BCR/ABL1 Multiplex RT-PCR, Qualitative

Background

The t(9;22)(q32;q22) *BCR/ABL1* translocation is found in all cases of chronic myeloid leukemia (CML) and approximately 25% of acute lymphoblastic leukemias (ALL).[1,2] Variations in translocation breakpoints in *BCR* and *ABL1* lead to the production of different *BCR/ABL1* fusion transcript isoforms. In 95% of CML, *BCR/ABL1* transcripts are either e13a2 or e14a2 fusions (p210 isoform). Approximately 70% of *BCR/ABL1* positive ALL contain e1a2 transcripts (p190 isoform), while 25% of cases contain either e13a2 or14a2 fusions.

While the e1a2, e13a2, e14a2 isoforms account for the vast majority of *BCR/ABL1* translocations, atypical transcripts are sometimes observed.[3,4] Breakpoints in *ABL1* intron 1 and *BCR* intron 6 (e6a2) or intron 19 (e19a2, p230 isoform) have been reported, as well as cases with a breakpoint in *ABL1* intron 2 leading to e1a3, e13a3 and e14a3 transcripts. The ability to detect and distinguish between *BCR/ABL1* isoforms, including atypical forms, is critical for appropriate diagnosis and selection of appropriate follow-up tests.

Cleveland Clinic Laboratories offers a multiplex RT-PCR assay that is capable of detecting and distinguishing between the following *BCR/ABL1* transcripts: e1a2, e1a3, e6a2, e13a2, e13a3, e14a2, e14a3 and e19a2.

Clinical Indications

This assay is intended to detect *BCR/ABL1* translocations in newly diagnosed or suspected cases of CML or ALL.

Interpretation

Positive results are reported as "*BCR/ABL1* transcripts detected," and the specific isoform identified is provided. Based on these results, suggestions for follow-up testing are provided.

Methodology

RNA is extracted from peripheral blood or bone marrow, and cDNA is prepared by reverse transcription. Multiplex RT-PCR is performed, and products visualized by capillary electrophoresis fragment length analysis on the ABI 3730 Genetic Analyzer (Applied Biosystems, Carlsbad, CA).

Limitations of the Assay

This assay is intended for initial diagnosis. The sensitivity of the assay corresponds to a percent ratio value of approximately 1% (*BCRABL1/ABL1*). For sensitive minimal residual disease detection, please order p190 *BCR/ABL1* RT-PCR, Quantitative or p210 *BCR/ABL1* RT-PCR, Quantitative.

References

1. Luu MH and Press RD. *BCR–ABL* PCR testing in chronic myelogenous leukemia: molecular diagnosis for targeted cancer therapy and monitoring. *Expert Rev. Mol. Diagn*. 2013;13:749–762.

2. Letizia F, Wilson G, Gerrard G, *et al*. Guidelines for the measurement of *BCR-ABL1* transcripts in chronic myeloid leukaemia. *Br J Haematol*. 2011;153:179-190.

3. Burmeister T, Reinhardt R. A multiplex PCR for improved detection of typical and atypical *BCR-ABL* fusion transcripts. *Leuk Res*. 2008;32:579-85.

4. Wada H, Mizutani S, Nishimura J, *et al*. Establishment and molecular characterization of a novel leukemic cell line with Philadelphia chromosome expressing p230 *BCR/ABL* fusion protein. *Cancer Res*. 1995;55:3192-3196.

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Test Overview

Test Name	*BCR/ABL1* Multiplex RT-PCR, Qualitative
Ordering Mnemonic	BCRQL
Reference Range	*BCR/ABL1* transcripts not detected
Specimen Requirements	10 mL Whole blood EDTA (Lavender). Place specimen on ice after draw. Specimen must be delivered to testing lab by 2 pm on Fridays.
Minimum Specimen Requirements	5 mL Whole blood EDTA (Lavender). Place specimen on ice after draw. Specimen must be delivered to testing lab by 2 pm on Fridays.
Alternate Specimen Requirements	5 mL Bone marrow EDTA (Lavender). Place specimen on ice after draw. Specimen must be delivered to testing lab by 2 pm on Fridays.
CPT Codes	81479, G0452

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