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NCCN Guidelines Panel: Prostate Cancer Treatment
Molecular and biomarker analysis of tumor:

On behalf of Myriad Genetic Laboratories, Inc., we respectfully request that the NCCN Prostate Cancer Panel review the enclosed request for modifications within the Prostate Cancer guideline, Version 1.2020 – March 16, 2020.

Specific changes:

1. We thank the committee for its recommendation of "Consider if life expectancy ≥ 10 y" in the Molecular/Biomarker Analysis of Tumor column on PROS-2. To have consistency throughout the Guideline, we request that on PROS-2A, footnote J, to read:

   "*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.* (delete: Men with low or favorable intermediate-risk disease and life expectancy ≥ 10 y may consider the use of the following tumor-based molecular assays: Decipher, Oncotype Dx Prostate, Prolaris, and ProMark). *Consider the use of Decipher and Prolaris tumor-based molecular assays in men with unfavorable intermediate- and high-risk disease and life expectancy ≥ 10 y.* Retrospective studies have shown that molecular assays performed on prostate biopsy or radical prostatectomy specimens provide prognostic information independent of NCCN or CAPRA risk groups. These include, but are not limited to, likelihood of death with conservative management, likelihood of biochemical progression after radical prostatectomy or external beam therapy, and likelihood of developing metastasis after radical prostatectomy or salvage radiotherapy."

2. On page MS-9, under Tumor Multigene Molecular Testing, 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) the *consideration of the use of tumor-based molecular assays such as Decipher, Oncotype Dx Prostate, Prolaris, or ProMark in men with clinically localized disease if life expectancy ≥ 10 y is warranted during initial risk stratification."* (Strike out) ~~men with low or favorable intermediate disease may consider the use of Decipher, Oncotype Dx Prostate, Prolaris, or ProMark during initial risk stratification.~~

Rationale and Summary:

Word changes are requested so that there is consistency with statements in the column titled "Molecular and biomarker analysis of tumor" on page PROS-2, where it states "Consider if life expectancy ≥ 10 y." Such consistency is important for providers and clinicians.

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

1. Bishoff JT, Freedland SJ, Gerber L, et al: Prognostic utility of the CCP score generated from biopsy in men treated with prostatectomy. *J Urol* 2014 Aug: 192(2):409-14.
2. Canter DJ, Reid, Latsis M, et al: Comparison of the prognostic utility of the cell cycle proliferation score for predicting clinical outcomes in African American and non-African American men with localized prostate cancer. *Eur Urol* 2019; 75:515-22.
3. Cuzick J, Swanson GP, Fisher G, et al. Transatlantic Prostate Group. Prognostic value of an RNA expression signature derived from cell cycle proliferation genes in patients with prostate cancer: a retrospective study. *Lancet Oncol*. 2011 Mar;12(3):245-55.
4. Cuzick J, Berney DM, Fisher G, et al. Transatlantic Prostate Group. Prognostic value of a cell cycle progression signature for prostate cancer death in a conservatively managed needle biopsy cohort. *Br J Cancer*. 2012 Mar 13;106(6):1095-9.
5. Cooperberg MR, Simko JP, Cowan JE, et al. Validation of a cell-cycle progression gene panel to improve risk stratification in a contemporary prostatectomy cohort. *J Clin Oncol*. 2013 Apr 10;31(11):1428-34.
6. Freedland SJ, Gerber L, Reid J, et al. Prognostic utility of cell cycle progression score in men with prostate cancer after primary external beam radiation therapy. *Int J Radiat Oncol Biol Phys*. 2013 Aug 1;86(5):848-53.
7. Cuzick J, Stone S, Fisher G, et al. Validation of an RNA cell cycle progression score for predicting death from prostate cancer in a conservatively managed needle biopsy cohort. *Br J Cancer*. 2015; 113:382–9.
8. Koch MO, Cho JS, Kaimakliotis HZ, et al. Use of the cell cycle progression (CCP) score for predicting systemic disease and response to radiation of biochemical recurrence. Cancer Biomark. 2016 Jun 7;17(1):83-8.
9. 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.
10. Lin DW, Crawford ED, Keane T, et al: Identification of men with low-risk biopsy-confirmed prostate cancer as candidates for active surveillance. Urol Oncol 2018 Jun;36(6):310.e7-310.e13. doi:10.1016/j.urolonc.2018.03.011. Epub Apr 11, 2018.
11. Stone S, Reid J, Brawer M: Patient NCCN Risk Classification Based on Combined Clinical Cell Cycle Risk (CCR) Score. Poster presented at: Genitourinary Cancers Symposium (ASCO-GU); 2017 Feb 17; Orlando, FL.

Sincerely,

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Myriad Genetic Laboratories, Inc.