable. Heparin (green top tube) is not acceptable for whole blood. Whole blood is recommended for serial analysis and MRD detection; each subsequent sample MUST be of the same sample type – e.g. only whole blood or only bone marrow. Consecutive samples of differing types will only provide a qualitative result.

Specimen Transport: Submit original Vacutainer tubes promptly at 4°C. Do not freeze. SAMPLES MUST ARRIVE IN THE LAB WITHIN 48 HOURS OF COLLECTION.

TAT: 2 – 9 days

Test Schedule: Weekly

Specimen Rejection Criteria: Whole blood in sodium heparin, serum/plasma, grossly hemolyzed sample, shared sample (other than bone marrow in sodium heparin), frozen sample, sample aliquots, leaky container, samples collected >2 days previous, improperly labeled specimens.

DESCRIPTION

METHOD

ORDER CODE

CPT CODE

SPECIMEN REQUIREMENTS

COMMENTS

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