Prospective Multicenter Evaluation of PCA3 and TMPRSS2-ERG Gene Fusions as Diagnostic and Prognostic Biomarkers for Prostate Cancer

Introduction and Objective: PCA3 and ets gene fusions are two prostate cancer specific biomarkers that can be measured in urine. Our aim was to evaluate the diagnostic and prognostic value of Progensa PCA3 and TMPRSS2-ERG gene fusions (as individual biomarkers and as a panel) in a prospective multicenter setting.
Materials and Methods: We prospectively collected post-DRE first-catch urine specimens prior to prostate biopsies in six clinics. We assessed the predictive value of Progensa PCA3 and TMPRSS2-ERG (quantitative nucleic acid amplification assay to detect TMPRSS2-ERG mRNA) for prostate cancer, Gleason score, and clinical tumour stage (individually and as a marker panel). This was compared to serum PSA and the ERSPC risk calculator. In a subgroup (n=61) we evaluated biomarker association with prostatectomy outcome.
Results: Of the 497 men that were included, urine samples of 443 men contained sufficient mRNA for marker analysis. Prostate cancer was diagnosed in 196/443 men. Serum PSA, PCA3 and TMPRSS2-ERG correlated all significantly with prostate cancer. Both PCA3 and TMPRSS2-ERG had significant additional predictive value to the ERSPC risk calculator parameters in multivariate analysis ($p<0{\cdot}001$ and resp. $p=0{\cdot}002$). The AUC increased from 0·799 (ERSPC risk calculator), to 0·833 (ERSPC RC+PCA3), to 0·842 (ERSPC RC+PCA3+TMPRSS2-ERG). Sensitivity of PCA3 increased from 68% to 76% when combined with TMPRSS2-ERG. TMPRSS2-ERG had significant additional predictive value to the ERSPC risk calculator to predict Gleason score and clinical tumour stage, whereas PCA3 did not.
Conclusions: PCA3 and TMPRSS2-ERG are valuable diagnostic markers for prostate cancer. TMPRSS2-ERG had independently additional predictive value to PCA3 and the ERSPC risk calculator parameters for predicting prostate cancer. Furthermore, TMPRSS2-ERG had prognostic value, whereas PCA3 did not. By implementing the novel biomarker panel PCA3 and TMPRSS2-ERG into clinical practice, this would lead to a considerable reduction of prostate biopsies.