Chronic Myelogenous Leukemia
BCR-ABL1 by PCR

**Introduction**

In the 2008 revision of the World Health Organization (WHO) classification of myeloid neoplasms, MPNs include: chronic myelogenous leukemia (CML), chronic neutrophilic leukemia, polycythemia vera (PV), primary myelofibrosis (PMF), essential thrombocythemia (ET), chronic eosinophilic leukemia, mastocytosis, and unclassifiable MPNs. CML is the only MPN that is characterized by the chromosomal translocation t (9;22), BCR-ABL fusion gene.
In most cases, diagnosis of CML is based on blood counts (leukocytosis and frequently also thrombocytosis) and differential immature granulocytes, from the metamyelocyte to the myeloblast, and basophilia). Splenomegaly is present in >50% of cases of CML in the initial chronic phase (CP), but about 50% of patients are asymptomatic. Proof of diagnosis is attained by demonstration of the Philadelphia (Ph) chromosome (22q-) resulting from the balanced translocation t(9;22) (q34;q11), and/or the BCR-ABL rearrangement in peripheral blood or bone marrow cells.

**Clinical Background**

The BCR-ABL1 fusion gene is formed by a translocation between chromosomes 9 and 22 [t(9;22)], which also results in an abnormally short chromosome 22 (the Philadelphia chromosome; Ph). The fusion gene is present in virtually all individuals with CML and is the hallmark diagnostic feature of the disease. The BCR-ABL1 rearrangement results in the production of a fusion protein with constitutive tyrosine...
kinase activity, which is thought to play a role in the development of leukemia.

**Methodology**
The Method used in this assay is reverse transcription polymerase chain reaction (RT-PCR) - GeneXpertDx System. The amount of BCR-ABL transcript is quantified as the ratio of BCR-ABL/ABL.

**Clinical Use of BCR-ABL1 RT-PCR**
- Diagnose chronic myelogenous leukemia (CML)
- Monitor the effectiveness of therapy
- Monitor minimal residual disease (MRD)
- Predict disease progression

**Interpretive Information**

**Diagnosis**
Along with characteristic cell morphology findings, presence of the P210 BCR-ABL transcript is consistent with CML.

**Typical testing strategy**
At diagnosis: BM cytogenetic studies and quantitative measurement of BCR-ABL1 transcript levels are recommended before treatment initiation

**Monitoring Progress**
The quantity of transcript detected in the initial test serves as a baseline for serial monitoring. An increasing BCR-ABL1/ABL1 percent ratio over time suggests an increase in tumor burden, while a decreasing ratio suggests a favorable response to therapy. For P210 transcription, a BCR-ABL1/ABL1 ratio of 0 represents a complete
molecular response to therapy. BCR-ABL1/ABL1 % (IS) values ≤0.1% correspond to a 3-log or greater reduction from the baseline, indicating a major molecular response (MMR) in CML patients and thus excellent progression-free survival.

**Monitoring response to TKI therapy in CML**

The goal of TKI therapy is to achieve a complete cytogenetic response within 12 months of initiation of therapy with goal of eventual major molecular response. A subset of individuals will eventually achieve a complete molecular response. The favorable prognosis is measured as a 3-log decrease in the level of BCR-ABL1 fusion transcripts (major molecular response) within 18 months of beginning TKI therapy is an indicator of favorable outcome.

The recommended strategy of monitoring using quantitative RT-PCR

1- Every 3 months when treatment response is evident
2- After complete cytogenetic response has been achieved and every 3 months for 3 years, and every 3-6 months thereafter
3- More frequent monitoring may be required in individuals with rising BCR-ABL1 transcripts to detect early relapse

**Sample Precautions**

- Specimen Required: 5.0 mL EDTA Blood
- Storage/Transport Temperature: Refrigerated
- Unacceptable Conditions: Bone marrow samples, Ambient temp or Frozen storage condition - Sample volume <1.0 mL - Samples exceeds 48 hour transport.
# Ordering Information

<table>
<thead>
<tr>
<th>Test Code</th>
<th>Test Name</th>
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<tbody>
<tr>
<td>1565</td>
<td>Major BCR-ABL Detection by Real Time PCR</td>
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<tr>
<td>1579</td>
<td>Major BCR-ABL Monitoring by Real Time PCR</td>
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**References:**

4. Serpa et al. (2010)