BCR-ABL RNA PCR Quantitation for Leukemia

Test Code: 4080

Department: Molecular Oncology

Test Synonyms:
- BCR-ABL RNA
- Philadelphia chromosome fusion transcript levels determination
- BCR-ABL PCR
- CML monitoring
- CML minimal residual disease

CPT Code(s):
- 82955
- 83891
- 83896 x 2
- 83902
- 83907
- 83908

Background:
Chronic myeloid leukemia (CML) is a clonal hematologic stem cell malignancy associated, in greater than 90% of cases, with the Philadelphia chromosome (Ph), a reciprocal translocation between the long arms of chromosomes 9 and 22 \( [t(9;22)(q34;q11)] \). 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. The resulting BCR-ABL fusion gene is transcribed and translated into a 210 kD (p210) or 185 kD (p185) BCR-ABL fusion product with dysregulated (significantly enhanced) tyrosine kinase activity. The aberrant growth and differentiation of leukemic cells in CML is caused by the constitutive expression of the BCR-ABL kinase, a chimeric fusion protein resulting from a leukemia-specific chromosomal translocation described above. Targeted inhibition of BCR-ABL with tyrosine kinase inhibitors (imatinib, dasatinib, nilotinib) is the standard treatment for CML (and Ph+ ALL).

The efficacy of TKI therapy is routinely monitored with serial BCR-ABL RNA PCR’s, which define the “molecular response”. A consensus treatment goal is the achievement of “major molecular response”, a 3-log drop in BCR-ABL RNA, defined as 0.1% on the BCR-ABL RNA PCR international scale (IS) of measurement.

Clinical Utility:
The quantitative BCR-ABL RNA assay is intended to monitor the level of minimal residual disease in TKI-treated Philadelphia chromosome positive leukemias (CML or ALL). High or rising BCR-ABL RNA levels have been shown to increase the risk of leukemic relapse and drug-resistance mutations during TKI therapy. The failure to achieve a “major molecular response”, a 3-log drop in BCR-ABL RNA, defined as 0.1% on the BCR-ABL RNA PCR international scale (IS), is the consensus definition of a “sub-optimal” treatment that requires an alternative treatment approach. The OHSU BCR-ABL RNA PCR assay has been calibrated to the International Scale, and is one of only a few US assays reporting results on the IS.

Methodology:
By measuring BCR-ABL RNA levels using a sensitive real-time fluorescent PCR method, we are able to detect the presence of leukemic cells at a very low level. The sensitivity limit of the assay is approximately 1 tumor cell in 100,000 normal cells. A relative ratio (in percent) of BCR-ABL RNA to reference gene RNA is reported, as well as a value on the BCR-ABL international scale (which is the only way to assess major molecular response).
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Specimen Requirements:
- Blood or Bone Marrow: 10-20 mL purple (EDTA) or yellow (ADC) tube (unspun)
- Deliver to lab at shipping address above within 24 hours of collection, if sample cannot arrive within 24 hours, refrigerate until sample can be transported, then transport on ice packs; do not freeze.
- If sample is to be shipped overnight, pour blood/bone marrow into RPMI media at a 1:1 ratio (1 mL of RPMI to 1 mL of blood/bone marrow) and mix thoroughly.

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

Test Performed (Days):
4 times per week

Turn Around Time:
2 – 5 Days

Shipment Sensitivity Requirements:
Keep specimen cold during transit, but do not ship on dry ice. Contact Client Services for shipping kit and instructions at (855) 535-1522. Please 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.

References: