Introduction:

The ability to discriminate indolent from clinically significant prostate cancer (PCa) prior to initial biopsy remains an important health issue. Diagnostic assays that have been extensively evaluated in a prospective setting are necessary for efficacy and clinical adoption. We conducted a second independent validation study to assess outcome and cut-point performance of the ExoDx Prostate(IntelliScore) (EPI) (Figure 1) urine exosome assay vs. a standard of care model (SOCm) (i.e. prostate-specific antigen [PSA], age, race, and family history) for discriminating Grade group (GG) ≥2 PCa from GG1 PCa and benign disease reclassified from initial biopsy [1, 2, 3]. Exosomes are small vesicles released from cells into biofluids such as urine. These exosomes contain molecular information, including RNA signatures of tumor cells, which can be used to monitor disease status in real-time.

Methods:

This second independent validation study was designed as a two cohort, adaptive clinical implementation and utility study. In Phase 1 EPI test results were compared to biopsy outcomes for eligible subjects: ≥50 years, PSA 2-10ng/mL, scheduled for initial prostate needle biopsy. Here we report on the test performance in Phase 1 using the area under the receiver operating characteristic curve (AUC), negative predictive value (NPV), sensitivity, and specificity for discriminating aGG2 from GG1 and benign disease on initial biopsy. Results are compared to a previously published validation study [2] and other papers referring to the same cohort [13]. Please refer to Table 1: Cohort Information.

Results:

Phase 1 cohort consists of N=503 patients with median age 64 years, median PSA 5.4 ng/mL, 14% African American, 70% Caucasian, 53% positive biopsy rate (22% GG1, 17% GG2 and 14% >GG3). EPI shows an AUC of 0.70 superior to SOCm AUC of 0.62 and PSA AUC of 0.58 for discriminating aGG2 PCa from benign and GG1 PCa (Figure 2). (Comparison to the original validation cohort (N=519 patients, EPI AUC 0.71) demonstrated good agreement (Figure 3). Using the previously validated cut-point of 15.6 or alternative 20 (Figure 4) would avoid 26% (or 40%) of unnecessary prostate biopsies and 20% (or 31%) of total biopsies, with an NPV of 89% for both cut-points, and miss only 7% (or 11%) of aGG3, respectively (Table 1).

Conclusion:

EPI is an non-invasive, easy to use, world’s first exosome based 3-gen expression urine assay, which:

- has been validated in >1000 patients with PSA 2-10ng/mL
- discriminates high-grade (aGG2) from low-grade (GG1) PCa and benign disease
- accurately identifies patients with higher grade disease
- reduces the total number of unnecessary biopsies

References:

