

# Outcomes of Men with Prostate Cancer Managed with Active Surveillance and Tested with a Clinical Cell-Cycle Risk Score<sup>†</sup>

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## BACKGROUND

- Many prostate cancers are indolent, making some men eligible to undergo active surveillance (AS) instead of immediate definitive treatment based on their risk of disease progression.
- The combined clinical and molecular cell-cycle risk (CCR) score provides improved prognostic information about tumor aggressiveness over clinical parameters alone.
- This study evaluated the clinical outcomes of men with low-risk prostate cancer by both National Comprehensive Cancer Network (NCCN) guidelines and CCR score who selected AS.

## METHODS

- This study included 664 men with localized prostate cancer who received CCR testing between 2013 and 2017.
  - All men had low-risk disease by NCCN guidelines and CCR score [risk of disease-specific mortality (DSM) <3.2%].
- Men selected AS (no treatment within 6 months of diagnosis) or underwent immediate definitive treatment.
- Durability of AS was evaluated from diagnosis to initiation of definitive therapy.
- Outcomes were determined by reporting adverse events, including biochemical recurrence (BCR), progression to metastasis as confirmed by radiographic imaging, or DSM.
- Wilcoxon Rank Sum test and Fisher’s exact test were used to evaluate differences.
  - p-value <0.05 was considered statistically significant.

## RESULTS

- Men who received immediate definitive treatment (N=117) had more aggressive disease characteristics than those who selected AS (N=547; Table 1).
  - Median follow-up for the full cohort was 2.2 years (IQR 1.4, 3.0).

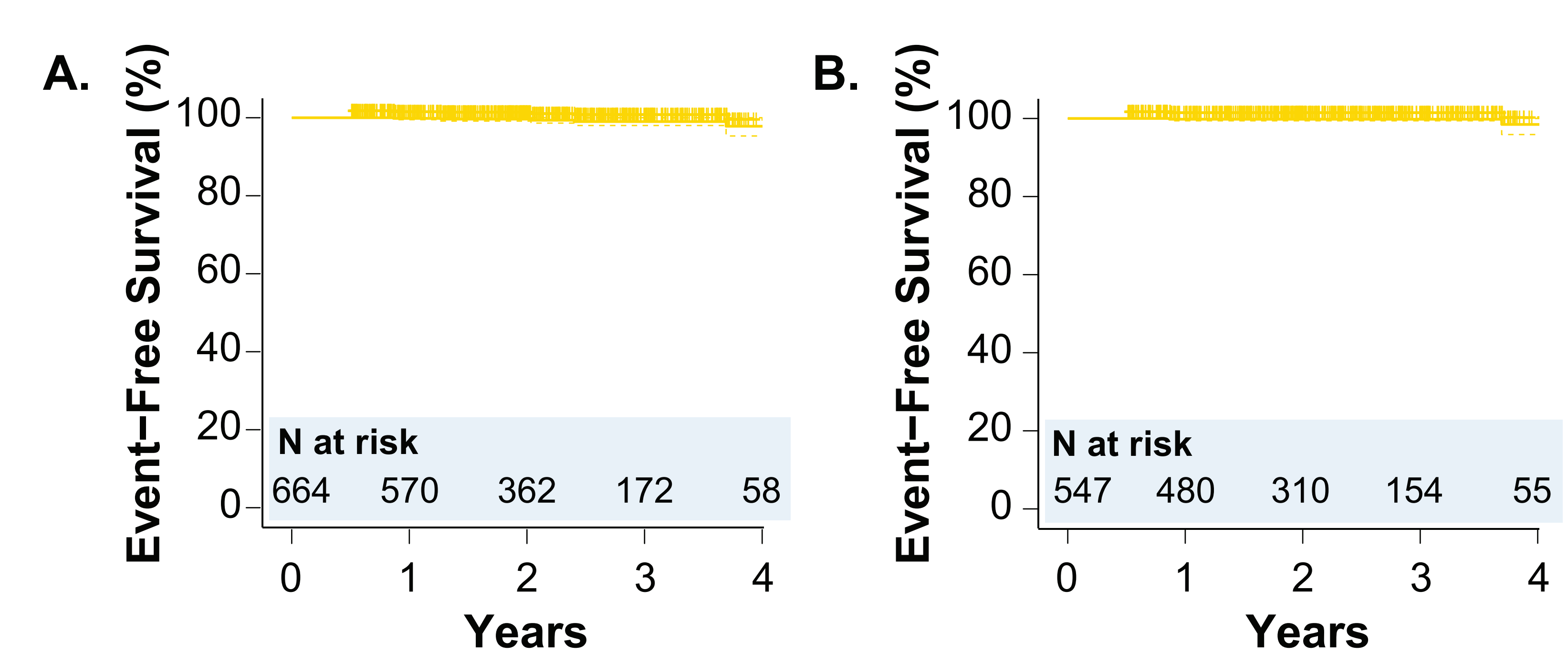
**Table 1. Disease Characteristics by Cohort.**

Variable	Statistic/Category	AS cohort (N=547)	Treated cohort (N=117)	p-value
Prebiopsy PSA (ng/mL)	Median (IQR)	4.8 (3.9, 6.0)	5.1 (3.8, 6.4)	0.263
Tumor Stage N (%)	T1a	134 (24.5%)	9 (7.7%)	<0.001
	T1c	367 (67.1%)	95 (81.2%)	
	T2a	42 (7.7%)	13 (11.1%)	
% Positive Cores	Median (IQR)	16.7 (8.3, 25.0)	20.1 (10.8, 33.3)	0.010
# Positive Cores N (%)	≤2	366 (66.9%)	60 (51.3%)	0.003
	>2	180 (32.9%)	56 (47.9%)	
CCR Score	Median (IQR)	-0.07 (-0.30, 0.22)	0.10 (-0.24, 0.43)	0.024

IQR: interquartile range; Some were missing information on tumor stage and # positive cores.

- Only 0.8% (5/664) of the full cohort experienced an adverse event (Figure 1A).
  - 0.4% (2/547) of the men managed by AS experienced an adverse event (Figure 1B).
  - One man experienced BCR 3.7 years post-diagnosis (underwent radical prostatectomy at 2.1 years).
  - The other experienced metastasis 0.9 years post-diagnosis and underwent definitive treatment.
  - There were no reported cases of DSM.

**Figure 1. Event-Free Survival in the Full Cohort (A, N=664) and Among Men Who Selected AS (B, N=547).**



- Among patients who initially selected AS, most (69.6%) remained on AS for >3 years (Table 2).

**Table 2. Durability of AS.**

Year	Evaluable men (N)	Treatment-free survival (95% CI)*
1	441	91.2% (88.4%, 93.3%)
2	260	78.9% (74.8%, 82.4%)
3	123	69.6% (64.5%, 74.1%)
4	45	65.2% (58.9%, 70.8%)

\*Based on Kaplan-Meier estimates.

- Reasons for leaving AS included patient choice (27.1%), increase in Gleason score (23.3%), and change in PSA (10.5%; Table 3).
  - Only 4 who exited due to PSA change (N=14) exhibited a clinically-significant increase in PSA (>10 ng/mL).

**Table 3. Reasons for Leaving AS.**

Reason	N (%) of AS cohort (N=547)	% of patients who left AS (N=133)
Gleason score	31 (5.7%)	23.3%
PSA*	14 (2.6%)	10.5%
Imaging	6 (1.1%)	4.5%
Tumor volume	3 (0.5%)	2.3%
Patient choice	36 (6.6%)	27.1%
Other/missing	43 (7.9%)	32.3%

\*There was no PSA doubling in this cohort.

## CONCLUSIONS

- Most men with NCCN low-risk prostate cancer confirmed by CCR score selected AS in this cohort
- The incidence of metastatic disease or BCR was rare and the majority of men who selected AS remained on AS for the duration of the study.
- Utilizing the CCR score during risk assessment may allow more patients to safely avoid unnecessary over-treatment, thus reducing the financial and physical costs related to treatment of prostate cancer and treatment-related morbidities.

<sup>†</sup>Kaul, S, et al. *Per Med.* 4 September 2019