BCR-ABL IS (International Scale) Transcript fusion Quantification

Test Principle : Real Time PCR

Equipment : Rotor Gene 3000 from Corbett Research, Australia

Specimen : Blood

Result :

M-BCR-ABL IS count %	**0.4382 %**
ABL (Control Gene)	**42353 copies**

Result Interpretation:

- The international reporting scale (IS) has been established which expresses detectable disease as a percentage (0.1 % is corresponds to MMR) and is essentially identical to that used in the IRIS trial to achieve Major molecular response (MMR).
- BCR-ABL transcript quantification is expressed as a % of the control gene i.e., ABL. The sample showing amplification curve for both BCR/ABL transcript fusion gene (FG) and (CG) are considered as positive for the test and are reported as a % expression of BCR/ABL over ABL.
- In the absence of amplification curve for the CG or copies < 10000, the test is reported as invalid, denoting degradation of RNA.
- This test is directed for the quantification of Major breakpoint at e14a2 and e13a2 corresponding p210 transcript, which is found in 95 % of CML patients.

Reference Range of Major Molecular Response (MMR) Status:

IS BCR-ABL/ABL %	Log Reduction	Response
IS BCR-ABL/ABL% < 0.001	5.0	Deep Molecular Response (DMR)
IS BCR-ABL/ABL% < 0.0032	4.5	Deep Molecular Response (DMR)
IS BCR-ABL/ABL% < 0.01	4	Deep Molecular Response (DMR)
IS BCR-ABL/ABL% < 0.1	3	Major Molecular Response (MMR)
0.1 < IS BCR-ABL/ABL% < 0.15	-	Around the MMR cut –off
IS BCR-ABL/ABL% > 0.15	-	No Major molecular Response

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Clinical Background:

- Quantitative analysis of BCR/ABL transcript level by real time PCR should ideally be performed before the start of the therapy in order to determine the baseline value and for minimal residual disease (MRD) estimation.
- Since the introduction of BCR-ABL kinase inhibitor therapy, molecular monitoring after
- achieving complete cytogenetic response (CCR) post- initiation therapy has become particularly relevant & crucial.
- The BCR-ABL gene translocation or t(9;22) is found in more than 95% CML patients, 5% of paediatric ALL-B CALLA positive and 15-30% of adult ALL-B CALLA positive patients. This genetic aberration is a balanced reciprocal translocation between ABL gene on chromosome 9 and BCR gene on chromosome 22. This test is performed for the quantitative detection and differentiation of BCR-ABL fusion gene transcripts, Major (M), minor (m) and micro in bone marrow or peripheral blood samples of ALL or CML using real time PCR. Follow-up is recommended, if clinically indicated. A repeat testing after 6 months is additionally recommended.
- The lower limit of BCR-ABL transcript detection in the assay is dependent on the quality of RNA obtained and the cellularity of the sample. Since genetic variation and other problems can affect the accuracy of PCR based testing, the result should always be interpreted in light of clinical data.

Limitation of Assay:

- Other Transcripts p230 and p190 cannot be detected by this assay.
- PCR is a highly sensitive method; common reasons for paradoxical results are contamination during specimen collection, selection of inappropriate specimens and inherent PCR inhibitors in the specimen.

Reference:

- BACCARANI et al., European LeukemiaNet recommendations for the management of chronic myeloid
- leukemia: 2013, BLOOD, 8 AUGUST 2013, VOLUME 122, NUMBER 6
- ChaoJie Zhen and Y. Lynn Wang, Molecular Monitoring of Chronic Myeloid Leukemia: International
- Standardization of BCR-ABL1 Quantitation, J Mol Diagn 2013, 15: 556e564

-- End of Report --

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