Evaluation of a predefined active surveillance threshold in a large cohort of men with localized prostate cancer

Daniel Canter, MD[1]; Julia E. Reid, MStat[2]; Saradha Rajamani, MStat[2]; Maria Latsis, MS[1]; Margaret Variano[1]; Shams Halat, MS[1]; Kristen E. Gurtner, MD[1]; Michael K. Brawer, MD[2]; Steven Stone, PhD[2]; Stephen Bardot, MD[1]

[1]Ochsner Clinic, Department of Urology, New Orleans, LA [2]Myriad Genetics, Inc., Salt Lake City, UT

BACKGROUND

- Men with newly diagnosed, localized prostate cancer (PC) have historically been selected for active surveillance (AS) using clinicopathologic features.
- However, a clinical cell−cycle risk (CCR) score has been developed to include both molecular [cell cycle progression (CCP) RNA signature] and clinical [Cancer of the Prostate Risk Assessment (CAPRA[1])] features.[2]
- Previous validations have demonstrated that this combined CCR score provides improved prognostic information relative to molecular or clinical features alone.
- As such, a CCR threshold score has been recently developed and validated to identify men with low−risk disease who may be candidates for AS.[3]
- Here, we have evaluated the performance of the AS threshold for discriminating risk of biochemical recurrence (BCR), metastatic disease, and disease-specific mortality in a contemporary cohort of men with newly diagnosed localized PC.

METHODS

COHORT

- Men with localized adenocarcinoma of the prostate who were treated at the Ochsner Clinic between 2006 and 2011 (4 patients were diagnosed in 2012−2014) were evaluated.

MOLECULAR TESTING

- Formalin−fixed paraffin embedded biopsy tissue was analyzed for the RNA expression of 46 genes (31 CCP genes and 15 housekeeping genes) to obtain a CCP score.[4]
- The CCR score was calculated as (0.57xCCP) + (0.39xCAPRA).[2]
- A CCR score threshold of 0.8 has been previously validated in a cohort of conservatively managed men.[3]

STATISTICAL ANALYSIS

- Men with a CCR score equal to the threshold had an estimated 10−year disease−specific mortality risk of 3.3%, while men with scores below the threshold had a 2.7% risk.
- All patients were censored at 7 years from initial diagnosis date.

Presented at ASCO-GU on February 8, 2018.

RESULTS

- Complete molecular and clinical information were available for 767 men with a median clinical follow−up time of 5.2 years measured from date of diagnosis.
- 217 men had CCR scores ≤ 0.8 (Table 1).
  - Of these, 125 were treated by radical prostatectomy, 61 with radiation, 2 with radiation with hormones, 2 with hormones only, and 19 with watchful waiting. Treatment for eight men were unknown.
- One patient (0.5%) with a CCR score below the AS threshold progressed to metastatic disease, and was initially treated with radiation (Figure 1).

Table 1. AUA Risk Category among Men with CCR Scores Below Threshold (n=217)

AUA category	N	%
Low	181	83.4
Intermediate	31	14.3
High	5	2.3

Figure 1. 7-year Prostate Cancer Metastasis Risk (N=767)

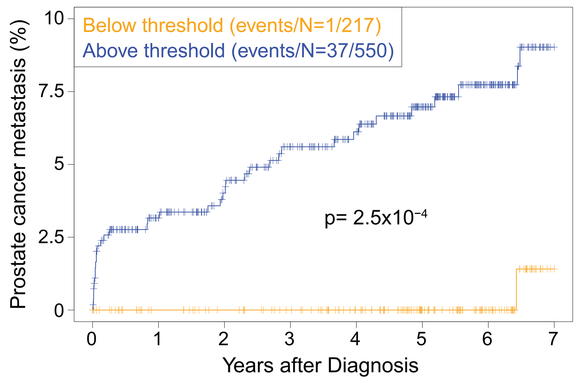
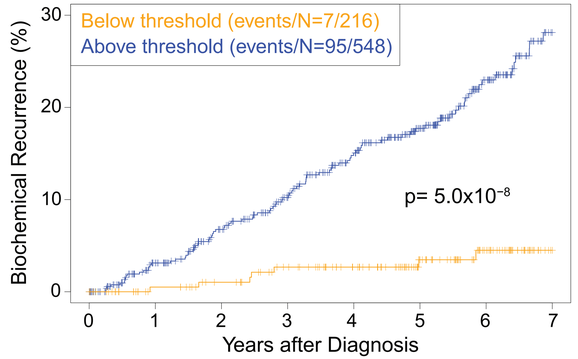


Figure 2. 7-year Prostate Cancer BCR Risk (N=764*)



*1 man below threshold and 2 above threshold were missing BCR event information

Figure 3. 7-year Prostate Cancer BCR Risk by CCR Threshold and AUA Category

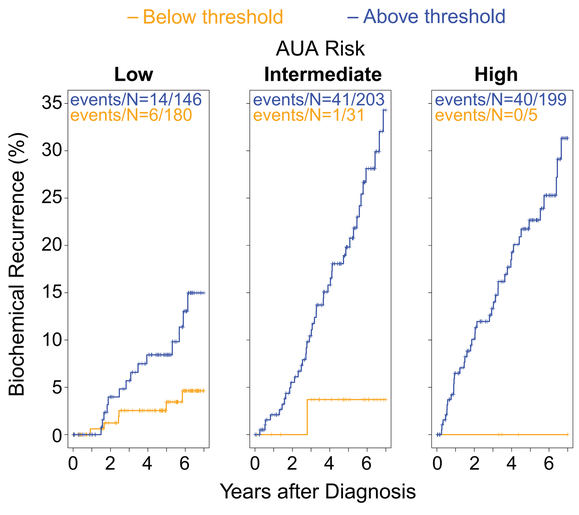
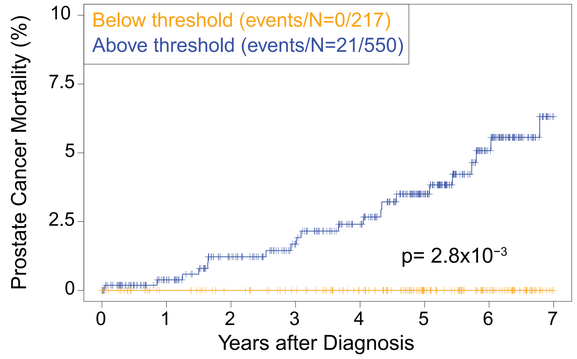


Figure 4. 7-year Prostate Cancer Death Risk (N=767)



- Seven patient (3.2%) with a CCR score below the AS threshold experienced BCR, and were initially treated with prostatectomy (Figures 2 and 3).
  - Kaplan-Meier plot for each AUA category is not generated for prostate cancer mortality and metastasis endpoints due to small event rate.
- There were no prostate-cancer specific deaths among men with scores below the threshold (Figure 4).

CONCLUSIONS

- We evaluated the performance of a previously validated AS threshold on a contemporary US cohort.
- The observed adverse event risk estimates in this cohort are in line with the established risk estimates from previous studies.
- The CCR threshold can be used safely to identify candidates for active surveillance in treated patients.

REFERENCES

1. Cooperberg M, et al. J Urol. 2005;173(6):1938-42.
2. Cuzick J, et al. *Br J Cancer.* 2015;113:382-389.
3. Lin D, et al. Presented at American Urological Association Western Section, 2016.
4. Cuzick J, et al. Lancet Oncol. 2011;12(3):245-25.

PLEASE EMAIL DANIEL CANTER (DANIEL.CANTER@OCHSNER.ORG) WITH ANY QUESTIONS OR COMMENTS