

MOLECULAR MONITORING OF CHRONIC MYELOID LEUKEMIA (CML): ASSESSMENT OF MAJOR MOLECULAR RESPONSE (MMR) BY A ONE-STEP RT-REAL-TIME PCR ASSAY

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Chronic myeloid leukemia (CML) is a cancer of the white blood cells which is characterized by a BCR-ABL fusion gene, commonly known as the Philadelphia chromosome (Ph). This marker is importantly present of CML cases and in 3% to 30% of patients with acute lymphoblastic leukemia (ALL) (Eide et al. 2015). It is caused by a reciprocal translocation between chromosome 9 and 22, t(9; 22)(q34; 11) (Bartram et al. 1983). Ph contains the chimeric oncogene BCR-ABL, which produces an active BCR-ABL tyrosine kinase that is involved in the pathogenesis of CML. The introduction of the first target-specific tyrosine kinase inhibitor (TKI) into the clinical practice has been a significant progress in the treatment of CML.

To help understanding whether a patient is responding optimally or not to therapy, international treatment recommendations incorporate specific time-dependent molecular landmarks. Molecular measurements are made by reverse transcriptase quantitative polymerase chain reaction (RT-qPCR) to estimate the amount of BCR-ABL mRNA relative to internal reference gene, typically ABL or GUSB. The results are expressed on an International Scale (IS) as a percentage, with 100% BCR-ABLIS corresponding to the IRIS study standardized baseline and 0.1% BCR-ABLIS being defined as a major molecular response (MMR or MR3; 3 log reduction from the standardized baseline) (Zhen et al. 2013).

AB ANALITICA designed and developed a One-Step RT-qPCR assay, called REALQUALITY RQ-BCR-ABL p210 One-Step, that starts directly from extracted RNA. The assay was designed according to the EAC guidelines and has passed the internal validation necessary to obtain the CE-IVD mark.

In this study, the IVD device has been subjected to a clinical validation, focused on the definition of MMR class. The same thirty RNA samples of CML patients were tested with REALQUALITY RQ-BCR-ABL in three different laboratories, using in parallel their own certified method. A total of 6 different results on the same RNA sample were obtained. The assessment data of MMR were compared and analyzed.

Eide et al (2015). "Chronic myeloid leukemia: advances in understanding disease biology and mechanisms of resistance to tyrosine kinase inhibitors." Current hematologic malignancy reports 10.2: 158-166.

Bartram et al (1983). "Translocation of c-abl oncogene correlates with the presence of a Philadelphia chromosome in chronic myelocytic leukaemia." 277-280.

Zhen et al. "Molecular monitoring of chronic myeloid leukemia: international standardization of BCR-ABL1 quantitation." The Journal of Molecular Diagnostics 15.5: 556-564.

