Changes in the levels of WT1, Bcl-2, p21Cip, mBCR-ABL, and Ki-67 transcripts in the course of chronic myeloid leukemia (CML)

Imatinib mesylate is a prototype of a molecular targeted therapy now used succesfuly in clinical practice in treatement of CML and other diseases. Some patients with CML, however, experience primary or secondary resistace to this drug. The aim of this study was to determine potencial new markers of resistance to this type of therapy.

We monitored changes in the levels of WT1, Ki-67, p21Cip, mBCR-ABL, and Bcl-2 transcripts by reverse transcriptase real-time PCR using TaqMan probes. After comparing both today used quantitative methods – 1) with the use of standard curve and 2) the two delta delta Ct method, we chose the latter one. The first step in finding a new marker was statistical analysis of differences in gene expression in various types of response to the treatement. For statistical analysis we used ANOVA test or Kruskal-Wallis test. As the tests for multiple comparision, the Tukey´s and Dunn´s tests were used.

The results of statistical analysis showed that the only possible early marker of relapse on therapy from the genes monitored in this study was WT1. The others were rather possible markers of blastic phase of the disease (p21Cip, Bcl-2) or poor response to treatment (Ki-67). The results of monitoring kinetics of changes in 18 patients mostly confirmed the results obtained from statistical analysis. Mutations in BCR-ABL kinase domain do not seem to have any influence on the expression of all those genes.

The amounts of mBCR-ABL were very low or undetectable in patients' blood samples. Therefore, it was not possible to quantify it. The mBCR-ABL was detected rather in cells from patients with suboptimal response or resistance to treatement.

Key words: CML, BCR-ABL, imatinib, resistance, mutation, marker, gene expression, WT1, p21Cip, Bcl-2, Ki-67, mBCR-ABL

Klíčová slova: CML, BCR-ABL, imatinib, rezistence, mutace, marker, genová exprese, WT1, p21Cip, Bcl-2, Ki-67, mBCR-ABL