**Background:**
Chronic myeloid leukemia (CML) is a clonal hematologic stem cell malignancy associated, in ~90% of cases, with a somatically-acquired tumor-specific chromosomal alteration - the Philadelphia chromosome (Ph). The molecular consequences of the Philadelphia translocation are the physical juxtapositioning of sequences from the chromosome 22 **BCR** gene (breakpoint cluster region) adjacent to sequences from the chromosome 9 c-**ABL** gene encoding a non-receptor tyrosine kinase. Depending on the precise site of the Ph translocation breakpoint, the resulting **BCR-ABL** fusion gene is transcribed and translated into a 210 kD (p210) or 185 kD (p185) **BCR-ABL** fusion product with deregulated (significantly enhanced) tyrosine kinase activity. The p210 **BCR-ABL** protein is expressed not only in ~95% of patients with CML but also in ~15% of adult-onset cases of acute lymphoblastic leukemia (ALL) and ~5% of adults with acute myeloid leukemia (AML). The alternative p185 **BCR-ABL** product is expressed in ~15% of adult-onset cases of ALL and in ~5% of pediatric-onset cases of ALL. Patients with these **BCR-ABL** positive acute leukemias have a significantly poorer prognosis than patients with acute leukemias lacking the Philadelphia chromosome.

Imatinib’s targeted inhibition of the **BCR-ABL** kinase activity specifically represses the leukemic clone without the typical toxicity of conventional non-specific cancer drugs. Despite its promising efficacy, imatinib fails to produce either an initial response or a durable response in a subset of treated patients. This heterogeneity of responses suggests the pressing need for better laboratory methods to monitor and predict treatment efficacy to identify patients who likely will (or will not) have a durable response to the relatively non-toxic imatinib regimen. Other more toxic alternative therapies could then be reserved only for those patients most likely to benefit from the additional risk. By measuring **BCR-ABL** RNA levels using a sensitive RT-PCR method, and then reflex negative cases to nested PCR, we will be able to detect the presence of leukemic cells at very low levels (before clinical relapse). Current literature suggests a role for this approach in risk assessment of relapse events to allow preventive interventions.

**Clinical Utility:**
The quantitative **BCR-ABL** RNA assay is intended to monitor the post-therapy level of minimal residual disease in Philadelphia chromosome positive leukemias (CML or ALL). High or rising **BCR-ABL** RNA levels have been shown to predict the risk of leukemic relapse in patients treated by bone marrow transplantation, interferon, and/or tyrosine kinase inhibitors. Per clinical indication, cases with negative results on the quantitative **BCR-ABL** RNA assay are reflexed to a nested RT-PCR assay. This test combination is available as a single test performed in our laboratory.
Methodology:
The assay utilizes nested primers that cover ABL and BCR specific sequences in two separate rounds of reverse-transcription polymerase chain reaction to amplify the p210 (major) and p185 (minor) BCR-ABL fusion transcripts within the same reaction tube.

Sensitivity: This assay has a sensitivity for detecting BCR-ABL levels at approximately 4.0-log below the pretreatment baseline in the International Randomized Study of Interferon versus STI 571.

Specimen Requirements:
- 20 mL of blood or bone marrow — yellow (ACD) or purple (EDTA) tube (unspun).
- Please maintain sample at refrigerated temperatures and deliver to lab at shipping address above within 24 hours of collection.

A REQUISITION FORM MUST ACCOMPANY ALL SAMPLES. Please include detailed clinical information.

Test Performed (Days):
Monday - Friday

Turnaround Time:
3-6 days

Shipment Sensitivity Requirements:
Keep specimen cold during transit, but do not ship on dry ice. Please contact Client Services at (855) 535-1522 for shipping kits and instructions. Use the cold pack provided in the KDL shipping kit. Ship the specimen overnight express, using the FedEx priority overnight label provided. The specimen must arrive at the lab no more than 24 hours after collection.

Reference:


