Evaluating the ExoDx™ Prostate Test in Men with Grade Group One Cancer on Active Surveillance – A Multi-Center Prospective Trial

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Key Takeaways

- ExoDx and MRI can be used interchangeably to inform a shared decision to defer a confirmatory biopsy for men on Active Surveillance.
- Furthermore, in a population of men with negative MRI (PI-RADS 1-2), a low-risk ExoDx test has a 100% negative predictive value.

Background

The ExoDx™ Prostate Test (ExoDx)† is a unique genomic urine liquid biomarker test that can be collected at home or in the office to inform initial and repeat prostate biopsy decisions. The test was validated in multiple prospective multi-center trials. [1-3]

For men on Active Surveillance (AS), NCCN guidelines recommend a repeat confirmatory biopsy and mpMRI - usually within one year of diagnosis, to confirm AS eligibility. The guidelines acknowledge that a negative mpMRI does not exclude the possibility of prostate cancer, and biomarkers can be considered in the decision process to biopsy this population. [4-6] Biomarkers can provide an orthogonal risk assessment and complementary information to mpMRI for the biopsy decision. [7]

The ExoDx assay cut-point (15.6) was developed for men being considered for an initial or repeat biopsy. This study investigates the potential clinical benefit of ExoDx, with or without mpMRI, with respect to confirmatory biopsy deferral in men on AS.

Methods

Men on AS protocols with Grade Group 1 (GG1) on a diagnostic biopsy from 14 practices consented to provide a urine sample within a month prior to a subsequent confirmatory biopsy. The clinical data captured included patient demographics, PSA, DRE, mpMRI, and both diagnostic and confirmatory biopsy pathology data (Table 1). An interim analysis was performed on 330 patients, with enrollment currently on-going. Metrics were calculated based on the highest GG between the diagnostic and confirmatory biopsies.

Demographics in the Primary Endpoint (n=330)	
Age, median (IQR)	65.5 (60.0-71.0)
PSA, median (IQR)	5.3 (3.8-7.7)
DRE, n (%)	
Non-suspicious	160 (48.5%)
Suspicious	24 (7.3%)
Not Available	146 (44.2%)
Race, n (%)	
American Indian or Alaska Native	3 (0.9%)
Asian	9 (2.7%)
Black or African American	51 (15.5%)
Hispanic	29 (8.8%)
Native Hawaiian or Other Pacific Islander	2 (0.6%)
Other	10 (3.0%)
White	226 (68.5%)

Table 1. Patient Demographics from Interim Analysis Cohort

PI-RADS, n (%)	
1	23 (7.0%)
2	50 (15.2%)
3	89 (27.0%)
4	121 (36.7%)
5	47 (14.2%)
Confirmatory GG, n (%)	
Benign	71 (21.5%)
1	125 (37.9%)
2	103 (31.2%)
3	23 (7.0%)
4	5 (1.5%)
5	3 (0.9%)

Results

In this interim cohort of men on AS protocols (n = 330), 40.6% upgraded from GG1 to ≥GG2.

The ExoDx scores ranged from 5.3 to 95.1 with a median score of 35.2.

When mpMRI or ExoDx were evaluated independently (Table 2), the ExoDx test (at validated cut-point of 15.6) and mpMRI (PI-RADS 1-2 vs 3-5) had similar negative predictive values (NPVs) of 72.2% vs 72.6%, respectively.

In the subset of men with PI-RADS 1-2, the NPV for the ExoDx test was 100% (Table 1). Moreover, in a subset of men with PI-RADs 3, the ExoDx NPVs for ruling out an upgrade to GG≥2 and GG≥3 were 81.8% (Table 2) and 100% (not shown), respectively.

Clinical scenarios are modeled in Figures 1-2 assuming a cohort size of 1000:

Figure 1 (below) shows that high-grade prostate cancer (≥GG2) was missed similarly in men with either ExoDx or mpMRI low-risk results (28% vs. 27% respectively, p=0.97). Detection of ≥GG2 in high-risk PI-RADS was proportionately similar to high-risk ExoDx results (44% vs 42%, p=0.61). Figure 2 (right) shows that men with both low-risk ExoDx and mpMRI results have a 0% upgrade to ≥GG2, though there were only 21 men in the extrapolated group.

Table 2. Interim Analysis Performance Metrics

	ExoDx ≤15.6 (n=330)	mpMRI (n=330)	ExoDx ≤15.6 in PI-RADS 1-2 (n=73)	ExoDx ≤15.6 in PI-RADS 3 (n=89)
Sensitivity	92.5	85.1	100	93.1
NPV	72.2	72.6	100	81.8

Figure 1. Detection of HGPCA (≥GG2) In Extrapolated Cohort of n=1000 in ExoDx or mpMRI

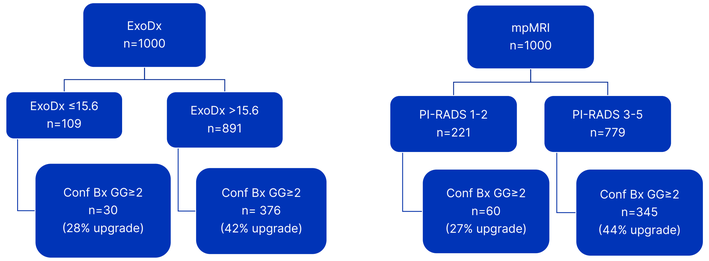
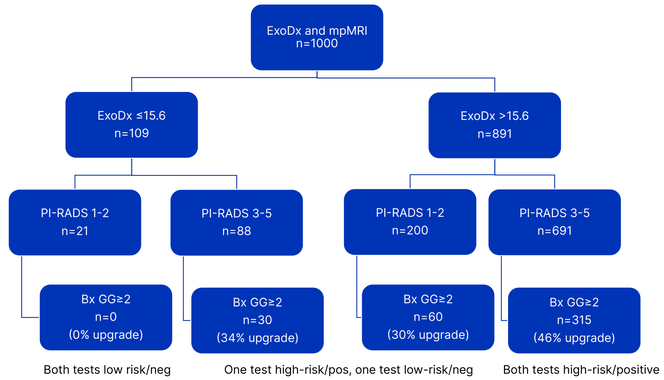


Figure 2. Detection of HGPCA (≥GG2) In Extrapolated Cohort of n=1000 in ExoDx and mpMRI



Conclusions

In a cohort of men getting *confirmatory biopsy after a GG1 diagnosis,* interim results demonstrate that:

- Patients on AS with a subsequent mpMRI PI-RADS of 1-2 and a negative ExoDx test could avoid repeat confirmatory biopsy without an increased risk of progressing to ≥GG2 prostate cancer.
- ExoDx may be valuable for men on AS protocols either as a standalone tool with a comparable NPV to mpMRI, or as a valuable complement to mpMRI results.

This urine-based test with equivalent NPV to mpMRI, in which samples can be collected at home or in the clinic, can provide a cost-effective and faster-turnaround time alternative to mpMRI as the test expands access to care. Additional studies should be performed to confirm these findings to influence clinical guidelines.

1. McKiernan J, Donovan MJ, O'Neill V, et al. A novel urine exosome gene expression assay to predict high-grade prostate cancer at initial biopsy. JAMA Oncol 2016; 2(7):1-8.
2. McKiernan J, Donovan MJ, Margolis E, et al. A prospective adaptive utility trial to validate performance of a novel urine exosome gene expression assay to predict high-grade prostate cancer in patients with prostate-specific antigen 2-10 ng/mL at initial biopsy. Eur Urol 2018; 74: 731-738.
3. Tutrone R, Donovan M, Torkler P, et al. Clinical Utility of the exosome bases ExoDx Prostate (Intelliscore) test in men presenting for initial biopsy with a PSA 2-10 ng/ml. Prostate Cancer and Prostatic Disease 2020.
4. Brandon R. Mason DO, James A. Eastham MD, Brian J. Davis MD, PhD, Lance A. Mynderse MD, MS, Thomas J. Pugh MD, Richard J. Lee MD, PhD, and Joseph E. Ippolito MD, PhD "Current Status of MRI and PET in the NCCN Guidelines for Prostate Cancer" Volume/Issue: Volume 17: Issue 5 Online Publication Date: May 2019
5. NCCN Guidelines insights – V3 2024
6. Henrik Olsson, Tobias Nordström, Fredrik Jäderling, et. al. Incorporating Magnetic Resonance Imaging and Biomarkers in Active Surveillance Protocols - Results From the Prospective Stockholm3 Active Surveillance Trial (STHLM3AS)
7. AJ Vickers, G Russo, C Evans, et al. How should molecular markers and magnetic resonance imaging be used in early detection of prostate cancer?

†ExoDx™ Prostate Test is a laboratory developed test (LDT). The Test and its clinical performance characteristics were established by Exosome Diagnostics, Inc. for initial and repeat prostate biopsy decisions in men. It has not been cleared or approved by the U.S. Food and Drug Administration (FDA). Exosome Diagnostics, Inc. is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high-complexity testing.
NOTE: The ExoDx Prostate Test (LDT) is being used within the study, *Evaluating the ExoDx™ Prostate Test in Men with Grade Group One Cancer on Active Surveillance – A Multi-Center Prospective Trial*, to explore new potential clinical benefits. The Test has not been validated or approved for the new exploratory applications.