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NCCN Guidelines Panel: Prostate Cancer Early Detection

On behalf of Myriad Genetic Laboratories, Inc., we respectfully request that the NCCN Prostate Cancer Early Detection Panel review the enclosed request for modifications within the Prostate Cancer Early Detection guideline, Version 2.2020 – August 24, 2020.

Specific changes:

On PROSD-2, BASELINE EVALUATION, History and physical (H&P) including:

- Family cancer history. Please include the following footnote to provide guidance on the specific types of family cancer history to consider.
    - Family cancer history includes, but is not limited to, a first- or second-degree relative with metastatic prostate cancer, ovarian cancer, male breast cancer, female breast cancer ≤45, colorectal or endometrial cancer ≤50, or pancreatic cancer or two or more first- or second-degree relatives with breast, prostate, colorectal or endometrial cancer at any age. See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian and Pancreatic (CRIT-1) and NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal (LS-1). For patients who meet hereditary risk assessment criteria established in these guidelines, germline genetic testing is recommended.
- Replace footnote b as follows:
    - If there is a known or suspected cancer susceptibility gene mutation in the family, germline genetic testing is recommended and referral to a cancer genetics professional or urology professional should be considered. Certain germline mutations increase the risk for prostate cancer, earlier onset prostate cancer and/or more aggressive prostate cancer.
- On PROSD-2, RISK ASSESSMENT, Age column
    - Revise the following in the flow chart to:
        - Age 40-75 y for African American men or those with germline mutations which increase the risk for prostate cancer[a,*]
        - Age 45-75 y
        - Age >75 y, in select patients
    - Add new Footnote (*): Men with *BRCA1/2* or *HOXB13* pathogenic mutations have a significantly increased risk for prostate cancer before age 65 years. Prostate cancer in men with *BRCA2*

mutations occurs earlier and is more likely to be associated with prostate cancer mortality. Certain germline mutations increase the risk for prostate cancer, earlier onset prostate cancer and/or more aggressive prostate cancer. Consequently, for men with *BRCA2* mutations it is reasonable to recommend shared decision-making about annual PSA screening beginning at age 40 years, or 10 years before the youngest prostate cancer diagnosis in the family. For men with *BRCA1, HOXB13, ATM*, or mismatch repair (*MLH1, MSH2, MSH6, PMS2*) germline gene mutations it is reasonable to consider shared decision-making beginning at age 40 years.

FDA Clearance: Not applicable

Rationale and Summary:

Knowledge regarding germline mutation and the implications for prostate cancer risk and management is rapidly evolving.[1] The NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian and Pancreatic[2] and Genetic/Familial High-Risk Assessment: Colorectal[3] contain specific germline genetic testing criteria based on cancer family history risk assessment that is pertinent to men who may be at risk of carrying a prostate cancer associated gene. There are specific management recommendations and considerations noted for men with pathogenic mutations in several genes (*BRCA1, BRCA2, HOXB13, ATM, MLH1, MSH2, MSH6, PMS2*).[1,2] In addition, the identification of a germline mutation may increase the risk for other cancers for which surveillance strategies are available.[1-3]

It is imperative that health care providers incorporate a complete, extensive cancer family history that encompasses a wide range of cancers; it is no longer sufficient to just consider a family history of prostate cancer. Consequently, providing guidance on the family cancer history indicators within the Early Detection guideline would alert health care providers to the need for a quality family cancer history assessment. Clear guidelines regarding germline genetic testing will allow health care providers to appropriately stratify their patients' risk, an essential element of the prostate cancer risk-benefit discussion, and to help modify their treatment and management protocols.

Literature support: A list of select above referenced publications supporting the relevance of germline genetic testing to inform prostate cancer screening is below.

1. Giri VN, Knudsen KE, Kelly WK, et al. Implementation of Germline Testing for Prostate Cancer: Philadelphia Prostate Cancer Consensus Conference 2019. Journal of Clinical Oncology. 2020;38:24(2798-2811).
2. Daly MB, Pilarski R, Berry MP, et al. NCCN Clinical Practice Guidelines in Oncology. Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. Version1.2020 – December 4, 2019.
3. Gupta S, Weiss JM, Axell L, et al. NCCN Clinical Practice Guidelines in Oncology. Genetic/Familial High-Risk Assessment: Colorectal. Version1.2020 – July 21, 2020.

Sincerely,

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