Poster #30 Influence of Cell Cycle Progression Molecular Testing on Selection and Durability of Active Surveillance in Patients with NCCN Intermediate-Risk Prostate Cancer

Lauren Lenz[1]; Wyatt Clegg[1]; Diana Iliev[1]; Elizabeth Cogan[1]; Howard Korman[2]; Todd Morgan[3]; Jason Hafron[4]; Alexander DeHaan[5]; Carl Olsson[6]; Ronald Tutrone[7]; Timothy Richardson[8]; Kevin Cline[9]; Paul Yonover[10]; Todd Cohen[1]; Robert Finch[1]; Thomas Slavin[1]

1. Myriad Genetics, Inc.;   2. Comprehensive Urology / Wayne State University;   3. University of Michigan;
4. Michigan Institute of Urology, Troy;   5. Urologic Consultants;   6. IMPPLLC;   7. Chesapeake Urology;
8. Wichita Urology;   9. Regional Urology;   10. UroPartners, LLC

INTRODUCTION

- Clinicopathologic features, such as Prostate Specific Antigen (PSA) and Gleason Score have been considered the gold standard for predicting disease severity and for guiding decision-making to pursue Active Surveillance (AS) or Definitive Treatment (DT).
- Prolaris is a commercially available test that combines a molecular score with clinicopathologic features to produce a Combined Clinical Risk (CCR) score; this score can be used to predict the likelihood of disease specific mortality and metastasis.
- This test has been clinically validated in untreated patients across all National Comprehensive Cancer Network (NCCN) risk groups, and clinical utility studies in different risk groups are ongoing.
- This prospective study evaluated the clinical utility of Prolaris to guide medical decisions on the selection and durability of AS in patients with NCCN Intermediate-risk prostate cancer.

METHODS

- Patients were tested with Prolaris between 09/2015-12/2018, following diagnosis with NCCN favorable- or unfavorable-intermediate risk prostate cancer at 10 community or academic urology clinics.
- CCR scores were calculated based on UCSF Cancer of the Prostate Risk Assessment (CAPRA) score and molecular variables identified from the sample submitted for testing.
- Patients with CCR-based 10-year disease specific mortality risk of ≤3.2% were considered below the AS threshold. Clinical follow-up data were reported by the clinics.
- Patients were required to have at least six months of follow-up to establish AS selection, which was defined as six or more months without DT following diagnosis.
- For patients who initially selected AS, AS durability was defined as the time from diagnosis to first DT.
- Logistic regression was used to predict binary AS selection. Cox proportional hazards models and Kaplan-Meier methods were used to describe AS durability at three years post-diagnosis.

RESULTS

Figure 1: Distribution of Combined Clinical Risk Scores Relative to Active Surveillance Threshold
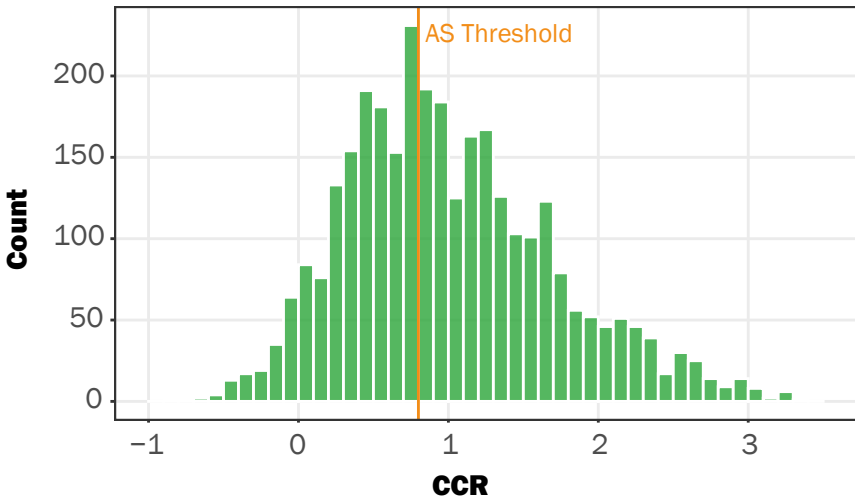
- The analysis set consisted of 3,138 patients (56% favorable-intermediate, 44% unfavorable-intermediate), 1,439/3,138 (46%) of whom had CCR-based mortality risks below the AS threshold (Figure 1).
- Patients with CCR-based mortality risk above the AS threshold were significantly less likely to initially select AS (20.4%, 95% confidence interval (CI) 18.5%-22.4%) than patients with risk below the threshold (42.2%, 95% CI 39.6%-44.8%; OR 0.41, 95% CI 0.36-0.47, p<0.001) (Figure 2).

Figure 2. Proportion Initially Selecting Active Surveillance Based on Prolaris Recommendation
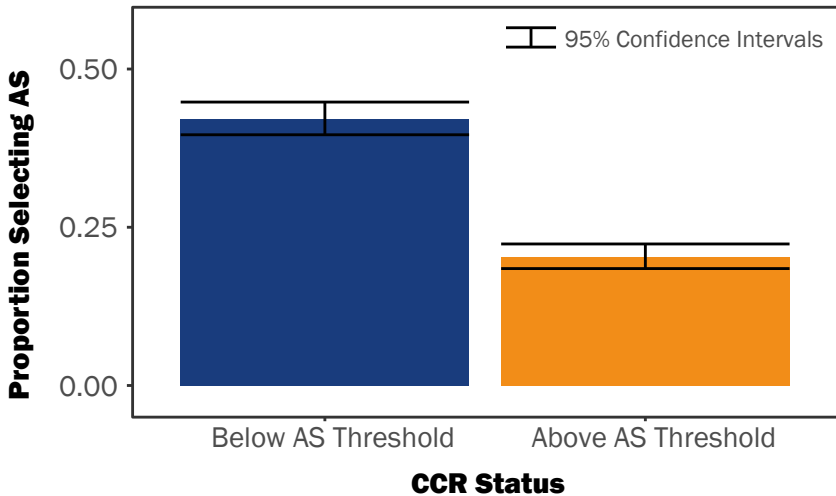
- In a bivariable model predicting initial AS vs DT selection, AS threshold status added significant, predictive information over CAPRA alone (AS threshold status OR 0.57, 95% CI 0.50-0.65, p<0.001; CAPRA OR .81, 95% CI 0.76-0.85, p<0.001).

Figure 3. Kaplan-Meier Plot for Active Surveillance Durability by Active Surveillance Threshold Status
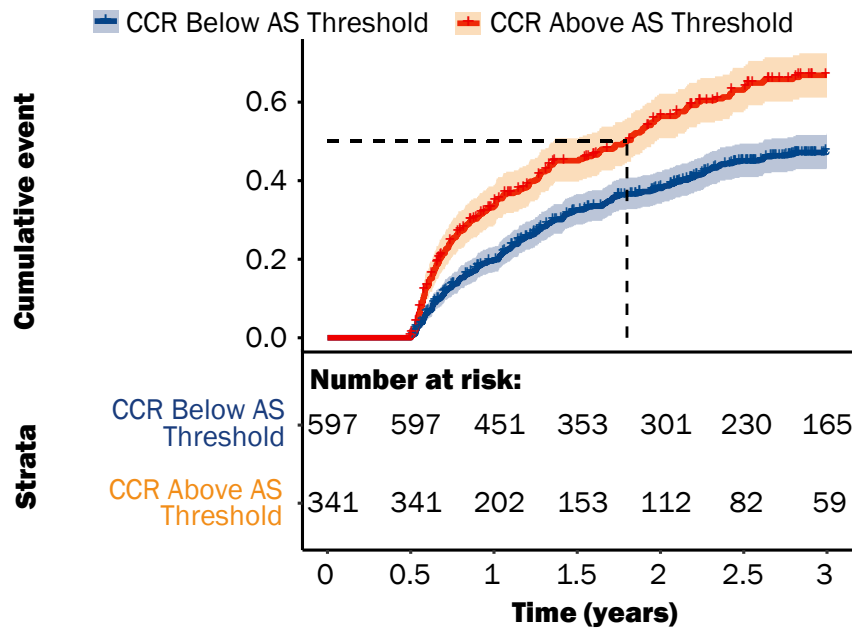
- Patients with CCR-based mortality risk above the AS threshold were more likely to exit AS for DT than patients with risk below the threshold (HR 1.68, 95% CI 1.38-2.03, p<0.001) (Figure 3).
- The three-year AS durability rate was 52.5% (95% CI 48.0%-56.8%) for patients below the AS threshold, and 33.2% (95% CI 27.6%-38.9%) for patients above the threshold (Figure 3).

CONCLUSIONS

- Patients with CCR-based mortality risk below the AS threshold were more likely to initially select AS compared to patients with scores above the threshold.
- Patients with CCR-based mortality risk below the AS threshold also experienced higher durability of AS.
- Prolaris provides important clinical information that significantly impacts treatment decisions in patients with NCCN favorable- and unfavorable-intermediate risk prostate cancer.