15-8025

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.

James McKiernan*, Michael Donovan, NYC, NY, Vince O'Neill, Cambridge, MA, Stefan Bentink, Mikkel Noerholm, Martinsried, Germany, Susan Belzer, St. Paul, MN, Johan Skog, Cambridge, MA, Alan Partin, Baltimore, MD, Gerald Andriole, St. Louis, MO, Gordon Brown, Vorhees, NJ, James Cochran, Dallas, TX, John Wei, Livonia, MI, Ian Thompson, San Antonio, TX, Peter Carroll, San Francisco, CA

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, >/=GS7 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. 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 ('expanded gray zone'), 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). Primary objective was achieved: EXO106+SOC AUC 0.72 (95% CI 0.68-0.77) > SOC AUC 0.63 (95% CI0.58-0.68), 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.