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NCCN Guidelines Panel: Prostate Cancer Treatment

On behalf of Myriad Genetic Laboratories, Inc., I respectfully request that the NCCN Prostate Cancer Panel review the enclosed request for modifications in order to have consistency in the manner with which tumor-based molecular assays are presented within the guidelines.

Specific changes:

1. On page PROS-3, Footnote L. Change to: "*Consider the use of tumor-based molecular assays (Decipher, Oncotype DX Prostate, Prolaris, Promark) in men with low or favorable intermediate risk disease with life expectancy of ≥10 y.* Retrospective studies have shown…."

2. On page PROS-3, Footnote C, please insert the following sentence following the Footnote. (Insert) *"Consider germline testing when personal history of high-grade prostate cancer (Gleason score ⩾ 7) at any age with ⩾ 1 close blood relative with ovarian carcinoma of any age or breast cancer ⩽ 50 y or two relatives with breast, pancreatic, or prostate cancer (Gleason score ⩾ 7 or metastasis) at any age."*

3. On page MS-5, please modify the following sentence. "Although full assessment of their clinical utility requires prospective randomized clinical trials, which are unlikely to be done, the panel believes that (change to) *consideration of the use of tumor-based molecular assays in men with clinically localized disease if life expectancy ≥ 10 y is warranted."*

4. On page MS-6, please modify the following paragraph. "The panel recommends inquiring about family and personal history of cancer, with ~~referral to genetic counseling~~ (insert) *consideration of genetic counseling and testing* if a familial cancer syndrome is suspected. In addition, due to the high prevalence of germline mutations, the panel recommends consideration of germline testing for all men with metastatic and high-/very-high-risk clinically localized prostate cancer (insert) *with* genetic counseling *provided by a qualified healthcare professional* ~~before and after such testing is essential~~.

Rationale: The NCCN Prostate Cancer Guidelines Version 2.2018 (March 8, 2018) has included clarification of the use of molecular testing in Risk Stratification and Staging Workup on page PROS-2. With respect to Specific change #1, Footnote L on page PROS-3, the word changes are requested to have consistency with the statements in the "Molecular testing of tumor" on page PROS-2, where it states "Consider if life expectancy ≥ 10 y."

With respect to Specific change #2, Footnote C on page PROS-3, the word changes are requested to have consistency with the statements in the "Germline testing" on page PROS-2, where it states "Consider if strong family history". In addition, the changes requested are consistent (and identical) with statements on page BRCA-1 of the NCCN Genetic/Familial High-Risk Assessment: Breast and Ovarian Guidelines Version 1.2018 (October 3, 2017) for personal history of prostate cancer Gleason score ≥ 7.

With respect to Specific change #3, page MS-5, again the word changes are requested to have consistency with the statements in the "Molecular testing of tumor" on page PROS-2, where it states "Consider if life expectancy ≥ 10y."

For Specific change #4, page MS-6, the requested wording recognizes ASCO, ACOG and other professional society position statements affirming that physicians with the necessary training can and should provide genetic counseling to their patients (i.e., see https://www.asco.org/about-asco/press-center/news-releases/asco-releases-updated-policy-statement-genetic-and-genomic, https://www.acog.org/Clinical-Guidance-and-Publications/Position-Statements/Access-to-Genetic-Testing).

Since the first mention of tumor-based molecular assays in the 2015 NCCN Prostate Cancer guidelines, data have been published in support of the Prolaris® test, a 46-gene RNA-expression assay that directly measures tumor cell growth characteristics to generate a cell-cycle progression (CCP) score. In multiple published studies, the CCP score proved to be an independent and the most powerful variable in predicting the risk of lethal prostate cancer, as determined by the clinically meaningful oncologic endpoints of prostate cancer-specific mortality, metastasis, and biochemical recurrence after radical prostatectomy. [1-10]

Given the existing published data and Medicare coverage for Prolaris and other prostate cancer prognostic tests, as well as tests for germline mutations, physicians have incorporated these tests into routine clinical practice. Our request for word changes is to allow for consistency of the recommendation already noted by the panel. We believe that these changes will facilitate the improved access to such testing for appropriate patients.

Literature support: A list of all publications supporting the use of Prolaris to predict lethal prostate cancer is referenced below.

Sincerely,

Todd Cohen, MD.
VP of Medical Affairs, Urology
Myriad Genetic Laboratories, Inc.

Johnathan Lancaster, MD, PhD.
Chief Medical Officer
Myriad Genetic Laboratories, Inc.

References:

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8. Tosoian JJ, Chappidi MR, Bishoff JT, et al: Prognostic utility of biopsy-derived cell cycle progression score in patients with National Comprehensive Cancer Network low-risk prostate cancer undergoing radical prostatectomy: implications for treatment guidance. *BJU Int* 2017; 120:808-4.
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10. Bardot S, Reid J, Latsis S, et al: Evaluating the prognostic utility of the CCP score for predicting prostate cancer aggressiveness in African American men. *J Urol* 194, issue 4, e346 (abstract MP28-19).