Undetectable Prostate-Specific Antigen After Short-Course Androgen Deprivation Therapy for Biochemically-Recurrent Patients Correlates with Time to Metastasis and Prostate Cancer-Specific Survival

Daniel M. Lim¹, Roman Gulati², Serge Aleshin-Guendel², Agnes Gawne², Jonathan T. Wingate², Heather H. Cheng¹, Ruth Etzioni², and Evan Y. Yu¹

¹Department of Medicine, Division of Oncology, University of Washington, Seattle Cancer Care Alliance, Seattle, WA

²Biostatistics and Biomathematics, Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA

Abstract

Background: Optimal utilization of novel therapies for advanced prostate cancer is challenging without a validated surrogate efficacy endpoint. Ongoing trials are using durable undetectable prostate-specific antigen (PSA) levels as a marker of efficacy. The clinical relevance of prolonged undetectable PSA after a short course of androgen deprivation therapy (ADT) is uncertain.

Methods: The University of Washington Caisis database was queried for radical prostatectomy patients who received 6–12 months of ADT after biochemical recurrence (BCR), defined as PSA 0.2 ng/mL and no radiographically detectable metastasis. Proportions of men with undetectable PSA 12 and 24 months after ending ADT were compared to a hypothesized 5% rate using exact binomial tests. Associations with patient and tumor characteristics were examined using logistic regression, and associations with risk of subsequent metastasis and death were evaluated by log-rank tests.

Results: After ineligibility exclusions, 23/93 (25%; 95% CI 16–35%; $P<0.001$) and 14/93 (15%; 95% CI 9–24%; $P<0.001$) had undetectable PSA 12 and 24 months after ending ADT, respectively. Detectable PSA at 12 months was associated with increased risk of metastasis ($P=0.006$), prostate cancer-specific death ($P=0.028$), and death from any cause ($P=0.065$). Being 1 year older at diagnosis was associated with a 14% (95% CI 5–24%; $P=0.006$) decrease in the odds of having a detectable PSA after controlling for PSA at diagnosis, PSA doubling time, grade group, and time from initial therapy to BCR.

Conclusions: This single-institution retrospective analysis shows that it is not uncommon to have undetectable PSA 12 or 24 months after a short course of ADT. No baseline prognostic

Corresponding Author Contact Information: Evan Y. Yu, M.D., University of Washington, Seattle Cancer Care Alliance, 825 Eastlake Ave E, G4-800, Seattle, WA 98109-1024, evanyu@u.washington.edu, (206) 606-6292.

Disclosure Statement

No relevant disclosures from all coauthors.

characteristic other than age was associated with a durable (12 month) undetectable PSA. Because a durable undetectable PSA was associated with lower risks of metastasis and prostate cancer-specific death, it may be a reasonable clinical trial endpoint.

Keywords

landmark; surrogate; endpoint

INTRODUCTION

After radical prostatectomy for localized prostate cancer, approximately 20% of men will have biochemical recurrence (BCR) within 10 years.¹ Even after salvage therapy with curative intent, prostate-specific antigen (PSA) levels may continue to rise, and there is no known survival-prolonging treatment for this patient population.² For these men, intermittent androgen deprivation therapy (ADT) is a reasonable standard of care with non-inferior survival and an improved side-effect profile for the patient compared to continuous ADT.³ It has previously been established that the duration of the first off-cycle correlates with overall survival.⁴ Additionally, time to PSA recurrence during the first off-cycle correlates with progression to castration-resistant prostate cancer (CRPC).⁵

Even with ADT for the BCR disease state, some patients have excellent results while others respond only for a short duration. For instance, in the same study that demonstrated the correlation of first-off cycle with overall survival, median times from primary treatment to CRPC and death were 8.6 years (range, 2.8 to 21.0 years) and 11.5 years (range, 5.0 to 21.6 years), respectively.⁴ These wide ranges reflect heterogeneity in this patient population. Although some patients who receive a single short-course of ADT (e.g., 6–12 months) maintain low PSA levels for years, the conventional wisdom is that such outcomes are rare.⁶

There are currently several low-toxicity therapies that have demonstrated efficacy in the treatment of metastatic CRPC (mCRPC), such as sipuleucel-T, abiraterone acetate, and enzalutamide.⁷ These active therapies, however, are not generally introduced until many years after BCR, as they are only FDA-approved for mCRPC. Recent data support the early use of both docetaxel chemotherapy or abiraterone acetate in combination with ADT for metastatic hormone-sensitive prostate cancer, with dramatic survival benefits.^{8–11} Although intriguing, investigating survival at earlier disease time points (e.g., at BCR) is challenging, as median time to clinical metastasis was 10 years in an untreated BCR cohort.¹² Therefore, it is important to establish an early indicator of therapeutic efficacy, and several studies are using the undetectable PSA rate after a short course of therapy after 12 or 24 months with and without the recovery of testosterone in this fashion. The ongoing Abicure trial (NCT01751451), for example, would benefit from an analysis demonstrating that their primary endpoint of undetectable PSA with a recovered testosterone level of >150 ng/dL at 18 months is clinically meaningful.

To reliably evaluate whether these novel agents are effective before developing evidence of metastasis using undetectable PSA as an early endpoint, it is necessary to establish the rate at which patients have durable responses after ADT is discontinued. Furthermore, identifying baseline clinical characteristics associated with durable response may help to

identify patient populations with more versus less aggressive disease and help inform appropriate therapy and clinical trial eligibility. Finally, it is informative to empirically assess whether durable response is associated with long-term outcomes, including metastasis, prostate cancer-specific death, and death from any causes. These are the three goals of this study.

METHODS

Patients:

This is a single-center retrospective study of men with nonmetastatic prostate cancer who received a short course of ADT for BCR. The medical records for this analysis were abstracted from the Caisis database from March 1986 to September 2017, an in-house repository that stores the patient medical information for all genitourinary cancer patients seen at the University of Washington Medical Center and Seattle Cancer Care Alliance. To determine the patients eligible for this analysis, the Caisis database was queried for patients with a histological diagnosis of prostate cancer with any T and N stage without metastasis (M0) from bone and computed tomography scans. The search query was then narrowed to those who underwent radical prostatectomy for localized disease as primary treatment. Finally, patients who underwent 6–12 months of subsequent short-term ADT were included. Baseline characteristics, laboratory, pathology, treatment, and outcome data were collected and compiled. The study was reviewed and approved by the institutional review board of the Fred Hutchinson Cancer Consortium.

Patients who received adjuvant therapy after surgery were included in this analysis with or without simultaneous ADT. For patients who received ADT with radiation therapy concurrently, the following cycle of ADT, which was the first cycle of ADT with non-curative intent, was used in this analysis only if testosterone had recovered to ≤ 50 ng/dL. Similarly, patients were considered eligible for this analysis if they previously received ADT prior to surgery and testosterone was proven to have recovered to ≤ 50 ng/dL at the time of ADT initiation with non-curative intent. Following surgery or adjuvant therapy, patients must have had BCR, defined as PSA ≥ 0.2 ng/mL on a lab draw and >0.2 ng/mL on the following lab draw, with at least 1 month between obtained values.¹³ Time to recovery of testosterone to non-castrate levels during the off cycle was also abstracted and defined separately for separate analyses as testosterone ≤ 50 ng/dL and ≤ 150 ng/dL. Patients were then evaluated for PSA recurrence following completion of short-term ADT using the same definition as for initial BCR.

Study Design:

Our primary aim was to determine the proportion of men with undetectable PSA 12 and 24 months after short-term ADT for BCR. Proportions were calculated with and without conditioning on testosterone recovery to non-castrate levels (≤ 50 ng/dL and ≤ 150 ng/dL).

A secondary aim of this study was to evaluate associations between PSA status at these times and demographic and clinico-pathologic characteristics, namely patient age and PSA at diagnosis, grade group, time from prostatectomy to BCR, and PSA doubling time. PSA

doubling time from BCR to initiation of ADT was calculated using all values from BCR after last local definitive therapy to the initiation of ADT using the Memorial Sloan Kettering prostate cancer nomogram.¹⁴ Definitive local therapy included primary, adjuvant, or salvage radiation therapy or surgery.

The final aim of this study was to determine associations between PSA status and long-term outcomes, namely metastasis-free survival, prostate-cancer specific death, and death from any cause. Date of metastasis was defined by RECIST 1.1 criteria with any lymph nodes >1.5 cm on the short axis, nodules >1 cm on the long axis, or new skeletal metastasis identified by bone or computed tomography scans.¹⁵

Statistical Methods:

To test whether proportions of men with undetectable PSA 12 and 24 months after completing ADT for BCR exceeded a nominal level, exact binomial tests were used to determine whether the true proportion was equal to 5%. The test was repeated among subgroups of men who recovered testosterone to non-castrate levels of 50 ng/dL and 150 ng/dL. To evaluate associations between PSA status and baseline characteristics, logistic regressions were fit using complete case analyses. To evaluate associations between PSA status and long-term outcomes, Kaplan-Meier estimation and log-rank tests were used. To explore whether associations remained after accounting for any significant baseline characteristics variables, Cox proportional hazards regressions were fit and likelihood ratio tests were used in complete case analyses.

RESULTS

From the initial Caisis query, 190 men were evaluated under study criteria. After data abstraction, 93 men met the eligibility criteria for this analysis (Figure 1). Characteristics of the eligible patients are presented in Table 1. At diagnosis, the median age was 60 years (range, 44 – 76 years) with a median PSA of 8.5 ng/mL (range, 1.1 – 131.0 ng/mL). The median grade group was 3 (range, 1 – 5), and the median time from initial local definitive therapy to BCR was 1.5 years (range, 15 days – 10 years). Prior to short-term ADT for BCR, the median PSA doubling time was 6.0 months (range, 1.0 – 33.0 months). In addition to radical prostatectomy as primary therapy, 12 patients received adjuvant radiation therapy, 40 received salvage radiation therapy, and 10 received salvage ADT concurrent with salvage radiation. All patients received 6–12 months of ADT after BCR and had at least 12 months of subsequent follow-up.

Of the 93 eligible patients who received ADT after radical prostatectomy, 23/93 (25%; $P<0.001$) of men had undetectable PSA at 12 months and 14/93 (15%; $P<0.001$) of men had undetectable PSA at 24 months (Table 2). Among men who recovered testosterone to 50 ng/dL, 13/65 (20%; $P<0.001$) had undetectable PSA at 12 months and 10/65 (15%; $P=0.001$) had undetectable PSA at 24 months. For men who recovered testosterone to 150 ng/dL, 13/60 (22%; $P<0.001$) had undetectable PSA at 12 months and 10/60 (17%; $P<0.001$) had undetectable PSA at 24 months.

Results of the logistic regression to evaluate associations between PSA status and baseline characteristics are presented in Table 3. There was a significant association between age at diagnosis and undetectable PSA at 12 months ($P=0.006$). Specifically, being 1 year older at diagnosis was associated with a 14% (95% CI 5–24%; $P=0.006$) decrease in the odds of having a detectable PSA at 12 months after controlling for PSA at diagnosis, grade group, time from initial therapy to BCR, and PSA doubling time. No other baseline characteristics were significantly associated with PSA status at 12 months. In this analysis, only 59 patients were included because they had complete data. In a separate analysis excluding PSA doubling time, similar results were obtained using data from 81 patients with complete data.

Metastasis-free survival, prostate cancer-specific survival, and overall survival given PSA status at 12 months after completing ADT for BCR are presented in Figures 2 and 3. Detectable PSA at 12 months was strongly associated with increased risk of metastasis ($P=0.006$), moderately associated with increased risk prostate cancer-specific death ($P=0.028$), and marginally associated with increased of death from any cause ($P=0.065$). Median time from completion of ADT to metastasis for all men was 3.9 years (range, 0.29 – 15.3 years), for men with undetectable PSA at 12 months was 6.8 years (range, 0.56 – 11.6 years), and for men who had detectable PSA at 12 months was 3.5 years (range, 0.29 – 15.3 years). Having detectable PSA at 12 months was associated with a 3-fold increase in the hazard of metastasis ($P=0.013$), a 4.5-fold increase in the hazard of prostate cancer-specific death ($P=0.042$), and a 2.5-fold increase in the hazard death from any cause ($P=0.042$) after controlling for patient age at diagnosis.

Discussion

This single-institution retrospective analysis shows that it is not uncommon to have undetectable PSA 12 or 24 months after a short course of ADT and that these rates of undetectable PSA are higher than previously expected. It is possible that the rate of undetectable PSA in our primary analysis could be explained by a low rate of testosterone recovery. However, we observed that in the subset of men whose testosterone recovery could be confirmed, the rate of undetectable PSA was comparable to the overall population in this analysis. Therefore, if undetectable PSA at a pre-specified landmark is used as an early endpoint to evaluate therapy efficacy, it may not be necessary to condition on testosterone recovery. Of course, this conclusion depends on the type and duration of experimental agents used. For example, our patients received only short-term ADT. If they received long-term ADT (e.g., 2 years), testosterone recovery might have greater impact on results.

In our dataset, undetectable PSA at the 12 or 24-month landmark was associated with long-term outcomes of metastasis and death, demonstrating the potential utility of using PSA status as an early indicator of efficacy in clinical trials (e.g. NCT01786265, NCT02319837, NCT02203695, NCT03047135, NCT01751451). Specifically, future trials may utilize our findings as a possible null hypothesis for study design. As demonstrated in a recent study by the Intermediate Clinical Endpoints in Cancers of the Prostate (ICECaP) working group, metastasis-free survival correlates with overall survival.¹⁶ From our analysis, median time from completion of ADT to metastasis varied from 3.5 to 6.8 years. Rather than waiting years to identify metastasis radiographically, as a marker for therapeutic efficacy,

undetectable PSA at 12 months could be further evaluated as an earlier endpoint, given the association to both metastasis and death. However, the association between PSA status at 12 months and the risk of prostate cancer-specific death in this analysis was only suggestive, as there were only 2 prostate cancer-specific deaths among men with undetectable PSA at 12 months.

Other possible prognostic endpoints, including PSA_{dt}, duration of the first off cycle of intermittent ADT, or time to PSA recurrence during first off cycle were considered. However, while PSA_{dt} has historically been valuable in establishing prognosis, it has not been ideal as a treatment response marker. Notably, in single-arm trials it has been shown that calculated PSA_{dt} may naturally increase due to the influence of the duration of PSA follow up.¹⁷ A demonstrated increase in PSA_{dt} even with the lack of active treatment weakens the clinical utility of this endpoint in trials without a placebo arm. Furthermore, it has been shown that patients who receive ADT have altered PSA_{dt} when testosterone and PSA are rising concomitantly.¹⁸ As a result, we restricted our analysis to include PSA_{dt} only as a baseline prognostic marker and did not try to correlate PSA_{dt} after initial ADT and testosterone recovery with metastasis-free survival or overall survival.

As demonstrated by the CHAARTED, STAMPEDE, and LATITUDE trials, there is a proven benefit to more aggressive systemic treatment earlier in the disease course for men with metastatic prostate cancer. Moving efficacious agents earlier in the disease course is currently being explored and greatly increases the need for a reliable clinical trial endpoint. In addition, staging and identification of oligometastatic prostate cancer is improving with next generation imaging, such as 18F-fluciclovine (FACBC) and prostate-specific membrane antigen (PSMA) positron emission tomography scans. These imaging modalities are uncovering previously undetected disease, leading to many metastasis-directed therapies of uncertain benefit. Hence, this new field would also benefit from an early endpoint, such as time to PSA progression.¹⁹ Thus, as research protocols continue to explore treatment intensification for both BCR and oligometastatic disease states, undetectable PSA at a pre-specified landmark may prove to be an effective marker with a wide breadth of applications if correlations with long-term outcomes can be confirmed in other patient populations.

Designing effective clinical trials relies on identifying the men who may benefit most from novel and experimental therapies. Our multivariate analysis indicates that being older at diagnosis is protective of PSA progression within 12 months. Although it could be suggested that the significant rate of undetectable PSA could be attributed to an older age and thus longer duration of undetectable PSA or time to testosterone recovery, the median age at diagnosis for the cohort of men in this study was only 60 years. The remainder of the known prognostic predictor variables, including PSA doubling time, were not significantly associated with PSA status at 12 months. Thus, this analysis was unable to determine which patients were more likely to respond favorably to ADT beyond the trend for patients with advanced age. This suggests that PSA status may provide independent clinical information.

The patients in this study could not be said to have indolent prostate cancer, so that cannot explain the unexpectedly high proportions with undetectable PSA at 12 or 24 months. For example, median PSA doubling time of this cohort was 6 months, highlighting that this was

a patient population with relatively aggressive disease biology (Table 1).²⁰ Median time to BCR in the population was less than 2 years, which is also indicative of men with more aggressive prostate cancer.²¹ So, although the proportion of men with undetectable PSA at 12 months indicated in this analysis is greater than previously expected, it is unlikely due to patient selection of an indolent cohort of patients that did not require therapy.

Limitations to this analysis include the sample size, especially in the evaluation of association between PSA status and baseline characteristics. The single-institution data source and limited number of providers warrants independent confirmation in other patient populations. Also, PSAdt was unable to be calculated for men without three PSA values and these men may be more likely to have detectable PSA at 12 months due to shorter follow up, introducing possible bias to this measure. Finally, as in all retrospective analyses, this study is subject to possible confounding and other biases.

Conclusion

In this single-institution study, a significant proportion of biochemically-recurrent prostate cancer patients had undetectable PSA after short course ADT at 12 or 24 months. Undetectable PSA at 12 or 24 months was associated with risks of metastasis and death. Hence, PSA status at one of these landmarks may be further evaluated as an early endpoint for use in clinical trials. Additional analyses should be performed in larger, multi-institutional data sets to confirm the clinical value of this endpoint.

Acknowledgements

None.

Funding: NIH/NCI P50 CA097186 and Drive Fore the Cure Northwest and R50 CA221836

References

1. Stephenson AJ, Scardino PT, Eastham JA, et al. Postoperative nomogram predicting the 10-year probability of prostate cancer recurrence after radical prostatectomy. *J Clin Oncol* 2005;23(28): 7005–7012. doi:10.1200/JCO.2005.01.867 [PubMed: 16192588]
2. Punnen S, Cooperberg MR, Amico AV, et al. Management of Biochemical Recurrence After Primary Treatment of Prostate Cancer: A Systematic Review of the Literature. *Eur Urol* 2013;64(6): 905–915. doi:10.1016/j.eururo.2013.05.025 [PubMed: 23721958]
3. Crook JM, O'Callaghan CJ, Duncan G, et al. Intermittent Androgen Suppression for Rising PSA Level after Radiotherapy. *N Engl J Med* 2012;367(10):895–903. doi:10.1056/NEJMoa1201546 [PubMed: 22931259]
4. Yu EY, Gulati R, Telesca D, et al. Duration of first off-treatment interval is prognostic for time to castration resistance and death in men with biochemical relapse of prostate cancer treated on a prospective trial of intermittent androgen deprivation. *J Clin Oncol* 2010;28(16):2668–2673. doi: 10.1200/JCO.2009.25.1330 [PubMed: 20421544]
5. Kuo KF, Hunter-Merrill R, Gulati R, et al. Relationships between times to testosterone and prostate-specific antigen rises during the first off-treatment interval of intermittent androgen deprivation are prognostic for castration resistance in men with nonmetastatic prostate cancer. *Clin Genitourin Cancer* 2015;13(1):10–16. doi:10.1016/j.clgc.2014.08.003 [PubMed: 25242417]
6. Bruchovsky N, Klotz L, Crook J, Phillips N, Abersbach J, Goldenberg SL. Quality of life, morbidity, and mortality results of a prospective phase II study of intermittent androgen suppression for men with evidence of prostate-specific antigen relapse after radiation therapy for locally

- advanced prostate cancer. *Clin Genitourin Cancer* 2008;6(1):46–52. doi:10.3816/CGC.2008.n.008 [PubMed: 18501083]
7. Choong K, Basaria S. Emerging cardiometabolic complications of androgen deprivation therapy. *aging male Off J Int Soc Study Aging Male* 2010;13(1):1–9. doi:10.3109/13685530903410625
 8. Sweeney CJ, Chen Y-H, Carducci M, et al. Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer. *N Engl J Med* 2015;373(8):737–746. doi:10.1056/NEJMoa1503747 [PubMed: 26244877]
 9. James ND, Sydes MR, Clarke NW, et al. Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): Survival results from an adaptive, multiarm, multistage, platform randomised controlled trial. *Lancet* 2016;387(10024):1163–1177. doi:10.1016/S0140-6736(15)01037-5 [PubMed: 26719232]
 10. Fizazi K, Tran N, Fein L, et al. Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer. *N Engl J Med* 2017;377(4):352–360. doi:10.1056/NEJMoa1704174 [PubMed: 28578607]
 11. James ND, de Bono JS, Spears MR, et al. Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy. *N Engl J Med* 2017;377(4):338–351. doi:10.1056/NEJMoa1702900 [PubMed: 28578639]
 12. Antonarakis ES, Chen Y, Elsamanoudi SI, et al. Long-term overall survival and metastasis-free survival for men with prostate-specific antigen-recurrent prostate cancer after prostatectomy: analysis of the Center for Prostate Disease Research National Database. *Bju Int* 2011;108(3):378–385. doi:10.1111/j.1464-410X.2010.09878.x [PubMed: 21091976]
 13. Cookson MS, Aus G, Burnett AL, et al. Variation in the definition of biochemical recurrence in patients treated for localized prostate cancer: the American Urological Association Prostate Guidelines for Localized Prostate Cancer Update Panel report and recommendations for a standard in the re. *J Urol* 2007;177(2):540–545. doi:10.1016/j.juro.2006.10.097 [PubMed: 17222629]
 14. Prostate cancer nomograms: PSA doubling time. Memorial Sloan Kettering Cancer Center. https://www.mskcc.org/nomograms/prostate/psa_doubling_time. Accessed July 1, 2017.
 15. Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer* 2009;45(2):228–247. doi:10.1016/j.ejca.2008.10.026 [PubMed: 19097774]
 16. Xie W, Regan MM, Buyse M, et al. Metastasis-Free Survival Is a Strong Surrogate of Overall Survival in Localized Prostate Cancer. *J Clin Oncol* 2018;35(27). doi:10.1200/JCO.2017.73.9987
 17. Paller CJ, Olatoye D, Xie S, et al. The effect of the frequency and duration of PSA measurement on PSA doubling time calculations in men with biochemically recurrent prostate cancer. *Prostate Cancer Prostatic Dis* 2014;17(1):28–33. doi:10.1038/pcan.2013.40 [PubMed: 24100642]
 18. Keizman D, Huang P, Antonarakis ES, et al. The change of PSA doubling time and its association with disease progression in patients with biochemically relapsed prostate cancer treated with intermittent androgen Deprivation. *Prostate* 2011;71(15):1608–1615. doi:10.1002/pros.21377 [PubMed: 21432863]
 19. Ost P, Reynders D, Decaestecker K, et al. Surveillance or Metastasis-Directed Therapy for Oligometastatic Prostate Cancer Recurrence: A Prospective, Randomized, Multicenter Phase II Trial. *J Clin Oncol* 2017;36(5):446–453. doi:10.1200/JCO.2017.75.4853 [PubMed: 29240541]
 20. Wei XX, Perry J, Chang E, et al. Clinical Variables Associated With Overall Survival in Metastatic Castration-Resistant Prostate Cancer Patients Treated With Sipuleucel-T Immunotherapy. *Clin Genitourin Cancer* 3 2018. doi:10.1016/j.clgc.2017.12.004
 21. Freedland SJ, Humphreys EB, Mangold LA, et al. Risk of prostate cancer-specific mortality following biochemical recurrence after radical prostatectomy. *JAMA* 2005;294(4):433–439. doi:10.1001/jama.294.4.433 [PubMed: 16046649]

Figure 1.

Consort diagram on patient eligibility to determine eligible and excluded patients for this analysis from the initial Caisis query.

Figure 2.
Kaplan Maier curves for time to metastasis stratified by detectable PSA at 12 months (n=78).

Figure 3A.

Kaplan Maier curves for time to prostate-specific death stratified by detectable PSA at 12 months (n=86).

Figure 3B.

Kaplan Maier curves for time to death from any cause stratified by detectable PSA at 12 months (n=86).

Table 1.

Patient characteristics.

Age at Diagnosis, years	No. of patients	Percent
40–49	8	9%
50–59	36	39%
60–69	38	40%
70–79	7	8%
Unknown	4	4%
Race		
Caucasian	75	81%
Black or African American	3	3%
Asian/Hawaiian or Pacific Islander	2	2%
Unknown	13	14%
PSA at Diagnosis, ng/mL		
0–9	49	53%
10–19	21	23%
20–39	12	13%
> 40	4	4%
Unknown	7	8%
Grade Group		
Grade Group 1	14	15%
Grade Group 2 & 3	51	55%
Grade Group 4 & 5	26	28%
Unknown	2	2%
Time to BCR, years		
0–1	38	41%
1–2	15	16%
2–5	18	20%
>5	21	23%
Unknown	1	1%
Therapy		
Adjuvant Radiation Therapy	12	13%
Salvage Radiation Therapy	40	43%
Salvage ADT	10	11%

Table 2.

Proportion of men with undetectable PSA at 12 and 24 months. Subanalysis with recovery of testosterone 50 ng/dL and 150 ng/dL also included.

Proportion of Men with Undetectable PSA at 12 Months				
Group	n	Proportion	95% CI	P-value
All	23/93	25%	16% – 35%	< 0.0001
Testosterone 50	16/65	20%	15% – 37%	< 0.0001
Testosterone 150	15/60	22%	15% – 38%	< 0.0001
Proportion of Men with Undetectable PSA at 24 Months				
Group	n	Proportion	95% CI	P-value
All	14/93	15%	8.5% – 24%	0.0002
Testosterone 50	10/65	15%	7.6% – 27%	0.0014
Testosterone 150	10/60	17%	8.3% – 29%	0.0007

Table 3.

Multivariate analysis using a logistic regression model of having PSA detectable at 12 months. A complete case analysis was performed, including only subjects with no missing data, reducing the sample size from 93 to 59.

Covariate	OR	95% CI	P-Value
Age at Diagnosis	0.86	0.76 – 0.95	0.0061
Surgical Gleason	0.97	0.50 – 1.9	0.93
PSA at Diagnosis	1.0	0.97 – 1.1	0.59
Time to BCR	1.0	1.0 – 1.0	0.95
PSA DT	0.99	0.89 – 1.1	0.88