ABSTRACT:

Introduction: Together with the introduction of new therapeutic options in castration-resistant prostate cancer (CRPC), an advance in individual disease characterization is required. Since common biopsy methods are not suitable for the majority of CRPC patients, one possible solution is the liquid biopsy that is, the analysis of circulating tumor cells (CTCs) isolated from the cancer patients' blood.

Methods: A method based on the immunomagnetic enrichment of CTCs and subsequent PCR detection of tumor-associated genes (AdnaTest, Qiagen) was characterized and used for the detection of CTCs in 41 CRPC patients. Each patient was screened at the time of CRPC diagnosis and after the 3rd cycle of docetaxel therapy. A panel of genes associated with therapeutic decision-making was established and validated. Quantitative PCR (qPCR) method on a BioMark platform (Fluidigm, USA) was used to determine the expression of the gene panel in the CTC-enriched and primary tumor samples and the results were analyzed.

Results: CTCs were found in 85% and 45% of CRPC patients before and during the therapy, respectively. The presence of CTCs, as well as EGFR and AR PCR fragments, was associated with a decreased sPSA response and lower survival. The gene expression of the CTC-enriched and primary tumor samples differed significantly. The semi-quantitative AdnaTest results correlated with the gene expression measured by the BioMark. The Inter-individual differences in gene expression were higher than intra-individual differences at various time points. AR splice variant 7 (AR-V7) was present in 38% of AR positive samples. Both variants were associated with a decreased sPSA response. Twelve out of 27 genes from the monitored panel were found in the CTC negative samples.

Conclusions: AdnaTest proved its value as a CTC detection method in clinical practice and as a liquid biopsy method for individual characterization. The expression of the established gene panel differs between CTC-enriched and primary tumor samples as well as between samples taken before and during the therapy. The presence of mRNA from leukocytes has to be taken into account while using CTC-enriched samples for gene expression analysis. The expression of AR-related genes proved to have a prognostic value and is connected with the therapy response in CRPC.

Key words: circulating tumor cells; castration-resistant prostate cancer; immunomagnetic detection; personalized therapy