<table>
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<th>Guideline Page and Request</th>
<th>Panel Discussion/References</th>
<th>Institution Vote</th>
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| **PROS-1**                                                                                | External submission from Myriad Genetic Laboratories, Inc. requesting addition of the following statement as a distinct step immediately to the right of “life expectancy >5y or symptomatic: “Tumor-based molecular assay if therapeutic decisions would be altered by estimating:  
  - prostate cancer-specific mortality  
  - metastasis-free survival  
  - risk of surgical findings showing adverse pathology.”  
  Based on a review of data and discussion, the panel did not use the language proposed in the submission. However, the panel supported adding a new page Risk Stratification and Staging Workup (PROS-2), which includes consideration for tumor-based molecular testing for certain patients.  
  See Submission for References. | YES 0 | NO 23 | ABSTAIN 0 | ABSENT 5 |
| **PROS-1**                                                                                | External submission from Myriad Genetic Laboratories, Inc. requesting an update to footnote “l” as shown below:  
  “Men with clinically localized disease may consider the use of tumor-based molecular assays. Retrospective case cohort studies have shown that molecular assays performed on biopsy or prostatectomy specimens provide prognostic information independent of NCCN 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 of salvage radiotherapy.”  
  Based on the data in the noted references, the panel consensus supported the modification of footnote “l” as shown below:  
  “Men with low or favorable intermediate risk disease may consider the use of the following tumor-based molecular assays: Decipher, Oncotype DX Prostate, Prolaris, ProMark. Retrospective studies have shown that molecular assays performed on prostate biopsy or radical prostatectomy specimens provide prognostic information independent of NCCN 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. See Discussion.”  
  See Submission for References. | YES 23 | NO 0 | ABSTAIN 0 | ABSENT 5 |
| **PROS-2**                                                                                | External submission from Genomic Health requesting review of potential inconsistencies in NCCN Guidelines regarding use of tumor markers. Clarify the levels of evidence and consensus review for physicians, patients and payers.  
  Based on a review of data and discussion, the panel supported adding a new page, Risk Stratification and Staging Workup (PROS-2), which includes consideration for molecular testing for certain patients.  
  See Submission for References. | YES 23 | NO 0 | ABSTAIN 0 | ABSENT 5 |

Process document updated 3.9.18
### PROS-2
External submission from Genomic Health requesting that “Consider tumor-based molecular assay” be added to the algorithm for all patients with prostate cancer and life expectancy >5 years or who are symptomatic.

Based on a review of data and discussion, consensus did not support consideration of molecular testing for all patients with prostate cancer with prostate cancer and life expectancy >5 years or who are symptomatic.

See Submission for References.

| 0 | 20 | 1 | 5 |

### PROS-2 through 6
External submission from GenomeDx Biosciences, Inc requesting modification as described below:
When considering adjuvant therapy, given the relatively high number needed to treat (NNT) to prevent metastasis seen in randomized controlled studies (NNT=121), we contend that individualized risk assessment and shared decision making should be employed. In PROS-2 through 6, when adverse pathological features are present after prostatectomy we suggest the inclusion of bullet points to calculate nomogram predictors of clinical or biochemical progression (i.e. CAPRA-S which has been validated in this setting) and additionally a bullet point for the Decipher GC as an independent prognostic marker that can augment the accuracy of these nomograms [1-6, 12-29], can reduce NNT to 3 [4] and can help decrease decision uncertainty and patient anxiety [6] (see appendix)

Based on a review of data and discussion, the panel consensus did not support the addition of these specific recommendations into the Guidelines.

See Submission for References.

| 10 | 11 | 2 | 5 |

### PROS-3 and 4
External submission from GenomeDx Biosciences, Inc requesting, for patients considering EBRT, the addition of a footnote stating “Decipher assay can be considered to provide an additional independent measure of metastasis risk.”

Based on the data in the noted references, the panel consensus supported the modification of footnote “I” as shown below:

“Men with low or favorable intermediate risk disease may consider the use of the following tumor-based molecular assays: Decipher, Oncotype DX Prostate, Prolaris, ProMark. Retrospective studies have shown that molecular assays performed on prostate biopsy or radical prostatectomy specimens provide prognostic information independent of NCCN 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. See Discussion."

See Submission for References.

| PROS-9 | External submission from Janssen Biotech, Inc. requesting addition of abiraterone plus prednisone with androgen deprivation therapy (ADT) as a systemic therapy for locally advanced and metastatic castration-sensitive prostate cancer. | Based on a review of data and discussion, the panel consensus supported the inclusion of abiraterone acetate plus prednisone with ADT as an option for systemic therapy for regional castration-naive prostate cancer, in patients with life expectancy >5 years. This is a category 2A recommendation. | See Submission for References. | 18 | 1 | 3 | 6 |

PROS-8
External submission from GenomeDx Biosciences, Inc requesting, in addition to PSADT, the addition of a bullet point for the Decipher GC as an independent predictor of metastatic progression in the setting of clinical M0 disease and a persistent or recurrent PSA after treatment.

Based on the data in the noted references and discussion, the panel consensus was to include Decipher molecular assay. This is a category 2B recommendation.

See Submission for References.

PROS-13
External submission from Janssen Biotech, Inc. requesting addition of abiraterone plus prednisone with androgen deprivation therapy (ADT) as a systemic therapy for locally advanced and metastatic castration-sensitive prostate cancer.

Internal submission, Institutional Review comment to review the data for the use of ADT and abiraterone acetate based on Latitude and STAMPEDE.

Based on the data in the noted references and discussion, the panel consensus was to include ADT and abiraterone with prednisone as a systemic therapy option for patients with M1 castration-naive prostate cancer. This is a category 1 recommendation.

See Submission for References.

PROS-16, PROS-G
External submission from Merck & Co. requesting the addition of pembrolizumab as a systemic treatment option for patients with unresectable or metastatic, microsatellite

Based on a review of data and discussion, the panel consensus supported the inclusion of pembrolizumab as an option for subsequent systemic therapy for patients with MSI-H or dMMR metastatic castration-resistant prostate cancer. This is a category 2B recommendation.

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<thead>
<tr>
<th>External submission from Prostate Cancer Patient Education and Advocacy Organizations:</th>
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<tbody>
<tr>
<td>- National Alliance of State Prostate Cancer Coalitions</td>
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<tr>
<td>- Prostate Cancer Conditions and Education Council</td>
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<tr>
<td>- Prostate Health Education Network</td>
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<tr>
<td>- Us TOO International Prostate Cancer Education &amp; Support</td>
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<tr>
<td>- ZERO- The End of Prostate Cancer</td>
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Request NCCN Guidelines to encourage clinicians to use the three molecular tests recommended by the “Molecular Diagnostic Services Program.”

| See Submission for references. |

| Based on review of the data and discussion the Panel supported modification of footnote "l": |

"Men with low or favorable intermediate risk disease may consider the use of the following tumor-based molecular assays: Decipher, Oncotype DX Prostate, Prolaris, Promark. Retrospective studies have shown that molecular assays performed on prostate biopsy or radical prostatectomy specimens provide prognostic information independent of NCCN 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. See Discussion." |

| 23 | 0 | 0 | 5 |