Summary

The detection of residual tumor cells in patients with chronic lymphocytic leukemia (CLL) was the goal of this study. Since there is no CLL-specific molecular marker, minimal residual disease detection (MRD) is not simple.

The outcome of 29 patients treated with fludarabine, cyclophosphamide and rituximab (FCR) was monitored using PCR with "consensus" primers and comparative PCR. 16 patients subsequently underwent autologous stem cell transplantation (ASCT) which did not significantly prolong the length of molecular remission reached by these patients in comparison to patients treated with FCR only. However, it seems that the length of molecular remission of transplanted patients was not affected by eventual contamination of progenitor cells with leukemic cells while it was affected by the presence of detectable CLL cells in their bone marrow at the time of ASCT.

Since "consensus" PCR is not a method sufficiently sensitive for MRD detection in CLL the usefulness of detection of DNA methylation was explored for this purpose. Methylation status of 5 genes (DLC1, SHP1, p15, p16 and lamin A/C) was analyzed in the tested group of patients. DLC1 methylation was detected in the majority of patients so changes in its methylation levels in relation to disease evolution were further analyzed using real time PCR. DLC1 was found to be a putative surrogate marker for quantitative detection of CLL cells.

In addition, statistical analysis revealed a correlation between simultaneous methylation of at least 2 genes and high Rai stage. Results of this analysis were verified (and confirmed) on a cohort of 82 patients. Furthermore, it was found that methylation of SHP1 and p15 genes might be involved in progression of CLL.

Key words: chronic lymphocytic leukemia, DNA methylation, minimal residual disease, tumor suppressor gene, polymerase chain reaction