Cell-free DNA for prostate cancer progression monitoring

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Background: Prostate cancer (PC) is the second most commonly occurring cancer as well as the second leading cause of cancer-related deaths in men in Western countries. Androgen deprivation therapy in combination with androgen receptor (AR) targeted therapy (ARTA) represents a current standard of therapy in both patients with metastatic hormonal sensitive (mHSPC) or castration-resistant PC (CRPC). However, despite therapeutical advancement, all patients eventually become resistant to therapy.

Objectives: Our goal is to monitor changes that may indicate ARTA failure, disease progression, and metastatic activity of PC.

Methods: We collect plasma samples of advanced PC patients treated by ARTA before, during, and after the treatment. The circulating cell-free DNA was isolated from 2 ml of plasma and was used for the analysis of AR gene amplification by modern and highly sensitive digital droplet PCR (Qiagen).

Results: Our data suggests a connection between AR gene amplification and ARTA failure in baseline samples (before the start of ARTA) of patients with metastatic PC (n=110). The AR gene amplification was found in 14 (15.4%) of patients and they have more often high-volume disease at the time of diagnoses compared to the patients without AR amplification (p=0.0286). Interestingly, 86 % (12 of 14) patients with AR gene amplification had bone metastases compared to 66 % of patients without CNV of AR (p=0.0757). Furthermore, the positive patients had significantly shorter time between castration and CRPC occurrence (p=0.0122), elevated levels of clinically relevant markers such as PSA, lactate dehydrogenase, and alkaline phosphatase (p=0.0006, 0.0073, and 0.0130, respectively), and decreased levels of haemoglobin (p=0.0001). Moreover, the amplification of the AR gene significantly correlated with time on ARTA in HSPC patients (p=0.017), but not in CRPC cohort (p=0.198).

Conclusion: The analysis of AR gene amplification and blood markers could provide useful information for the prognostic stratification of metastatic PC patients.