

## The Prognostic Benefit of Targeted Germline Sequencing in Men on Active Surveillance for Prostate Cancer

Category: Surgery & Surgical Specialties; Poster Presentation

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[Supplemental Video](#)

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**BACKGROUND/KNOWLEDGE GAP:** Prostate cancer (PCa) is the most commonly diagnosed male malignancy in the United States. Genetic inheritance portends significant risk of developing aggressive PCa, yet limited understanding exists of whether germline alterations play a significant role in localized disease for men on active surveillance (AS). This study aimed to determine whether germline screening in patients on AS for low-risk PCa provides prognostic information regarding risk of pathologic upgrading or disease progression.

**METHODS/DESIGN:** From a prospectively maintained Institutional Review Board approved cohort of men with localized low- or intermediate-risk PCa electing AS for their primary treatment modality, we queried patients with targeted germline screening to detect DNA alterations. Patients were subsequently followed with biannual prostate-specific antigen, annual digital rectal exam plus magnetic resonance imaging (MRI), and as-indicated biopsies.

**RESULTS/FINDINGS:** We identified 40 men with targeted germline screening using a commercial targeted platform. Of the 40 men, 15 (37.5%) had DNA alterations. Of those with DNA alterations, 6 had a known pathologic DNA mutation (e.g., WRN, MUTYH, HOXB13, CHEK2). At a median follow up of 5.5 years, of those without DNA alterations, 8 (32.0%) had been upgraded with the remaining still on AS. Of those with non-pathologic DNA alterations, 5 (55.6%) had been upgraded. Of those with known pathologic DNA mutations, 4 (66.7%) had been upgraded. Approximately half of the 40 men had underwent radical local curative therapy, and this rate was similar in both germline mutation and non-mutation cohorts.

**CONCLUSIONS/IMPLICATIONS:** This study analyzed 40 patients who underwent germline sequencing while on AS for low-risk PCa. A high rate of DNA alterations and thus mutational burden was detected in this cohort. The majority of those with DNA alterations, especially those with known pathologic mutations, were upgraded. Though larger sample sizes are needed to detect the true prevalence of germline aberrations in this population, these findings suggest germline sequencing may be of prognostic benefit to men on AS for low-risk PCa.

### Learning Objectives

1. Discuss the known DNA alterations that increase one's risk of malignancy.
2. Examine the relationship between DNA alterations and the risk of malignant progression of prostate cancer.