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Hsa-miR-181a-5p, hsa-miR-182-5p and hsa-miR-26a-5p as potential biomarkers for BCR-ABL1 among adult chronic myeloid leukemia treated with tyrosine kinase inhibitors at the molecular response

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Tyrosine kinase inhibitors (TKIs) as first-line therapy for Chronic Myeloid Leukemia (CML) show a high success rate. However, a low number of patients with long-term treatment-free remission (TFR) were observed. Molecular relapse after imatinib discontinuation occurred at 50% at 24 months, with 80% occurrence within the first 6 months. One of the reasons for relapse is untimely TKIs discontinuation caused by large errors from estimates at very low-level or undetectable disease, thus warranting new biomarkers for CML. Methods: Next Generation Sequencing (NGS) was used to identify microRNAs (miRNAs) at the molecular response in CML adult patients receiving TKIs treatment. A total of 86 samples were collected, 30 from CML patients responsive and 28 from non-responsive to imatinib therapy and 28 from blood donors. NGS was conducted whereby 18 miRNAs were selected and validated by real-time RT-qPCR in triplicate.

Results

Hsa-miR-181a-5p was expressed significantly (p -value <0.05) with 2.14 and 2.33-fold down-regulation in both patient groups, respectively meanwhile hsa-miR-182-5p and hsa-miR-26a-5p were significant only in the non-responsive group with 2.08 and 2.39 fold up-regulation. The

down-regulation was consistent with decreased amounts of BCR-ABL1 in patients taking TKIs regardless of molecular responses. The up-regulation was consistent with the substantial presence of BCR-ABL1 in CML patients treated with TKIs at the molecular response. Conclusions: Therefore, these miRNAs have potential as new therapeutic biomarkers for BCR-ABL1 status in adult CML patients treated with TKIs at molecular responses. These could improve current approaches and require further analysis to look for targets of these miRNAs in CML.

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