May 29, 2015
To: submissions@nccn.org
Re: Submission Request- Prostate Cancer

Submitted by:
Name: Phillip Febbo, M.D.
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Date of Request- May 1, 2015
NCCN Guidelines Panel: Prostate Cancer-June 2015

On behalf of Genomic Health Inc., I respectfully request the NCCN Prostate Panel review the enclosed data and include the Onco*type* DX Prostate Cancer Assay in the guidelines as a diagnostic that provides an independent assessment of the presence of aggressive prostate cancer for men with very low, low, and intermediate risk prostate cancer. The Onco*type* DX Prostate Cancer Assay has multiple peer-reviewed publications reporting analytic validation, clinical validation, and clinical utility. In patients considering active surveillance, use of the Onco*type* DX Prostate Cancer Assay provides a precise and more accurate risk estimation that helps inform discussions and decisions between immediate definitive treatment or active surveillance.

Specific change: In the NCCN Guidelines Version 1.2015, tumor-based molecular assays are included as a class in footnote "b" on page PROS-1. The Onco*type* DX Prostate Cancer Assay is discussed in the supporting text on page MS-4. We recommend the following changes:

1) Include Onco*type* DX Prostate Cancer Assay as "a 17-gene RT-PCR-based assay to predict adverse pathology" in footnote "b" on page PROS-1 and update the discussion with the second validation study and clinical utility studies in the text on MS-4.
2) Include Onco*type* DX Prostate Cancer Assay in footnote "f" on page PROS-2 and PROS-3 as "Use of a 17-gene RT-PCR assay to predict adverse pathology can be considered to assess biological risk and guide management in patients with >10 years of life expectancy".
3) Include Onco*type* DX Prostate Cancer Assay as the second bullet point on page PROS-C in the section "Principles of Active Surveillance and Observation" as
    - Use of a 17-gene RT-PCR assay can assess biological risk and refine risk assessment for men considering active surveillance.

FDA Clearance: Performance of the Onco*type* DX Prostate Cancer Assay is regulated and certified as a laboratory developed test under the Clinical Laboratory Improvement Amendments (CLIA) and the College of American Pathologists (CAP). FDA clearance is not required for this assay.

Rationale: The robust development of the Onco*type* DX Prostate Cancer Assay now includes two independent validation studies and two clinical utility studies that demonstrate the test is a strong predictor of aggressive prostate cancer and, most recently, the Palmetto GBA's MolDX program has reviewed the development plan and issued a positive draft Local Coverage Decision that, when finalized, will provide coverage for Medicare beneficiaries.

The following articles are submitted in support of this proposed change.

Analytical validation studies

1. Knezevic D, Goddard AD, Natraj N, et al. Analytical validation of the Onco*type* DX prostate cancer assay -- a clinical RT-PCR assay optimized for prostate needle biopsies. BMC Genomics. 2013:14:690.

Clinical validation studies

1. Klein EA, Cooperberg MR, Magi-Galluzzi C, et al. A 17-gene assay to predict prostate cancer aggressiveness in the context of Gleason grade heterogeneity, tumor multifocality, and biopsy undersampling. Eur Urol. 2014;66(3):550-60.
2. Cullen J, Rosner IL, Brand TC, et al. A biopsy-based 17-gene Genomic Prostate Score predicts recurrence after radical prostatectomy and adverse surgical pathology in a racially diverse population of men with clinically low- and intermediate-risk prostate cancer. Eur Urol. 2014. doi: 10.1016/j.eururo.2014.11.030.

Clinical utility studies

1. Andriole G, Kemeter M, Kassabian V, et al. Clinical utility of the Genomic Prostate Score (GPS) in decision making for newly diagnosed prostate cancer. Presented at the American Urological Association Meeting-South Central; October 2014; Rancho Mirage, CA.
2. Badani K, Kemeter M, Febbo P, et al. The impact of a biopsy based 17-gene Genomic Prostate Score on treatment recommendations in men with newly diagnosed clinically prostate cancer who are candidates for active surveillance. Urology Practice. In press. DOI: http://dx.doi.org/10.1016/j.urpr.2014.10.010
3. Dall'Era M, Maddala T, Polychronopoulos L, et al. Utility of the Onco*type* DX prostate cancer assay in clinical practice for treatment selection in men newly diagnosed with prostate cancer (PCa): a retrospective chart review analysis. Urology Practice. In press.

Sincerely,

Phil Febbo, MD

Additional Information: