

Seven-Month Prostate-Specific Antigen Is Prognostic in Metastatic Hormone-Sensitive Prostate Cancer Treated With Androgen Deprivation With or Without Docetaxel

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A B S T R A C T

Purpose

We evaluated the relationship between prostate-specific antigen (PSA) and overall survival in the context of a prospectively randomized clinical trial comparing androgen-deprivation therapy (ADT) plus docetaxel with ADT alone for initial metastatic hormone-sensitive prostate cancer.

Methods

We performed a landmark survival analysis at 7 months using the E3805 Chemohormonal Therapy Versus Androgen Ablation Randomized Trial for Extensive Disease in Prostate Cancer (CHAARTED) database (ClinicalTrials.gov identifier: NCT00309985). Inclusion required at least 7 months of follow-up and PSA levels at 7 months from ADT initiation. We used the prognostic classifiers identified in a previously reported trial (Southwest Oncology Group 9346) of PSA \leq 0.2, $>$ 0.2 to 4, and $>$ 4 ng/mL.

Results

Seven hundred nineteen of 790 patients were eligible for this subanalysis; 358 were treated with ADT plus docetaxel, and 361 were treated with ADT alone. Median follow-up time was 23.1 months. On multivariable analysis, achieving a 7-month PSA \leq 0.2 ng/mL was more likely with docetaxel, low-volume disease, prior local therapy, and lower baseline PSAs (all $P \leq .01$). Across all patients, median overall survival was significantly longer if 7-month PSA reached \leq 0.2 ng/mL compared with $>$ 4 ng/mL (median survival, 60.4 v 22.2 months, respectively; $P < .001$). On multivariable analysis, 7-month PSA \leq 0.2 and low volume disease were prognostic of longer overall survival (all $P < 0.01$). The addition of docetaxel increased the likelihood of achieving a PSA \leq 0.2 ng/mL at 7 months (45.3% v 28.8% of patients on ADT alone). Patients on ADT alone who achieved a 7-month PSA \leq 0.2 ng/mL had the best survival and were more likely to have low-volume disease (56.7%).

Conclusion

PSA \leq 0.2 ng/mL at 7 months is prognostic for longer overall survival with ADT for metastatic hormone-sensitive prostate cancer irrespective of docetaxel administration. Adding docetaxel increased the likelihood of a lower PSA and improved survival.

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INTRODUCTION

Some patients with metastatic prostate cancer have a prolonged survival of approximately 5 or more years from the diagnosis of metastasis.¹⁻⁴ This extended survival is in part a result of the advent of multiple effective second-line therapies for castration-resistant disease that, when used in sequence, contribute to prolonging life. These include taxane-based chemotherapies, next-generation

antiandrogens such as enzalutamide, biosynthesis inhibitors such as abiraterone acetate, bone metastasis-homing radiation with radium-223, and an autologous dendritic cell vaccine sipuleucel-T.⁵⁻¹² Given that these drugs yield only incremental survival benefits, attempts to improve the outcomes of this largely fatal disease have evolved to move these agents forward to the hormone-sensitive setting. In this setting, the disease burden is lower, and there may be fewer resistance mechanisms at play to evade elimination. Indeed, as of

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ASSOCIATED CONTENT

Appendix
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2017, we now have multiple lines of therapy with level 1 evidence showing that both docetaxel and abiraterone acetate increase survival and disease control when added to luteinizing hormone-releasing hormone agonists at the diagnosis of metastatic hormone-sensitive disease.¹⁻⁴

Three pivotal studies have investigated the use of docetaxel for metastatic hormone-sensitive prostate cancer (mHSPC). Although the first study, Groupe d'Étude des Tumeurs Uro-Génitales-Association Française d'Urologie (GETUG-AFU 15), did not show a benefit to adding docetaxel at the time of mHSPC, the subsequent two larger studies, Chemohormonal Therapy Versus Androgen Ablation Randomized Trial for Extensive Disease in Prostate Cancer (CHAARTED) and Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy (STAMPEDE), have demonstrated a significant overall survival advantage to early docetaxel administration.^{3,4,13}

CHAARTED was a phase III, open-label study that randomly assigned 790 patients to receive either androgen-deprivation therapy (ADT) plus six cycles of docetaxel or ADT alone. It revealed a greater than 12-month overall survival benefit to adding docetaxel to ADT compared with ADT alone. Integrated into the stratification and analysis of the study was characterization of outcomes based on volume of disease. High-volume disease was defined by the presence of four or more bone lesions with at least one beyond the vertebral bodies or pelvis or any site of visceral metastasis. A planned subgroup analysis of CHAARTED based on volume of disease showed that the survival advantage of early chemotherapy administration was restricted to patients with high-volume cancer (hazard ratio, 0.6).¹⁴ As such, early docetaxel administration in combination with ADT is an option in 2017 in patients with high-volume mHSPC who are fit for chemotherapy.¹⁵

Prior work from the Southwest Oncology Group (SWOG) 9346 trial, a phase III study that compared continuous versus intermittent androgen blockade in treatment-naïve, hormone-sensitive disease, revealed that patients who achieved a prostate-specific antigen (PSA) ≤ 0.2 ng/mL at 7 months had a significantly longer overall survival compared with patients who did not achieve this milestone.¹⁶ Similarly, in that same study, patients whose PSA declined to between 0.3 and 4 ng/mL had improved outcomes compared with those whose PSA remained > 4 ng/mL at 7 months after ADT initiation. Thus, failure to achieve a PSA ≤ 0.2 ng/mL may identify patients who might benefit from earlier intensification of therapy. In addition to enhancing clinical discussions and improving patient morale, the availability of a biomarker that could detect clinical benefit (or lack thereof) earlier than our current longer term time-to-event end points such as time to progression or overall survival would aid in trial design and drug development.

The current treatment armamentarium for metastatic prostate cancer offers multiple nonchemotherapeutic agents that improve survival, and given the results of the CHAARTED and STAMPEDE trials, we have witnessed a transition to using docetaxel earlier in the metastatic disease course over the past few years. We sought to evaluate whether achieving an optimal 7-month PSA ≤ 0.2 ng/mL after treatment initiation remained prognostic of superior overall survival when docetaxel was added to ADT for initial mHSPC treatment using the CHAARTED database of patients with mHSPC with its prospectively cataloged clinical outcomes.

METHODS

With institutional review board and ethics committee approval, we interrogated the CHAARTED Eastern Cooperative Oncology Group 3805 database (ClinicalTrials.gov identifier: NCT00309985) of 790 patients with mHSPC enrolled from July 2006 to December 2012. Inclusion in this planned secondary analysis of on-therapy PSA changes required the following: at least 7 months of follow-up after ADT initiation (if ADT started before random assignment) or after random assignment (if ADT started after random assignment) and PSA levels at 7 months from ADT initiation. Data on baseline clinical and demographic characteristics, such as age at ADT initiation, race, Gleason score, baseline PSA, disease volume, presence of visceral disease, prior local therapy, and presence of bone pain or weight loss at baseline, were procured. Patients were allowed to start hormonal therapy up to 120 days before random assignment.

Statistical Analyses

Patient data from the original 2015 published analysis⁴ were used. Landmark survival analyses were performed at 7 months after ADT initiation. For patients who started hormonal therapy before random assignment, overall survival was defined as the time from 7 months after ADT initiation to death or date when last known to be alive. For patients who started hormonal therapy after random assignment, overall survival was defined as the time from 7 months after randomization to death or date last known to be alive in follow-up. Landmark survival analyses were performed at 7 months after ADT initiation. The SWOG 9346 PSA cut points of ≤ 0.2 , > 0.2 to 4, and > 4 ng/mL were used a priori.¹⁶ Patients who experienced progression or received non-protocol therapy (NPT) before 7 months were included in the 7-month PSA > 4 ng/mL group.

The Fisher's exact test and Kruskal-Wallis test were used to evaluate the associations between baseline patient characteristics and PSA status at 7 months. Multivariable logistic regression models with stepwise selection were constructed to predict 7-month PSA ≤ 0.2 using the significant covariates from the univariable analysis. Multivariable proportional hazards regression models stratified by stratification factors at random assignment were developed for overall survival using stepwise selection. All variables associated with PSA ≤ 0.2 ng/mL were included in the model selection, and treatment arm was included in the final model regardless of significance.

RESULTS

Of the 790 patients enrolled onto the CHAARTED study, 719 patients were eligible for this landmark analysis; 358 patients were treated with ADT plus docetaxel, and 361 patients were treated with ADT alone (Table 1). Patients were excluded if they had less than 7 months of follow-up after starting ADT ($n = 36$) or no PSA assessments during the 4 to 7 months after ADT initiation ($n = 35$; Appendix Table A1, online only). Patients who experienced progression before 7 months were included in the 7-month PSA > 4 ng/mL group. Patients who did not experience progression and did not have PSA assessments during months 4 to 7 were excluded from the analysis. The protocol did not specify a time frame for starting ADT after random assignment. From the database, 92 of 96 patients who began ADT after random assignment started it within 10 days of random assignment. Median follow-up, which started after 7 months of ADT, was 23.1 months (range, 0.2 to 72.8 months).

Among all patients, median overall survival was significantly longer if PSA at 7 months reached ≤ 0.2 ng/mL compared with > 4 ng/mL ($P < .001$; Table 2). Across the three different cut points identified in SWOG 9346, the lower the PSA at 7 months, the longer

Table 1. Patient Characteristics by 7-Month PSA Level

Characteristic	All Patients	PSA Status at 7 Months			P
		PSA ≤ 0.2 ng/mL	PSA > 0.2-4.0 ng/mL	PSA > 4.0 ng/mL	
Age at ADT start, years					.003
Median	63	64	63	61	
Range	36-88	44-83	36-83	41-88	
Treatment arm, No. (%)					< .001
ADT + docetaxel	358 (49.8)	162 (60.9)	109 (50.9)	87 (36.4)	
ADT alone	361 (50.2)	104 (39.1)	105 (49.1)	152 (63.6)	
Race, No. (%)					.006
White	609 (88.1)	238 (92.6)	184 (88.9)	187 (82.4)	
Black	72 (10.4)	16 (6.2)	19 (9.2)	37 (16.3)	
Other	10 (1.5)	3 (1.2)	4 (1.9)	3 (1.3)	
Missing	28	9	7	12	
Performance status, No. (%)					< .001
0	503 (70.1)	201 (75.6)	157 (73.7)	145 (60.7)	
1-2	215 (29.9)	65 (24.4)	56 (26.3)	94 (39.3)	
Missing	1	0	1	0	
Gleason score, No. (%)					< .001
4-6	36 (5.6)	20 (8.3)	11 (5.8)	5 (2.4)	
7	166 (25.9)	78 (32.2)	47 (24.7)	41 (19.7)	
8-10	438 (68.4)	144 (59.5)	132 (69.5)	162 (77.9)	
Missing	79	24	24	31	
Disease volume, No. (%)					< .001
High	469 (65.2)	132 (49.6)	137 (64.0)	200 (83.7)	
Low	250 (34.8)	134 (50.4)	77 (36.0)	39 (16.3)	
Visceral disease (among patients with high-volume disease), No. (%)					.83
No	356 (76.1)	100 (75.8)	106 (77.9)	150 (75.0)	
Yes	112 (23.9)	32 (24.2)	30 (22.1)	50 (25.0)	
Missing	1	0	1	0	
Prior local therapy, No. (%)					< .001
No	524 (73.0)	146 (54.9)	163 (76.5)	215 (90.0)	
Yes	194 (27.0)	120 (45.1)	50 (23.5)	24 (10.0)	
Missing	1	0	1	0	
ADT before random assignment, No. (%)					< .001
No	96 (13.4)	54 (20.3)	18 (8.5)	24 (10.0)	
Yes	622 (86.6)	212 (79.7)	195 (91.5)	215 (90.0)	
Missing	1	0	1	0	
Bone pain at baseline, No. (%)					< .001
No	650 (90.4)	251 (94.4)	200 (93.5)	199 (83.3)	
Yes	69 (9.6)	15 (5.6)	14 (6.5)	40 (16.7)	
Weight loss at baseline, No. (%)					.47
No	707 (98.3)	262 (98.5)	212 (99.1)	233 (97.5)	
Yes	12 (1.7)	4 (1.5)	2 (0.9)	6 (2.5)	
Baseline PSA, ng/mL					< .001
Median	50.9	16.9	53.9	191.0	
Range	0.1-8,540.1	0.1-3,260.6	0.9-5,778.7	0.1-8,540.1	

Abbreviations: ADT, androgen-deprivation therapy; PSA, prostate-specific antigen.

was the survival. Median overall survival by 7-month PSA (all patients; Fig 1A and Table 2) was 60.4 months with PSA ≤ 0.2 ng/mL, 51.9 months with PSA of 0.3 to 4 ng/mL, and 22.2 months with PSA > 4 ng/mL. This trend held true across each of the study arms with ADT plus docetaxel (Fig 1B) or ADT alone (Fig 1C). The proportion of patients with visceral disease was greatest among the patients with a 7-month PSA > 4.0 ng/mL (20.9%; 50 of 239 patients) and significantly lower in the groups with PSA ≤ 0.2 (12%; 32 of 266 patients) and PSA of 0.2 to 4 ng/mL (14.1%; 30 of 213 patients; *P* = .02).

On multivariable analysis, achieving a PSA of ≤ 0.2 ng/mL at 7 months was more likely if patients had received docetaxel, had low-volume disease, had received prior local therapy, had started ADT after random assignment, and had lower baseline PSA levels (continuous variable; all *P* ≤ .01; Table 3).

On multivariate analysis, longer overall survival was associated with PSA ≤ 0.2 ng/mL at 7 months, low-volume disease, and higher baseline PSA (all *P* < .01; Table 4) but not docetaxel use. Despite the latter statistical finding, there was a higher percentage of patients who achieved PSA ≤ 0.2 ng/mL in the docetaxel arms regardless of volume status (Table 5). Of the ADT plus docetaxel patients, 45.3% achieved a PSA ≤ 0.2 ng/mL at 7 months compared with 28.8% of patients on ADT alone. More importantly than whether PSA reaches this level is whether achieving this landmark correlates with improved survival. In an exploratory subset analysis evaluating how 7-month PSA correlated with overall survival, patients with high-volume disease had a worse median overall survival if they did not experience a 7-month PSA ≤ 0.2 ng/mL. Overall, patients with high-volume disease who

Lower PSA at 7 Months Is Prognostic in CHARTED

Table 2. OS by PSA Status at 7 Months

OS	PSA ≤ 0.2 ng/mL	PSA > 0.2-4.0 ng/mL	PSA > 4.0 ng/mL	P (stratified log-rank)
All patients				< .001
Median, months (95% CI)	60.4 (45.6 to 72.8)	51.9 (40.0 to 68.9)	22.2 (19.8 to 27.3)	
3-year OS rate, % (95% CI)	77.7 (68.4 to 84.5)	61.4 (51.0 to 70.2)	31.5 (23.4 to 39.9)	
ADT + docetaxel				< .001
Median, months (95% CI)	60.4 (45.6 to NA)	45.5 (32.1 to 68.9)	25.2 (16.3 to 46.3)	
3-year OS rate, % (95% CI)	74.2 (61.9 to 83.1)	62.2 (46.9 to 74.2)	36.8 (22.9 to 50.8)	
ADT alone				< .001
Median, months (95% CI)	72.8 (38.8 to 72.8)	NR (27.7 to NA)	21.6 (18.0 to 27.2)	
3-year OS rate, % (95% CI)	84.4 (70.0 to 92.3)	60.3 (45.3 to 72.4)	28.8 (19.2 to 39.2)	

Abbreviations: ADT, androgen-deprivation therapy; NA, not available; NR, not reached; OS, overall survival; PSA, prostate-specific antigen.

received docetaxel had a higher median overall survival than patients on ADT alone, and patients who achieved a 7-month PSA ≤ 0.2 ng/mL had a longer median overall survival than those whose 7-month PSA remained > 0.2 ng/mL (Table 5). In patients with high-volume disease who received ADT alone, median overall survival was 40.1 months if their PSA hit the landmark, compared

with 25.4 months if PSA remained > 0.2 ng/mL at 7 months. The patients with high-volume disease who received docetaxel had a median overall survival time of 60.4 months if 7-month PSA was ≤ 0.2 ng/mL and 45.4 months if PSA was > 0.2 ng/mL. The median overall survival of patients with low-volume disease had not been reached in the majority of subsets.

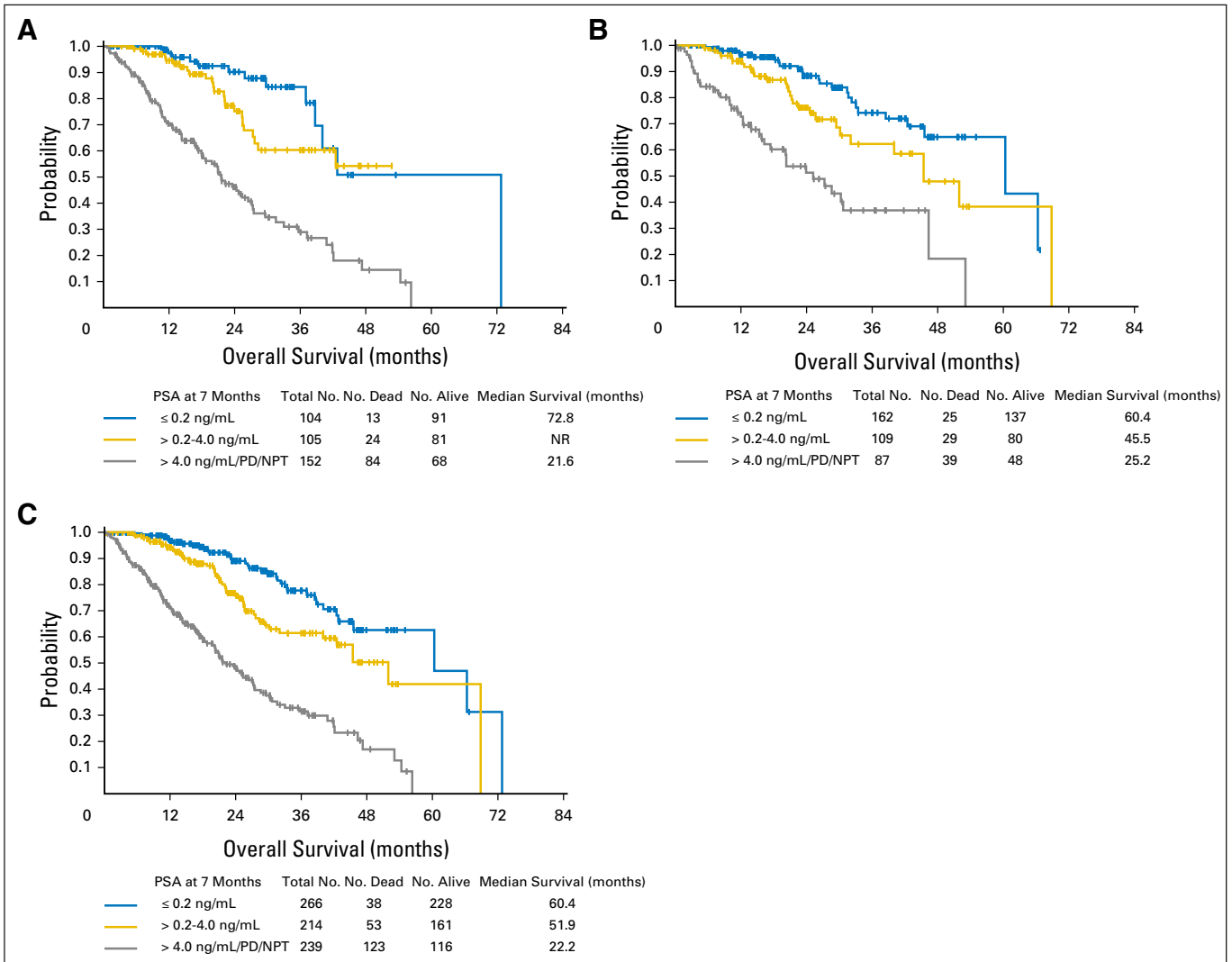


Fig 1. Kaplan-Meier analysis of overall survival by prostate-specific antigen (PSA) level at 7 months in (A) patients on ADT alone, (B) patients on androgen-deprivation therapy (ADT) plus docetaxel, and (C) all patients. NPT, non-protocol therapy; NR, not reached; PD, progressive disease.

Table 3. Multivariable Logistic Regression Model Predicting a PSA \leq 0.2 ng/mL at 7 Months

Variable	Odds Ratio*	95% CI	P
Assigned therapy (ADT+D v ADT alone)	2.58	1.82 to 3.64	< .001
Disease volume (low v high)	2.02	1.41 to 2.90	< .001
Prior local therapy (yes v no)	2.92	1.99 to 4.27	< .001
ADT started before random assignment (no v yes)	1.88	1.15 to 3.06	.01
Baseline PSA in 50-unit increments	0.96	0.94 to 0.98	< .001

NOTE. Stepwise selection was used with $P = .05$ as criterion for entry and removal (backward selection and forward selection both gave the same results). Seven hundred sixteen patients were included in the analysis.

Abbreviations: ADT, androgen-deprivation therapy; D, docetaxel; PSA, prostate-specific antigen.

*Odds ratio > 1 means more likely to achieve a PSA \leq 0.2 ng/mL at 7 months.

DISCUSSION

In the wake of the overall survival benefit demonstrated by the modern CHAARTED and STAMPEDE studies, there is now substantial rationale to support the use of docetaxel with ADT in the hormone-sensitive state, especially in fit patients with high-volume metastatic prostate cancer. The SWOG 9346 study, which was conducted in the 1990s, tested continuous versus intermittent androgen blockade in patients with mHSPC and revealed that patients with 7-month PSA \leq 0.2 ng/mL had significantly longer survival than patients who did not achieve this landmark.¹⁶ We sought to evaluate whether this potential on-therapy biomarker remained prognostic when docetaxel was added to ADT in the current treatment era in which multiple systemic agents are available that improve survival. CHAARTED also offered the first opportunity in the mHSPC setting to evaluate this landmark in the context of a randomized clinical trial in which one arm showed definite improved overall survival and to compare the percentage of patients who achieved an ideal 7-month PSA and survival associations between the different treatments.

We hypothesized that achieving a 7-month PSA \leq 0.2 ng/mL would remain prognostic for improved overall survival when docetaxel chemotherapy is added to ADT at the time of mHSPC. Using a more contemporary data set obtained from the CHAARTED study, we observed that achieving a PSA \leq 0.2 ng/mL at 7 months correlated with longer overall survival with ADT in patients with mHSPC, whether administered alone or with docetaxel. Further, when we incorporated the use of docetaxel into the analysis, its combination with ADT increased the likelihood of achieving a lower PSA and subsequent improved survival. Thus, while achieving a PSA \leq 0.2 ng/mL is prognostic, it remains a post-treatment variable and cannot direct upfront who should receive early docetaxel. Although we have shown that early docetaxel administration increases the likelihood of attaining this optimal biomarker state, whether the agents proven to prolong overall survival when added to ADT (ie, abiraterone acetate or docetaxel) should be reserved only for patients who do not achieve a 7-month PSA \leq 0.2 ng/mL has not yet been determined. In theory this tiered strategy might avoid therapy for some, however, it may also miss the possible benefit of attacking the cancer clones

at an earlier stage when they are more vulnerable and the associated survival benefits. Indeed, a phase II study of patients with mHSPC whose PSA did not decrease to \leq 4 ng/mL after 4 to 6 months of initial ADT showed that the addition of abiraterone acetate with prednisone can induce a PSA reduction to \leq 0.2 ng/mL in some patients.¹⁷

The recently reported findings of the LATITUDE and STAMPEDE phase III studies revealed a similar benefit to administering abiraterone acetate earlier at the diagnosis of hormone-sensitive metastatic disease.^{1,2} It will be interesting to see whether attaining a PSA \leq 0.2 ng/mL remains prognostic in these studies and in what time frame. Teasing out when to use docetaxel in light of the recent positive abiraterone studies and the upcoming enzalutamide studies (if positive) is the subject of much ongoing discussion in the field, and ultimate recommendations will likely take into account toxicity and administration profiles, quality of life, and financial repercussions.

Although PSA is an easy, inexpensive, and long-established clinical test, predictive pretreatment biomarkers are needed. By interrogating the tumor genetics (RNA and DNA), germline DNA, and circulating proteins and androgens from patients enrolled onto CHAARTED, we may identify more sophisticated biomarkers that are predictive of benefit with early docetaxel for patients and warrant its toxicity.

There are limitations inherent in any retrospective analysis. It is likely that the CHAARTED study as a whole was subject to selection bias in terms of which patients were referred for a study that included chemotherapy. This theory is possibly supported by the younger median age in the CHAARTED study (63 years) versus the LATITUDE and STAMPEDE (abiraterone arm) studies (68 and 67 years, respectively). The analysis was also limited to patients with at least 7 months of follow-up after ADT initiation and patients who had a 7-month PSA level available. These criteria may have biased the results somewhat toward patients with a better risk profile because they survived at least 7 months after ADT and/or were not lost to follow-up in that same time frame. However, only 36 patients of the 790 patients enrolled on CHAARTED were excluded for these reasons. In addition, patients with rapidly progressive disease do not need an intermediate clinical end point because their disease or other comorbidities will already be evident.

Table 4. Multivariable Proportional Hazards Model for Risk of Death After 7 Months of ADT

Variable	HR*	95% CI	P
PSA status at 7 months			
PSA > 0.2 –4.0 ng/mL v PSA > 4.0 ng/mL	0.33	0.23 to 0.47	< .001
PSA ≤ 0.2 ng/mL v PSA > 4.0 ng/mL	0.18	0.12 to 0.28	< .001
Assigned therapy (ADT+D v ADT alone)†	0.94	0.70 to 1.26	.68
Disease volume (low v high)	0.50	0.34 to 0.73	< .001
Baseline PSA in 50-unit increments	0.99	0.983 to 0.997	.009

NOTE. Stepwise selection was used with $P = .05$ as criteria for entry and removal (backward selection and forward selection both gave the same results) and the model was stratified by the stratification factors at randomization. Seven hundred sixteen patients were included in the analysis.

Abbreviations: ADT, androgen-deprivation therapy; D, docetaxel; HR, hazard ratio; PSA, prostate-specific antigen.

*HR < 1 means better survival.

†Treatment arm was included in the model regardless of P value.

Table 5. Distribution of Median OS After 7 Months of ADT by Treatment Arm, Disease Volume, and PSA Status at 7 Months

Disease Volume	ADT				ADT + D			
	PSA ≤ 0.2 ng/mL at 7 Months		Did Not Achieve PSA ≤ 0.2 ng/mL at 7 Months		PSA ≤ 0.2 ng/mL at 7 Months		Did Not Achieve PSA ≤ 0.2 ng/mL at 7 Months	
	% (No./total No.)	Median OS (months; 95% CI)	% (No./total No.)	Median OS (months; 95% CI)	% (No./total No.)	Median OS (months; 95% CI)	% (No./total No.)	Median OS (months; 95% CI)
High	19.7 (45/228)	40.1 (29.8 to 72.8)	80.3 (183/228)	25.4 (20.8 to 29.6)	36.1 (87/241)	60.4 (38.5 to NA)	63.9 (154/241)	45.4 (27.3 to 51.9)
Low	44.4 (59/133)	Not reached* (37.0 to NA)	55.6 (74/133)	Not reached (26.4 to NA)	64.1 (75/117)	Not reached† (NA to NA)	35.9 (42/117)	29.4 (24.6 to NA)

Abbreviations: ADT, androgen-deprivation therapy; D, docetaxel; NA, not available; OS, overall survival; PSA, prostate-specific antigen.

*Four deaths among the 59 patients.

†Six deaths among the 75 patients.

In conclusion, attaining a PSA ≤ 0.2 ng/mL at 7 months on ADT remains prognostic for improved overall survival in the more modern era, and the addition of docetaxel to androgen blockade increases the likelihood of achieving that milestone. Given the long times to an overall survival end point from the time of diagnosis of mHSPC, identification of an intermediate clinical end point for drug development is crucial to move the field forward in more tangible time frames. Our work suggests that 7-month PSA ≤ 0.2 ng/mL is worthy of prospective study as an intermediate clinical end point, and if proven, it could be a reasonable surrogate for overall survival in future trials. In addition, further prospective study is needed to investigate whether intensification of therapy in patients who do not reach a 7-month PSA ≤ 0.2 ng/mL is warranted and whether it will improve clinical outcomes. Future work modeling PSA dynamics, degree of decline, and different PSA time points and their association with improved clinical outcomes is planned. On-therapy biomarkers that are associated with improved outcomes are critical to improving patient mindset and to optimally identify patients for testing alternative therapies when the ideal prognostic metric is not achieved.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at jco.org.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Seven-Month Prostate-Specific Antigen Is Prognostic in Metastatic Hormone-Sensitive Prostate Cancer Treated With Androgen Deprivation With Or Without Docetaxel

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Appendix

Table A1. Specific Reasons Patients Were Excluded From the Analysis

Reason for Exclusion	No. of Patients	
	ADT Plus Docetaxel	ADT Alone
Death before 7 months	5	9
Patient withdrawal before 7 months	8	6
< 7 months of follow-up at time of the analysis	6	2
Survived beyond 7 months but no PSA assessments available during the 4-7 months after ADT	20	15

Abbreviations: ADT, androgen-deprivation therapy; PSA, prostate-specific antigen.