Prostate Cancer™ UPDATE

Conversations with Urologic Oncology Investigators

Bridging the Gap between Research and Patient Care

SPECIAL ISSUE
Proceedings from a Clinical Investigator "Think Tank"

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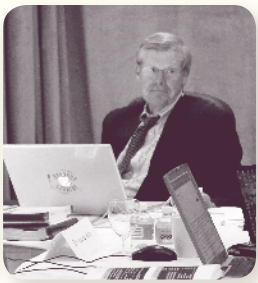


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STATEMENT OF NEED/TARGET AUDIENCE

Prostate cancer is one of the most rapidly evolving fields in urologic oncology. Published results from clinical trials lead to the emergence of new surgical and radiation therapy techniques and therapeutic agents, along with changes in the indications for existing treatments. In order to offer optimal patient care — including the option of clinical trial participation — the practicing urologist, radiation oncologist and medical oncologist must be well informed of these advances. To bridge the gap between research and practice, *Prostate Cancer Update* utilizes discussions with leading urologic oncology, radiation oncology and medical oncology investigators. By providing access to the latest research developments and expert perspectives, this CME program assists urologists, radiation oncologists and medical oncologists in the formulation of up-to-date clinical management strategies.

GLOBAL LEARNING OBJECTIVES

- Critically evaluate the clinical implications of emerging clinical trial data in prostate cancer screening, prevention and treatment and incorporate these data into management strategies in the local and advanced disease settings.
- Counsel appropriately selected patients about the availability of ongoing clinical trials.
- Inform prostate cancer patients about the specific risks and benefits of local and systemic therapies.
- Provide individualized counseling to patients regarding the choice and timing of endocrine therapy.
- Counsel appropriately selected patients in the high-risk or advanced disease settings about the risks and benefits of chemotherapy, including emerging data on taxane-based regimens.

PURPOSE OF THIS ISSUE OF *PROSTATE CANCER UPDATE*

The purpose of this special edition of *Prostate Cancer Update* is to support these global objectives by offering the perspectives of Drs Crawford, D'Amico, Freedland, Gomella, Keane, Klotz, Oh, Petrylak, Roach, Taplin and Zelefsky on the integration of emerging clinical research data into the management of prostate cancer.

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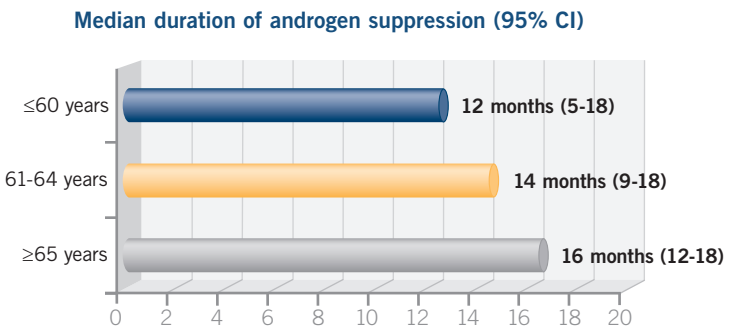
1.1 **Correlation Between Age and Duration of Androgen Suppression After Radiation Therapy and Six Months of Hormonal Therapy**



SOURCE: D'Amico AV et al. *Cancer* 2007;110:1723-8. **Abstract**

Select Excerpts from the Discussion

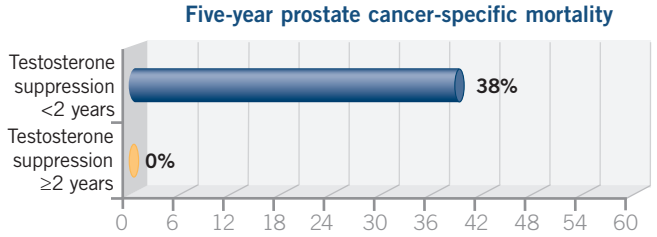
Tracks 1-2

DR LOVE: Can you discuss your work evaluating the correlation between clinical outcomes and the duration of testosterone suppression after the completion of six months of hormonal therapy in men with high-risk, localized prostate cancer who were treated with radiation therapy?

DR D'AMICO: Our study confirmed that as men age, six months of hormonal therapy provides a longer interval of testosterone suppression. In other words, it takes longer for their testosterone levels to return to baseline. If patients were younger than 60 years old, it took a year for testosterone levels to return to baseline. If patients were older than 70 years old, it took about a year and a half to two years for their testosterone levels to return to baseline. Approximately 10 percent of the patients never had a return to baseline testosterone levels following a minimum of five years of observation (D'Amico 2007; [1.1]).

As the duration of testosterone suppression after the completion of six months of hormonal therapy increased, the time to prostate cancer-specific and all-cause mortality increased. This suggests an association between the duration

1.2 **Five-Year Prostate Cancer-Specific Mortality (PCSM) According to Duration of Testosterone Suppression in Men with Gleason 8 to 10 Prostate Cancer Treated with Radiation Therapy and Six Months of Hormonal Therapy**



"...the duration of AS (androgen suppression) after RT and 6 months of HT increases as men age and is associated with the risk of PCSM."

SOURCE: D'Amico AV et al. *Cancer* 2007;110(8):1723-8. **Abstract**

of testosterone suppression and the likelihood of dying from prostate cancer in this particular cohort (D'Amico 2007; [1.2]).

When we evaluated the men with high-grade cancer (Gleason scores of 8 to 10) and plotted the cumulative incidence of prostate cancer deaths — stratified by whether their testosterone levels returned to baseline within two years or later — a striking difference was evident in those who died of prostate cancer.

Essentially, all the prostate cancer deaths in this observational study occurred in the men whose testosterone levels rebounded quickly. Prostate cancer deaths were not observed in those whose testosterone levels did not rebound within the first two years (D'Amico 2007).

Perhaps we've never been able to show in randomized trials with surgery a benefit from a short course of hormonal therapy because they included young men with a median age in the low sixties in whom the testosterone levels rebounded quickly.

Short-term hormonal therapy in that group may be homeopathic, whereas in the RTOG and European studies of radiation therapy, the patients tended to be a decade older, be less virile and have lower testosterone levels. This may be why even a short course of hormonal therapy in those men appears to be beneficial.

Track 3

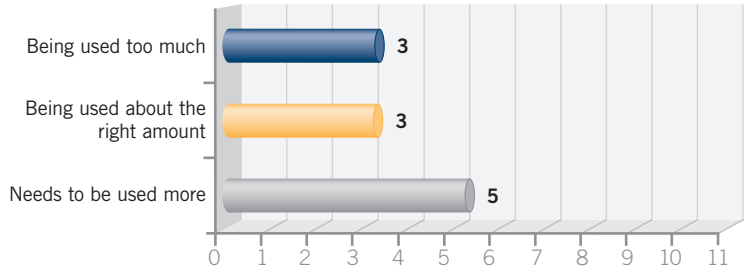
DR LOVE: What are your thoughts about these data, Laurie?

DR KLOTZ: One of the problems with the study is that recovery to baseline was utilized as the determinant, although a lot of data suggest that most men's

FACULTY POLL QUESTION 1

What is your general impression of the use of the following treatment approach in urology and radiation oncology practice in the US?

Androgen deprivation for patients with high-risk localized disease treated with radiation therapy



SOURCE: Survey of Think Tank Participants, June 21, 2007, Miami, Florida.

testosterone levels, after six or eight months of androgen deprivation, recover to approximately 50 percent of baseline.

If they achieve 80 or 90 percent of baseline, they still have, from the perspective of a prostate cancer cell, a pretty substantial androgenic stimulus.

DR D'AMICO: That's a good point. We evaluated several different cut points for testosterone levels: baseline, 200 ng/dL — which is hypogonadal — and 100 ng/dL.

As we went to lower numbers, from baseline to 200 ng/dL to 100 ng/dL, the effect remained but the *p*-value increased because the power to detect a difference was decreasing.

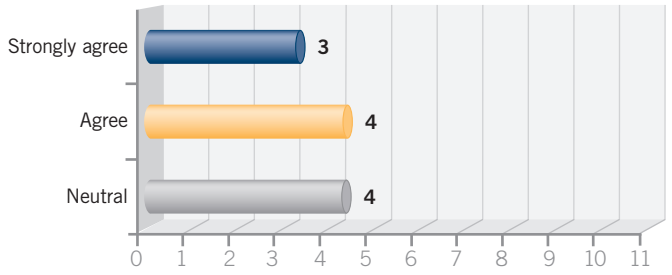
Again, perhaps the reason all five randomized trials of surgery with three months of hormonal therapy (Aus 2002; Klotz 2003; Selli 2002; Schulman 2000; Soloway 2002) did not show a benefit is that in these men, short-course hormonal therapy was homeopathic and their testosterone was not suppressed for long. I'm not convinced that adding hormonal therapy to surgery may not produce a benefit — it may.

DR KEANE: Laurie did a study comparing eight versus three months of neoadjuvant hormonal therapy, and hormonal therapy didn't work there (Gleave 2001).

DR KLOTZ: In an earlier Canadian study in the high-risk subset — in a retrospective stratification analysis — there was a benefit to three months of neoadjuvant therapy (Klotz 2003). Also, none of the neoadjuvant studies

FACULTY POLL QUESTION 2

Men with high-risk disease after radical prostatectomy should generally not receive off-protocol adjuvant androgen deprivation but should be followed for PSA progression and treated at some point during that time.



SOURCE: Survey of Think Tank Participants, June 21, 2007, Miami, Florida.

were enriched for patients with high-risk disease. So we don't know the answer in patients with high-risk disease.

DR CRAWFORD: I have to comment on these trials of neoadjuvant hormonal therapy with surgery. They have varied the duration of hormonal therapy from three, four or eight months. They all show some histologic benefit, but they don't show a difference in PSA recurrence or survival.

We have to remember that these are long-term studies in prostate cancer. Even in our adjuvant radiation therapy trial, for which the radiation oncologists love to talk about a big benefit, there is no survival benefit. Yet we accept radiation therapy as an adjuvant in high-risk prostate cancer.

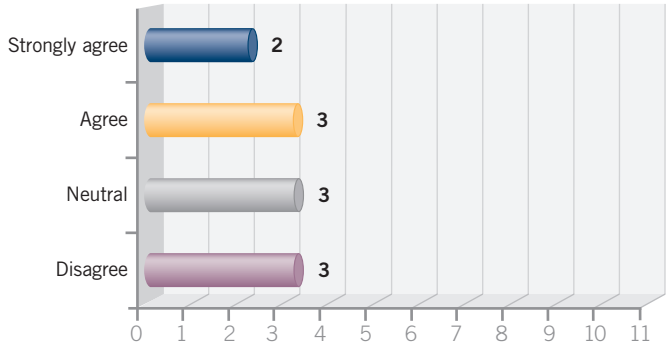
My bet is that the Soloway trial (Soloway 2002), the Debruyne trial (Schulman 2000) and the Canadian trial (Klotz 2003) will show a survival benefit at 15 years, similar to the Messing trial when it was first evaluated at five years (Messing 1999).

DR ROACH: I would like to take your bet, Dave. The fact is that these studies will not show a difference with long-term follow-up because no difference was evident in PSA failure. The risk of dying from prostate cancer in this patient population is too low, and the sample sizes from the studies are too small.

The bottom line is that 15 years from now, they will continue to be negative studies. The fact is that the benefit from hormonal therapy and radiation therapy results from a biologic interaction that does not occur with surgery. ■

FACULTY POLL QUESTION 3

Men with high-risk disease after radical prostatectomy should be told about the option of off-protocol adjuvant androgen deprivation and should be treated if they wish at that time.



SOURCE: Survey of Think Tank Participants, June 21, 2007, Miami, Florida.

SELECT PUBLICATIONS

Aus G et al. **Three-month neoadjuvant hormonal therapy before radical prostatectomy: A 7-year follow-up of a randomized controlled trial.** *BJU Int* 2002;90(6):561-6. **Abstract**

D'Amico AV et al. **Duration of testosterone suppression and the risk of death from prostate cancer in men treated using radiation and 6 months of hormone therapy.** *Cancer* 2007;110(8):1723-8. **Abstract**

Gleave ME et al; Canadian Uro-Oncology Group. **Randomized comparative study of 3 versus 8-month neoadjuvant hormonal therapy before radical prostatectomy: Biochemical and pathological effects.** *J Urol* 2001;166(2):500-6. **Abstract**

Klotz LH et al; Canadian Uro-Oncology Group. **Long-term follow-up of a randomized trial of 0 versus 3 months of neoadjuvant androgen ablation before radical prostatectomy.** *J Urol* 2003;170(3):791-4. **Abstract**

Messing EM et al. **Immediate hormonal therapy compared with observation after radical prostatectomy and pelvic lymphadenectomy in men with node-positive prostate cancer.** *N Engl J Med* 1999;341(24):1781-8. **Abstract**

Schulman CC et al. **4-year follow-up results of a European prospective randomized study on neoadjuvant hormonal therapy prior to radical prostatectomy in T2-3N0M0 prostate cancer. European Study Group on Neoadjuvant Treatment of Prostate Cancer.** *Eur Urol* 2000;38(6):706-13. **Abstract**

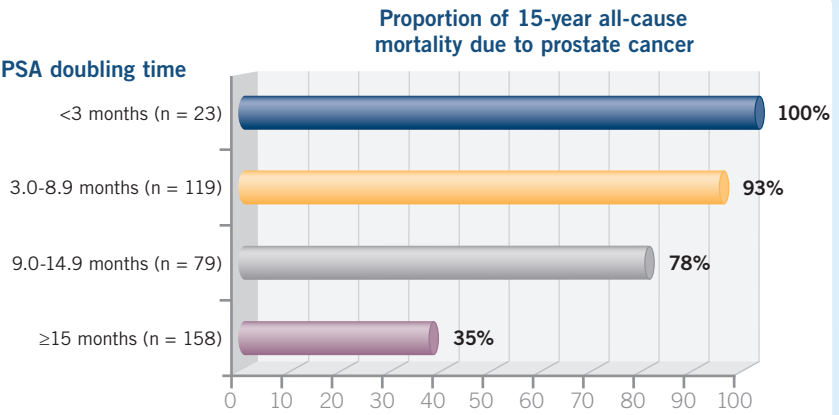
Seidenfeld J et al. **Competing risks for patients with localized prostate cancer.** *J Natl Cancer Inst* 2007;99(20):1498-9. No abstract available

Selli C et al; PROSIT Study Group. **Effects of complete androgen blockade for 12 and 24 weeks on the pathological stage and resection margin status of prostate cancer.** *J Clin Pathol* 2002;55(7):508-13. **Abstract**

Soloway MS et al; Lupron Depot Neoadjuvant Prostate Cancer Study Group. **Neoadjuvant androgen ablation before radical prostatectomy in cT2bNxMo prostate cancer: 5-year results.** *J Urol* 2002;167(1):112-6. **Abstract**

2.1

PSA Doubling Time and All-Cause Mortality Among Men with a PSA Recurrence After Radical Prostatectomy



"Although patients with a PSADT less than 3 months were at the greatest risk of prostate cancer-specific death, because of the small numbers in this group, these patients were estimated to account for only 13% of prostate cancer-specific deaths. Men with a PSADT 3.0 to 8.9 months, because of the larger numbers in this group and the elevated risk of prostate cancer-specific death relative to longer PSADT groups, were estimated to account for 58% of prostate cancer-specific deaths."

SOURCE: Freedland SJ et al. *J Clin Oncol* 2007;25(13):1765-71. **Abstract**

Select Excerpts from the Discussion

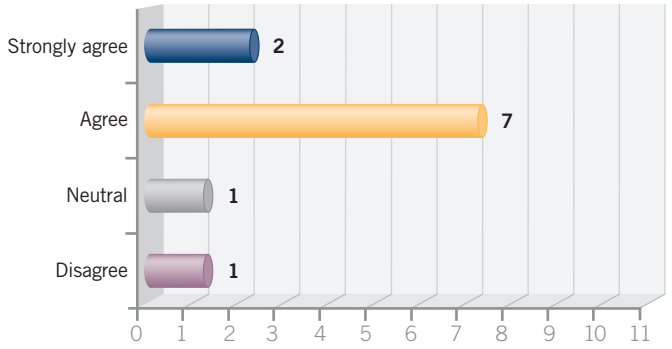
Tracks 21-23

DR LOVE: Steve, can you discuss your study evaluating the relationship between mortality and PSA doubling time following prostatectomy?

DR FREEDLAND: The PSA doubling time was calculated within the first two years after a PSA recurrence. Few men received hormonal therapy until the time of metastasis. Therefore, it is largely a natural history story (Freedland 2007; [2.1]). The question would be, if you take those men with PSA doubling times of less than three months and treat them with early hormonal therapy, will we see a better outcome? I don't know the answer.

FACULTY POLL QUESTION 4

It is reasonable to offer chemotherapy in a clinical setting to some patients with PSA-only relapse whose disease has become refractory to hormone therapy.



SOURCE: Survey of Think Tank Participants, June 21, 2007, Miami, Florida.

In Anthony's study published in the *JNCI*, he evaluated patients — from the CaPSURE and the Center for Prostate Disease Research databases — who were treated with radiation or surgery.

It was a much larger study than ours, and the median survival in patients with a PSA doubling time of less than three months was six years (D'Amico 2003). If you look at our study, the median survival was also six years.

DR OH: In looking at Steve's data, I am surprised that patients with a longer PSA doubling time had so many prostate cancer deaths. In patients with rapid PSA doubling times — where your data parallel Anthony's data — my guess would be that the practices are completely different at Hopkins and in the community in terms of when to initiate hormonal therapy. There's potentially no difference in outcomes. I'm not comparing the studies, but I don't think there seems to be an impact in those patients.

This brings up the question that perhaps, paradoxically, the benefits of hormonal therapy may actually be more dramatic in patients with moderate PSA doubling times.

If the patient's PSA is rapidly doubling, it may not matter whether you start hormonal therapy when the PSA is one or 10 or 20 ng/mL, but if a patient's PSA is doubling every 12 months, maybe it matters a lot. It may be that hormonal therapy is not being used enough.

DR LOVE: Steve, what about the use of intermittent hormonal therapy for patients with PSA-only disease?

DR FREEDLAND: I'm not a huge fan of intermittent hormonal therapy. In the man with a rapid PSA doubling time, the time off therapy — meaning the time he has a normal testosterone level — is extremely short. He actually derives a relatively low benefit.

I believe the patients who do have a significant quality-of-life benefit are the ones who, when their testosterone levels come back, stay off therapy for a year or two. In my experience, those are the patients with long PSA doubling times in whom I'm hesitant to use hormonal therapy in the first place.

For some patients, intermittent hormonal therapy would be better than continuous therapy because they don't need any treatment — some need continuous therapy. If you take "all comers," you're going to see no difference between intermittent and continuous hormonal therapy. If you risk stratify, however, I believe we can identify the group of patients that needs continuous hormonal therapy and the group that probably doesn't need any.

DR KLOTZ: We conducted a 100-patient prospective Phase II study of intermittent treatment, which was recently published (Bruchovsky 2007, 2006), and a lot from that study relates to these comments.

First, you can predict the off-treatment interval, in part, from the baseline PSA. The patients who do best are the ones who have a baseline PSA that is below 10 ng/mL (Bruchovsky 2007). Second, the PSA nadir is a huge predictor for the off-treatment interval and time to androgen-independent progression (Bruchovsky 2007).

DR LOVE: What about Steve's point about PSA-only disease and, for example, a patient with a rapid PSA doubling time?

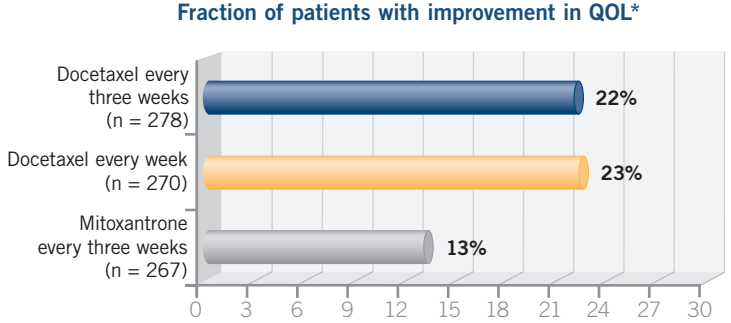
DR KLOTZ: For me, there are three groups of patients. The patients with a PSA doubling time that is less than three or six months should receive continuous hormonal therapy. The group with a slow PSA doubling time should have delayed hormonal therapy, which could be intermittent.

For the group in the middle — those with a PSA doubling time that is between six and 15 months — androgen deprivation therapy is warranted. However, no benefit of long-term, continuous hormonal therapy has been demonstrated. So other than for the patient with bad disease, I typically don't continue hormonal therapy beyond one or two years.

Track 25

DR LOVE: I've seen a change in the last couple of years in the approach to patients with hormone-refractory, PSA-only disease. Two or three years ago, I didn't hear much support for considering chemotherapy in these patients. I believe a lot of it is related to your work, Steve, on PSA doubling times and the idea that we can pick out the bad tumors and be more aggressive. What are your thoughts on that?

2.2 **TAX-327: Quality-of-Life (QOL) Outcomes**



* Improvement in QOL defined as a 16-point increase from baseline in the Functional Assessment of Cancer Therapy-Prostate (FACT-P) score on two measurements obtained at least three weeks apart

SOURCE: Tannock IF et al. *N Engl J Med* 2004;351(15):1502-12. **Abstract**

DR FREEDLAND: If you have a patient with hormone-refractory, PSA-only relapse, especially with a rapid PSA doubling time, you know what the future holds. If we have an effective therapy and our mantra is, "Effective therapy used earlier should be even more efficacious," I don't see a reason to hold that therapy.

Track 26

DR LOVE: What about the side effects of chemotherapy, specifically docetaxel? What's your take, Dan, in terms of how docetaxel affects quality of life?

DR PETRYLAK: The data from TAX-327, which evaluated the quality-of-life parameters for docetaxel versus mitoxantrone, are telling. The quality-of-life parameters improved more with weekly and every three-week docetaxel than with mitoxantrone (Tannock 2004; [2.2]).

It's different in an asymptomatic patient when you're not trying to treat bone pain and other issues. My general experience, however, has been — if you support the patients properly with growth factors and other measures — docetaxel is fairly well tolerated.

DR OH: If we properly select patients, we may not be making them feel better, but we're not making them miserable either. We're making them feel a little worse than they otherwise would in exchange for the probability that the longer-term picture might be better.

We don't have data in this setting, but we know the time to metastasis is short

2.3

Randomized Trials Comparing a Docetaxel-Containing Regimen to Mitoxantrone/Prednisone in Hormone-Refractory Metastatic Prostate Cancer

	SWOG-S9916[1]		TAX-327[2]*		
	D + E (n = 338)	M + P (n = 336)	D q3wk (n = 332)	D qwk (n = 330)	M (n = 335)
Median survival	17.5 mo[a]	15.6 mo	18.9 mo	17.4 mo	16.5 mo
Survival†	36%	30%	50%[b]	43%[c]	40%

D = docetaxel; E = estramustine; M = mitoxantrone; P = prednisone

* All patients in TAX-327 received prednisone in addition to chemotherapy.
† Median follow-up of 32 months for SWOG-S9916 and 20.7 months for TAX-327
[a] *p*-value = 0.02; [b] *p*-value = 0.009 versus mitoxantrone; [c] *p*-value = 0.36 versus mitoxantrone

SOURCES: [1] Petrylak DP et al. *N Engl J Med* 2004;351(15):1513-20. **Abstract**
[2] Tannock IF et al; TAX 327 Investigators. *N Engl J Med* 2004;351(15):1502-12. **Abstract**

in patients with rapid PSA doubling times. So, if a patient's PSA is doubling quickly in the absence of metastatic disease, even if he feels well, I believe docetaxel is a legitimate option to discuss, although it's not a standard practice.

Track 29

DR LOVE: How do you compare the quality-of-life impact from chemotherapy and androgen deprivation therapy?

DR FREEDLAND: I believe it's different in a lot of ways, but a lot of fatigue occurs with both therapies. Hormonal therapy dramatically affects quality of life, and we probably underestimate its effects.

DR OH: Docetaxel probably has greater global quality-of-life issues than hormonal therapy. Hormonal therapy is still a well-tolerated treatment, in general. I want to clarify that chemotherapy is not commonly used to treat patients with nonmetastatic, hormone-refractory disease. It's becoming more of an issue because men are increasingly receiving hormonal therapy in the absence of any metastatic disease.

In this setting, we'll often use second-line hormonal therapies — antiandrogens, ketoconazole, et cetera — in an effort to control the disease without having to use chemotherapy right away.

However, in a selected group of patients with aggressive, hormone-refractory prostate cancer, I don't believe it's wrong to have this conversation with the patient. In general, our surgical and radiation therapy colleagues ask us as medical oncologists, "Why aren't you using this treatment? It makes no sense not to."

Medical oncologists in the community have to balance this in the absence of data. They may say, "How do I take a patient who's feeling well and decrease his quality of life in the absence of data?" It's a fair point.

For many patients, once they have metastatic disease — whether they're symptomatic or asymptomatic — that's justification for chemotherapy. There is a survival benefit in that group of patients with metastases (Petrylak 2004; Tannock 2004; [2.3, 3.2, 3.3]).

In the patients with nonmetastatic disease, if they have a rapidly doubling PSA, it's predictive of time to metastasis. In that setting, if you're delaying chemotherapy by six months, is it meaningful to an extremely anxious young patient? My feeling would be that you're not buying much for that man by delaying chemotherapy. ■

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Bruchovsky N et al. **Locally advanced prostate cancer — biochemical results from a prospective phase II study of intermittent androgen suppression for men with evidence of prostate-specific antigen recurrence after radiotherapy.** *Cancer* 2007;109(5):858-67. **Abstract**

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D'Amico AV et al. **Surrogate end point for prostate cancer-specific mortality after radical prostatectomy or radiation therapy.** *J Natl Cancer Inst* 2003;95(18):1376-83. **Abstract**

Freedland SJ et al. **Death in patients with recurrent prostate cancer after radical prostatectomy: Prostate-specific antigen doubling time subgroups and their associated contributions to all-cause mortality.** *J Clin Oncol* 2007;25(13):1765-71. **Abstract**

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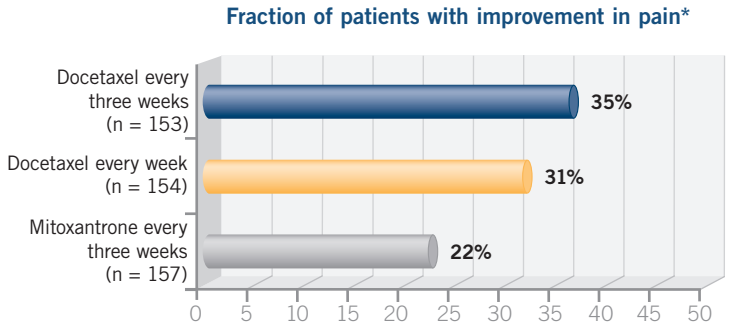
Southwest Oncology Group, Berry DL et al. **Quality of life and pain in advanced stage prostate cancer: Results of a Southwest Oncology Group randomized trial comparing docetaxel and estramustine to mitoxantrone and prednisone.** *J Clin Oncol* 2006;24(18):2828-35. **Abstract**

Tannock IF et al; TAX 327 Investigators. **Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer.** *N Engl J Med* 2004;351(15):1502-12. **Abstract**

Taplin ME et al. **Docetaxel, estramustine, and 15-month androgen deprivation for men with prostate-specific antigen progression after definitive local therapy for prostate cancer.** *J Clin Oncol* 2006;24(34):5408-13. **Abstract**

3.1

TAX-327: Pain Outcomes



* Improvement in pain defined as a two-point reduction in the Present Pain Inventory (PPI) score without an increase in the analgesic score or a reduction of at least 50 percent in the analgesic score without an increase in the PPI score, which was maintained for at least three weeks

SOURCE: Tannock IF et al. *N Engl J Med* 2004;351(15):1502-12. **Abstract**

Select Excerpts from the Discussion

Track 36

DR LOVE: Dan, what would you say to a patient with symptomatic prostate cancer about the potential impact of chemotherapy on his symptoms?

DR PETRYLAK: Data from TAX-327 demonstrated significant improvement in bone pain (3.1) and quality-of-life parameters (2.2) in favor of those symptomatic patients who received docetaxel compared to those who received mitoxantrone (Tannock 2004). I've seen symptomatic improvement in patients almost immediately — within a week or two of starting treatment. It's a fairly rapid response.

DR LOVE: Mike, what do you see when your patients come back from the oncologist after receiving chemotherapy?

3.2

TAX-327: A Phase III Randomized Trial of Docetaxel/Prednisone versus Mitoxantrone/Prednisone for Advanced Prostate Cancer

"Our findings provide evidence that cytotoxic chemotherapy can significantly prolong survival among men with hormone-refractory prostate cancer. Our data suggest that docetaxel plus prednisone is the preferred option for most patients with hormone-refractory prostate cancer."

SOURCE: Tannock IF et al. *N Engl J Med* 2004;351(15):1502–12. **Abstract**

3.3

SWOG-S9916: A Phase III Randomized Trial of Docetaxel/Estramustine versus Mitoxantrone/Prednisone for Advanced Refractory Prostate Cancer

"This randomized trial demonstrated that the treatment of androgen-independent metastatic prostate cancer with estramustine and docetaxel results in a longer median survival than treatment with mitoxantrone and prednisone (17.5 months vs 15.6 months, *P*=0.02)."

SOURCE: Petrylak DP et al. *N Engl J Med* 2004;351(15):1513–20. **Abstract**

DR ZELEFSKY: I would say that, in general, they do feel better in terms of pain. They also are psychologically happier when they see that their PSAs are dropping.

DR OH: I believe at least half of the symptomatic patients have a significant palliative benefit from chemotherapy — we're also extending their survival (3.2, 3.3). As Dr Zelefsky was pointing out, they want to know that their tumors are under control, which probably improves their quality of life above and beyond the pain benefit.

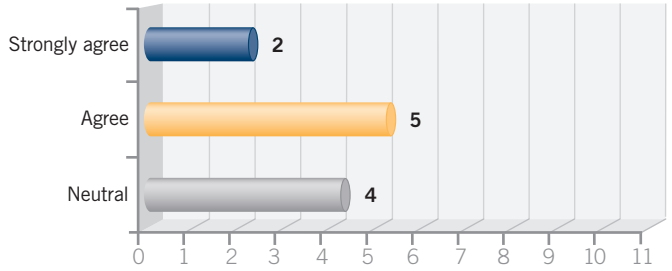
DR LOVE: Steve, for a patient with asymptomatic metastatic prostate cancer, how would you compare the ability to delay the onset of symptomatic disease and extend survival to the side effects and quality-of-life issues?

DR FREEDLAND: Patients don't walk in the door with metastatic hormone-refractory disease. They made a lot of choices along the way before they got there. It usually starts out with the choice to be screened for PSA, and they chose to be aggressive. They chose when it was positive to have the biopsy. They chose to undergo treatment — surgery or radiation. They chose to have the hormones before they had metastatic disease. So the patient often has chosen at every step of the game to be aggressive, based upon a PSA blood test. Now that we have a hormone-refractory rising PSA, I don't see why that mantra would be any different.

DR TAPLIN: I believe the asymptomatic patient with hormone-refractory prostate cancer is analogous to the patient with a rising PSA in that we have

FACULTY POLL QUESTION 5

For patients refractory to hormones who develop progressive disease on a first-line docetaxel regimen, satraplatin/prednisone represents a clinically meaningful option with the potential to improve quality of life and/or survival.



SOURCE: Survey of Think Tank Participants, June 21, 2007, Miami, Florida.

some predictors. Some of these patients have a slowly rising PSA, and you might hold back on chemotherapy in those patients and obtain intermittent scans. It could be a couple of years before they develop metastases. Other patients may have a rapidly rising PSA. They have had other predictors prior to this point that were negative, such as a short response to primary hormone therapy or no response to second-line hormone therapy. You know those patients are going downhill in a short time.

Track 42

DR LOVE: Dan, can you discuss the safety and efficacy profile of satraplatin?

DR PETRYLAK: The side-effect profile for satraplatin is remarkably benign. Our patient who was on it the longest received 14 cycles of treatment. He did extremely well while he was on the study. Moderate fatigue and minimal nausea occur with satraplatin. As the duration of therapy increases, more hematologic toxicity is observed, but it's a well-tolerated treatment.

Satraplatin has clear-cut clinical activity as evidenced from the pain data, PSA data and the objective response rate (Sternberg 2007; [3.4]). We are seeing a population of patients, as we saw with docetaxel, who will respond for a long time.

DR LOVE: Dan, if satraplatin was available today, how would you use it?

DR PETRYLAK: I would use satraplatin exactly as we did in the trial (Sternberg 2007), in patients who failed prior docetaxel.

3.4

A Phase III Randomized Trial of Satraplatin/Prednisone versus Prednisone Alone for Patients with Hormone-Refractory Prostate Cancer Who Were Treated with One Prior Chemotherapy: Efficacy Outcomes

	Satraplatin and prednisone	Placebo and prednisone	*p*-value
Pain response	85/351 (24.2%)	25/181 (13.8%)	0.005
Tumor response	23/352 (6.5%)	1/177 (0.6%)	0.001
PSA response	121/476 (25.4%)	28/225 (12.4%)	<0.001

SOURCE: Sternberg CN et al. *Proc ASCO* 2007;**Abstract 5019**.

DR OH: In patients who were previously treated with docetaxel, the difference in median progression-free survival was one week for satraplatin versus placebo (Sternberg 2007). One might ask, what's the point? However, it is important to go beyond the median because there is a platinum-sensitive subset of patients.

Data with other platinum drugs clearly demonstrate that some patients respond well to platinum-based agents. This large randomized trial demonstrates that exact fact. The problem is if you look at the median, you lose what might be a dramatic benefit in about a third of the patients (Sternberg 2007).

Tracks 44-45

DR LOVE: Steve, if a patient is symptomatic after progressing on hormones and then on docetaxel, what's the likelihood he will feel better after receiving satraplatin?

DR PETRYLAK: A clear-cut difference in pain response exists between satraplatin and placebo — 24 percent versus 14 percent (Sternberg 2007; [3.4]). So there's a fairly good chance this patient will feel better.

DR OH: I believe satraplatin might open the door to physicians who would otherwise feel that their patients are not candidates for chemotherapy. It may, therefore, open the door to using docetaxel subsequently.

Biologically, there's no reason to believe that docetaxel and satraplatin should be cross reactive in terms of sensitivity. We don't know yet because satraplatin hasn't been evaluated in the first-line setting. ■

SELECT PUBLICATIONS

Sternberg CN et al. **Satraplatin (S) demonstrates significant clinical benefits for the treatment of patients with HRPC: Results of a randomized phase III trial.** *Proc ASCO* 2007;**Abstract 5019**.

Tannock IF et al; TAX 327 Investigators. **Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer.** *N Engl J Med* 2004;351(15):1502-12. **Abstract**

QUESTIONS (PLEASE CIRCLE ANSWER):

1. **As men age, the duration of testosterone suppression after the completion of six months of hormonal therapy _____.**
   a. Decreases
   b. Increases
   c. Stays the same
2. **As the duration of testosterone suppression after the completion of six months of hormonal therapy increases, the time to prostate cancer-specific and all-cause mortality _____.**
   a. Decreases
   b. Increases
   c. Stays the same
3. **Randomized trials of prostatectomy with three months of neoadjuvant hormonal therapy have not demonstrated a benefit to date.**
   a. True
   b. False
4. **Satraplatin is a novel oral platinum compound.**
   a. True
   b. False
5. **TAX-327 demonstrated that patients with advanced prostate cancer treated with every three-week docetaxel and prednisone had a superior survival rate compared to patients treated with mitoxantrone and prednisone.**
   a. True
   b. False
6. **In patients with hormone-refractory, metastatic prostate cancer, the use of docetaxel has led to improvements in quality of life, overall survival and pain relief.**
   a. True
   b. False
7. **In patients receiving intermittent hormonal therapy, which of the following parameters may predict the duration of the off-treatment interval?**
   a. Baseline PSA
   b. PSA nadir
   c. Both a and b
   d. None of the above
8. **Which of the following supported the clinical activity of satraplatin as second-line therapy for patients with metastatic prostate cancer?**
   a. Objective tumor response
   b. PSA response
   c. Pain response
   d. All of the above
9. **In patients previously treated with docetaxel, the difference in median progression-free survival was _____ for satraplatin versus placebo.**
   a. One month
   b. Three months
   c. One week
   d. Three weeks
10. **Among patients with hormone-refractory, metastatic prostate cancer treated with prednisone, _____ resulted in a significantly greater improvement in quality of life compared to mitoxantrone.**
    a. Every three-week docetaxel
    b. Weekly docetaxel
    c. Both a and b
    d. None of the above
11. **In a retrospective analysis of patients with PSA recurrence after radical prostatectomy, Freedland and colleagues demonstrated that although patients with a PSA doubling time (PSADT) <3 months were at the greatest risk of prostate cancer-specific death, patients with a PSADT of 3.0 to 8.9 months accounted for the greatest number of prostate cancer deaths in the cohort of men evaluated.**
    a. True
    b. False

Post-test answer key: 1b, 2b, 3a, 4a, 5a, 6a, 7c, 8d, 9c, 10c, 11a

EVALUATION FORM

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GLOBAL LEARNING OBJECTIVES

To what extent does this issue of *PCU* address the following global learning objectives?

- Critically evaluate the clinical implications of emerging clinical trial data in prostate cancer screening, prevention and treatment and incorporate these data into management strategies in the local and advanced disease settings. . . . . 5 4 3 2 1 N/A
- Counsel appropriately selected patients about the availability of ongoing clinical trials. . . . . 5 4 3 2 1 N/A
- Inform prostate cancer patients about the specific risks and benefits of local and systemic therapies. . . . . 5 4 3 2 1 N/A
- Provide individualized counseling to patients regarding the choice and timing of endocrine therapy. . . . . 5 4 3 2 1 N/A
- Counsel appropriately selected patients in the high-risk or advanced disease settings about the risks and benefits of chemotherapy, including emerging data on taxane-based regimens. . . . . 5 4 3 2 1 N/A

OVERALL EFFECTIVENESS OF THE FACULTY MEMBERS

To what extent do you feel the faculty members' comments were helpful or not helpful?

. . . . . .

. . . . . .

. . . . . .

OVERALL EFFECTIVENESS OF THE ACTIVITY

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Related to my practice needs. . . . . 5 4 3 2 1 N/A
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Will help me improve patient care. . . . . 5 4 3 2 1 N/A
Stimulated my intellectual curiosity. . . . . 5 4 3 2 1 N/A
Overall quality of material. . . . . 5 4 3 2 1 N/A
Overall, the activity met my expectations. . . . . 5 4 3 2 1 N/A
Avoided commercial bias or influence. . . . . 5 4 3 2 1 N/A

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Which of the modules did you find particularly relevant to your practice? Please elaborate on what about the topics and comments was helpful to you.

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.....

What other faculty would you like to hear interviewed in future educational programs?

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Additional comments about this activity:

.....

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As part of our ongoing, continuous quality-improvement effort, we conduct postactivity follow-up surveys to assess the impact of our educational interventions on professional practice. Please indicate your willingness to participate in such a survey:

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PCUTT107

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