Improving Utilization Rate of Germline Testing in Indicated Patients Diagnosed with Prostate Cancer at the Karmanos Cancer Center: A Quality Improvement Initiative

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1.0 Introduction - Background and Rationale

Purpose: To assess the current utilization rate of germline testing among prostate cancer patients and identify barriers to germline testing with the goal of increasing future offering of germline testing in individuals that meet NCCN prostate cancer criteria within Karmanos Genitourinary Cancer Clinic.

Background:

In recent years, our understanding of the role of pathogenic variants in prostate cancer has been rapidly evolving. While often an indolent disease, recent evidence has demonstrated that men with prostate cancer and certain germline mutations have worse oncologic outcomes and more aggressive disease compared with men with the wildtype variants of these genes. This has led to the NCCN (National Comprehensive Cancer Network) recommending prostate cancer screening at age 40 for men with BRCA2 pathogenic germline variants and consideration of screening at this age for men with other pathogenic germline variants, including BRCA1, ATM, and mismatch repair genes. Identifying patients with pathogenic germline variants is critical to determining which patients may benefit from targeted therapy or whose family members may benefit from cascade testing. This exemplifies the need for men with a family history or other risk factors to undergo germline testing to address their increased risk of prostate cancer.

2.0 Objectives

Primary Objective

2.1 Among patients eligible for germline testing per NCCN criteria, determine the proportion of patients with prostate cancer who have undergone germline testing

Secondary Objectives

2.2 Among patients with germline mutations, determine the proportion that were appropriately referred to a genetic counselor

2.3 Identify barriers to both germline testing and genetic counselor referral within the Karmanos Cancer Clinic

2.4 Develop an intervention to increase the proportion of patients receiving germline testing as recommended by the NCCN guidelines

2.5 To measure the proportion of patients receiving germline testing after the implementation of the intervention

3.0 Selection of Patients Meeting Criteria for Review

3.1 Inclusion Criteria:

- Patients seen in the KCI clinic since Jan 2021 that meet NCCN criteria for germline genetic testing (Figure 1)
- Diagnosis of prostate cancer

Exclusion Criteria:

- Patients with less than 6 months of follow-up
- Prior germline genetic testing
- Patients who do not meet NCCN criteria necessary for germline testing

4.0 Research Design and Methods

This is a retrospective chart review of Karmanos Cancer Center patients. Our plan is to first determine which new patients with a diagnosis of prostate cancer seen at the Karmanos Cancer Center Multidisciplinary Genitourinary clinic met NCCN criteria for germline testing (Figure 1). We will review if germline testing was ordered or discussed and if genetic counselor referral was placed. We will also collect demographic information including age, race (Caucasian, African American, Other, Unknown), and insurance status (Private, Medicare, Medicaid, Other) to determine if this varied based on patient specific characteristics. We will collect indication for germline testing (HR/VHR vs. Family history vs. TanyN+M+), and treating clinicians' specialty (urology, medical oncology, radiation oncology). Finally, we will assess patient and provider specific variables such as provider specialty to assess for provider specific characteristics associated with offering germline testing.

We will also conduct informal interviews with providers, clinic staff and patients to discern obstacles to obtaining germline testing

We will use the data obtained from this retrospective review set a SMART goal and design interventions to increase the proportion of qualified patients who receive germline testing. Interventions may include grand rounds presentations, posters in clinic, dot phrases within the medical record, etc. Following implementation of the intervention for 1 calendar year, we will then collect and reanalyze the proportion of patients meeting the primary endpoint in the baseline period and after the intervention.

5.0 Confidentiality of data

Data files pertaining to this project will be deidentified. The analytic dataset (consisting of PHI) will be fully deidentified, with each patient identified only by a study number consisting of consecutive integers. The analytic dataset will be password protected and stored on WSU issued computers. A second, password protected file will consistent of patient identifying information (such as name and DOB) as well as study number. This file will only exist for the purpose of chart review to generate the analytic cohort. Protected health information will not be reported or made public. Database access and research files will be restricted to IRB approved personally only. All electronic data files pertaining to this research will be password protected and any physical reports pertaining

to this research will be kept in a locked file cabinet. Electronic files will be password protected and stored and WSU issued computers.

6.0 Consent

This is a retrospective review. IRB approval will be obtained prior to data collection.

7.0 Statistical Considerations:

Summary statistics for the cohort will be reported as medians with interquartile ranges for continuous measures and counts and percentages for categorical variables. For the primary and secondary outcomes, we will estimate the proportion of patients meeting the outcome with the corresponding 95% CI utilizing the Wald method. To assess for the association of factors associated with the receipt of germline testing, we will fit a multivariable logistic regression model. Covariates that will be selected for inclusion in the model will primarily be hypothesis driven including: age, indication for testing (HR/VHR disease, family history, TanyN+M+), managing physician specialty (urology, medical oncology, radiation oncology), race (Caucasian, African American, Other, unknown), and insurance type (Private, Medicare, Medicaid, Other). For a model with 11 degrees of freedom, will require approximately 110-165 events. If we the sample size and event rate does not justify a model with 11 degrees of freedom, we will instead perform unadjusted simple logistic regression for each variable. After collection of data in the postintervention period, we will again compare the proportion of eligible patients meeting that obtained germline testing before and after the intervention with the chi-squared test. If the sample size and event rate justify, we will add intervention period (before vs. after) to the multivariable model with covariates described above.

9.0 Data Sharing

Data will not be shared.

Figure 1. NCCN Criteria for Hereditary Cancer Testing

PRINCIPLES OF GENETICS AND MOLECULAR/BIOMARKER ANALYSIS

Germline testing is recommended *in patients with a personal history of prostate cancer* in the following scenarios:

- **By prostate cancer stage or risk group (diagnosed at any age)**
  - **Metastatic, regional (node positive), very-high-risk localized, or high-risk localized prostate cancer**
- **By family history[a] and/or ancestry**
  - **≥1 first-, second-, or third-degree relative with:**
    - ◊ **breast cancer at age ≤50 y**
    - ◊ **colorectal or endometrial cancer at age ≤50 y**
    - ◊ **male (sex assigned at birth) breast cancer at any age**
    - ◊ **ovarian cancer at any age**
    - ◊ **exocrine pancreatic cancer at any age**
    - ◊ **metastatic, regional, very-high-risk, or high-risk prostate cancer at any age**
  - **≥1 first-degree relative (parent or sibling) with:**
    - ◊ **prostate cancer[b] at age ≤60 y**
  - **≥2 first-, second-, or third-degree relatives with:**
    - ◊ **breast cancer at any age**
    - ◊ **prostate cancer[b] at any age**
  - **≥3 first- or second-degree relatives with:**
    - ◊ **Lynch syndrome-related cancers, especially if diagnosed <50 y: colorectal, endometrial, gastric, ovarian, exocrine pancreas, upper tract urothelial, glioblastoma, biliary tract, and small intestinal cancer**
  - **A known family history of familial cancer risk mutation (pathogenic/likely pathogenic variants), especially in: *BRCA1, BRCA2, ATM, PALB2, CHEK2, MLH1, MSH2, MSH6, PMS2,* and *EPCAM***
  - **Ashkenazi Jewish ancestry**
- **Personal history of breast cancer**

Germline testing may be considered *in patients with a personal history of prostate cancer* in the following scenarios:

- **By prostate cancer tumor characteristics (diagnosed at any age)**
  - ◊ **intermediate-risk prostate cancer with intraductal/cribriform histology[c]**
- **By prostate cancer[b] AND a prior personal history of any of the following cancers:**
  - ◊ **exocrine pancreatic, colorectal, gastric, melanoma, upper tract urothelial, glioblastoma, biliary tract, and small intestinal**

[a] Close blood relatives include first-, second-, and third-degree relatives on the same side of the family. See Pedigree: First-, Second-, and Third-Degree Relatives of Proband (EVAL-B) in the NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic.

[b] Family history of prostate cancer should not include relatives with clinically localized Grade Group 1 disease.

[c] Acinar prostate adenocarcinoma with invasive cribriform pattern, intraductal carcinoma of prostate, or ductal adenocarcinoma component have increased genomic instability, and germline testing may be considered.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.