Validation of a Novel Non-Invasive Urine Exosome Gene Expression assay to predict High-grade prostate cancer in patients undergoing initial biopsy with an equivocal PSA.


INTRODUCTION AND OBJECTIVES: Better predictive tools are needed for men with equivocal PSA (2-10 ng/mL). EXO106 is a non-invasive, non-DRE urine assay utilizing a three-gene signature to predict Gleason score, >7 from GS6 and benign disease. Interim results on 255 patients from a prospective, observational, multi-institutional trial demonstrated an AUC of 0.74 with an NPV of 96% in differentiating higher risk disease. We now report on the final validation results of this trial.

METHODS: 1064 sequentially obtained first-catch non-DRE urine specimens from 25 urology practices (academic / community practices) were collected. Exosomes were isolated and RNA extraction performed. RT-qPCR RNA copy numbers of ERG and PCA3 were normalized to SPDEF. The primary objective of the trial: AUC EXO106 + standard of care (SOC=PSA, age, race, family history) > AUC SOC for discriminating GS7+ vs. GS6 and benign lesions. A training set cut-point, NPV, PPV, Sensitivity and Specificity were also assessed.

RESULTS: Urine samples from 519 men presenting for initial biopsy represented the intended use population (> 50 years, PSA 2-10 ng/mL, first biopsy, urine volume <50ml); median age 63 years, median PSA 5.12 ng/mL, 82% negative DRE, 77% no family history, 17% African American; 48% positive biopsy rate and 28% >/=GS7). The primary objective was achieved: EXO106+SOC AUC 0.72 (95% CI 0.68-0.77) > SOC AUC 0.63 (95% CI 0.58-0.68), p<0.00004. A dichotomous gene signature demonstrated excellent clinical performance in predicting high-grade disease; NPV 91%, PPV 36%, Sensitivity 92%, and Specificity 34%. Consistent for predicting high-grade disease, the EXO106 score significantly correlated with GS (p<0.001; Spearman’s rank-order). 27% (138/519) of men were predicted negative including 11% (9/84) Gleason score 3+4 (median age 66, lower volume) and only 5% (3/62) >/=4+3 patients.

CONCLUSIONS: We have validated a novel, non-invasive urine exosome gene signature and demonstrated excellent discrimination for the diagnosis of GS7+ prostate cancer for men presenting with indeterminate PSA results who would be candidates for initial biopsy. The assay should result in a 27% reduction of prostate needle biopsies while missing only 5% of higher grade >/= 4+3 cancers.

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