ABSTRACT

Introduction and aim of the study

Circulating tumor cells (CTCs) are a promising tool of identifying patients with castration-resistant prostate cancer (CRPC) who will benefit from often demanding cytotoxic therapy. The aim of this work was to evaluate the prognostic significance of CTC in docetaxel-treated CRPC patients. During the project, we also tested the various methods of CTC cultivation and studied their genetic profile as well as the genetic profile of histological specimen at the time of diagnosis.

Patients and methods

A total of 39 patients who met the CRPC criteria and were indicated for docetaxel chemotherapy were included in the prospective study. Blood collection for CTC analysis was done in all patients before chemotherapy and on the first day of the fourth or fifth cycle of docetaxel. In parallel, CTCs were cultivated. Isolation and detection of CTC was done using the AdnaTest system, which consists of immunomagnetic separation and subsequent detection of mRNA from the CTC lysate. The primary objective of the study was to evaluate the overall survival (OS) of patients. Survival analysis was performed using the Kaplan–Meier method of estimating the survival distribution function. The impact of individual factors was tested using the Log–rank test, the Wilcoxon test and the Cox regression model.

Results

Data of a total of 30 patients were used in the survival analysis. Circulating tumor cells were detected in a total of 33 out of 39 (84.6 %) patients before chemotherapy and 17 out of 32 (53.1 %) during docetaxel treatment. The mean OS was 15.3 (0.9–35.2) months. The longest OS was recorded in four patients who were CTC negative in both samples. During the project, we also tested the possibility of CTC detection in patients before radical prostatectomy. We did not detect CTC in any patient, including two patients with positive lymph nodes after surgery. We also tested two patients with high prostate-specific antigen levels and negative prostate biopsy, and no CTC were detected. In addition, we examined a total of 41 patients for the presence of androgen receptor (AR). The concentration of the AR fragment in the sample taken during docetaxel treatment was 1.5 to 11 times lower compared to the sample taken before chemotherapy. Regarding the methods of cultivation, the isolation of the mononuclear cell layer and its subsequent cultivation in the Roswell Park Memorial Institute medium with the addition of fetal calf serum proved to be the most efficient. We have also optimized the method of histological specimen processing for mRNA isolation and for subsequent analysis of expression of selected genes.

Conclusion

Analysis of CTC can help estimate the prognosis of CRCP patients who are indicated for docetaxel therapy. Cultivation of CTC and determination of their genetic profile, including comparison with the genetic profile of prostate cancer at the time of diagnosis, can further improve the estimation of response to cytotoxic therapy. The project was supported by grants IGA NT 12205–5 / 2011 and MZ ČR – RVO VFN64165.