BCR/ABL p210 Quantitative RT-PCR Assay with International Scale Reporting for Minimal Residual Disease in Chronic Myeloid Leukemia

Background Information

A translocation between chromosomes 9 and 22, resulting in the formation of a *BCR/ABL* fusion transcript, has long been recognized as a hallmark of chronic myeloid leukemia (CML). Although the breakpoints in *BCR* and *ABL* are variable, in >95% of cases of CML, the translocation results in production of the p210 isoform of the fusion protein (e13a2 or e14a2 fusion genes).

Modern therapy for CML, including tyrosine kinase inhibitors, has resulted in effective therapeutic options for CML patients. With this advance in treatment has come the need for effective monitoring for the presence of minimal residual disease (MRD) and the ability to recognize disease progression at an early stage. Techniques such as fluorescence *in situ* hybridization (FISH) and metaphase cytogenetics provide valuable information at the time of initial diagnosis of CML and metaphase cytogenetics is helpful for identifying the emergence of additional chromosomal abnormalities, however, neither of these techniques are sufficiently sensitive to monitor MRD.[1,2] For this reason, a *BCR/ABL* p210 quantitative real-time reverse transcriptase polymerase chain reaction (qRT-PCR) assay was developed, validated, and implemented in the Department of Molecular Pathology.

To facilitate comparison of quantitative RT-PCR results between laboratories and platforms, International Scale reference materials were established by the World Health Organization.[3] Results of this assay are now reported on the International Scale.

Clinical Indications

Quantitative detection of *BCR/ABL* p210 transcripts (e13a2 or e14a2) in patients with CML.

Interpretation

Results are reported as the percentage ratio of fusion gene transcripts to wild-type *ABL* transcripts (% *BCRABL/ABL*). Results are also converted to the International Scale. A *BCRABL/ABL* value of 0.1% on the International Scale represents a major molecular response by consensus criteria.

Methodology

Assay sensitivity was established using RNA extracted from K562 cultured cells suspended in normal buffy coat. This assay successfully detects p210 *BCR/ABL* transcripts in RNA extracted from one K562 cell in 100,000 peripheral blood leukocytes from a normal individual.

References

1. Hughes T, Deininger M, Hochhaus A *et al*. Monitoring CML patients responding to treatment with tyrosine kinase inhibitors: review and recommendations for harmonizing current methodology for detecting *BCR-ABL* transcripts and kinase domain mutations and for expressing results. *Blood*. 2006;108:28-37.

2. Druker BJ, Guilhot F, O'Brien SG *et al*. Five-year follow-up of patients receiving imatinib for chronic myelogenous leukemia. *N Engl J Med*. 2006;355:2408-2417.

3. White HE, Matejschuk P, Rigsby P, *et al*. Establishment of the first World Health Organization International Genetic Reference Panel for quantification of *BCR-ABL* mRNA. *Blood* 2010;116:e111-7.

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Test Overview

Test Name	*BCR/ABL* p210 RT-PCR, quantitative
Reference Range	*BCR/ABL* p210 transcripts not detected
Specimen Requirements	10 mL whole blood, EDTA (lavender), refrigerated OR 5 mL bone marrow, EDTA (lavender), refrigerated
Special Information	Clearly indicate specimen type on label. External client shipping instructions: Ship "Priority Overnight;" do not ship on Fridays or the day preceding a holiday. Stability Ambient: 1 hour. Refrigerated: 48 hours.
Billing Code	82737
CPT Codes	81206

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