Conversations with Urologic Oncology Leaders
Bridging the Gap between Research and Patient Care

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Prostate Cancer
Update

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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 and radiation oncologist must be well-informed of these advances. To bridge the gap between research and practice, Prostate Cancer Update utilizes one-on-one discussions with leading urologic oncology and radiation oncology investigators. By providing access to the latest research developments and expert perspectives, this CME program assists urologists and radiation oncologists in the formulation of up-to-date clinical management strategies.

GLOBAL LEARNING OBJECTIVES:
Upon completion of this activity, participants should be able to:

- Critically evaluate the clinical implications of emerging clinical trial data in prostate cancer screening, prevention and treatment.
- Inform prostate cancer patients about the specific risks and benefits of local and systemic therapies.
- Offer patients information regarding their prognosis with and without various therapeutic options.
- Provide individualized counseling to patients regarding the choice and timing of endocrine therapy.
- Discuss chemotherapy and biologic therapy options in the treatment of prostate cancer.

PURPOSE OF THIS ISSUE OF PROSTATE CANCER UPDATE:
The purpose of Issue 3 of Prostate Cancer Update is to support these global objectives by offering the perspectives of Drs Fradet, Thomas, Slovin and Picus on the integration of emerging clinical research data into the management of prostate cancer.

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### Pharmaceutical agents discussed in this program

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The culture of healthcare delivery for patients with prostate cancer is a highly unusual and interesting pocket of oncology therapeutics. From my perspective as a medical oncologist who has observed the evolution of the evidence-based interdisciplinary management of patients with common tumors like breast, colorectal and lung cancer, prostate cancer follows a very different model.

Specifically, men with prostate cancer receive initial systemic therapy from their primary urologist or radiation oncologist, and medical oncologists are not usually involved until patients become resistant to first- or second-line hormonal therapy, often many years later. Simply and humbly put, it is my opinion that this is not in the best interest of current or future patients. More bluntly, I suggest that clinical research is hampered by this management strategy. Equally troubling, patients may be receiving suboptimal care.

A major detrimental outcome associated with this prevailing treatment paradigm is the marginal integration of chemotherapy into the management of patients with prostate cancer. As discussed by medical oncologists Susan Slovin and Joel Picus in this program, studies in patients with advanced disease clearly demonstrate that chemotherapy, particularly taxane-based regimens, is as effective in prostate cancer as they are in many other solid tumors.

Unfortunately, more than 25 years after a mortality advantage was reported in women with breast cancer in the first adjuvant chemotherapy trials, we essentially still have no data about adjuvant chemotherapy in patients with prostate cancer.

At the recent 2004 American Society of Clinical Oncology (ASCO) annual meeting, two randomized trials reported a significant survival advantage for adjuvant chemotherapy in patients with non-small cell lung cancer (NSCLC). For years, NSCLC — like prostate cancer — was considered “chemoresistant,” but in retrospect, trials with adequate statistical power had not been executed.

When adequately powered trials were finally conducted in non-small cell lung cancer, the overall survival curves were very similar to those in the old breast and colorectal cancer studies. At the same ASCO meeting, two other studies demonstrated that docetaxel-based therapy extended survival in patients with metastatic prostate cancer. Those data are comparable to the results we saw 10 years ago in patients with metastatic lung cancer.
I would bet 10 bucks and dinner at Joe’s Stone Crab on South Beach that a similar survival benefit would be observed if an adjuvant docetaxel-based regimen were compared to placebo in men with high-risk prostate cancer.

I believe that clinical trials ultimately will demonstrate that, like breast cancer, the best strategy to remain free from prostate cancer recurrence and death will include short-term adjuvant chemotherapy followed by extended endocrine therapy. Sadly, it could take 10 to 15 years before we have an answer, and in the interim, many men will suffer and die from this disease.

As a corollary, it is astonishing that the research platform for the current use of endocrine therapy in patients with prostate cancer is almost nonexistent. The most common clinical scenario for the use of androgen deprivation involves the patient with a PSA-only relapse, and essentially no prospective randomized clinical trial data exist to support this treatment strategy. Not that treating at PSA relapse is an inherently bad idea, but if I were a person with cancer, I would prefer that research data guide my doctor’s decisions.

My comments are made with the full understanding that I am not a prostate cancer researcher or clinician, just a CME doc who likes to make people think and maybe push a few buttons. Putting all controversies aside, if you listen to Drs Slovin and Picus, it seems obvious that medical oncologists can be helpful at an earlier stage in the prostate cancer treatment paradigm.

Here is my suggestion, which totally ignores the practical obstacles to making it happen:

*Whenever systemic therapy is being considered for a man with prostate cancer, a medical oncologist should either be the primary treating physician or have a role equal to that of the urologist or radiation oncologist in managing the patient.*

There are institutions where this happens regularly, but these are primarily large tertiary care cancer centers. In community practice, where most men with prostate cancer are treated, medical oncologists see patients years after the initial systemic treatment decisions are made. This can and should change, and like everything else in the United States, all types of market forces are involved. However, if you’re a man with a prostate, or more importantly, if you’re a man without one, you want to see this happen a lot sooner than later.

— Neil Love, MD
NLove@ResearchToPractice.net

**Select Publications**

Eisenberger MA et al. *A multicenter phase III comparison of docetaxel (D) + prednisone (P) and mitoxantrone (MTZ) + P in patients with hormone-refractory prostate cancer (HRPC).* *Proc ASCO* 2004; Abstract 4.

Petrylak DP et al. *SWOG 99-16: Randomized phase III trial of docetaxel (D)/estramustine (E) versus mitoxantrone(M)/prednisone(p) in men with androgen-independent prostate cancer (AIPCA).* *Proc ASCO* 2004; Abstract 3.
Early Prostate Cancer Trials evaluating bicalutamide 150 milligrams

Prostate cancer research is about 10 to 15 years behind breast cancer research. For a long time, adjuvant tamoxifen in patients with breast cancer has been known to reduce mortality.

Prostate cancer is even more sensitive to hormonal manipulation. For example, many men with metastatic prostate cancer will have tumor regression with hormonal therapy, which I don’t believe is as striking in women with breast cancer.

The Early Prostate Cancer Trials evaluating bicalutamide 150 milligrams are certainly important in terms of size (1.1). These are important trials evaluating the reduction in mortality associated with adjuvant bicalutamide therapy.

As the data mature over the next several years, the truth will be evident. I hope these trials will demonstrate that the introduction of a hormonal manipulation early in the course of the disease might have an impact on survival, as is the case with breast cancer.

Use of bicalutamide 150 milligrams in a nonprotocol setting

I present bicalutamide 150 milligrams as an option because the European studies found equivalent survival for patients with MO disease who were treated with either an LHRH agonist or bicalutamide 150 milligrams. If the patient’s disease fails on bicalutamide 150 milligrams, then an LHRH agonist can be used.

If a man will be on hormonal therapy for a long time, the side effects of an LHRH agonist should be considered — the effect on sexuality, bone density, muscle strength and hot flashes. Studies have demonstrated that hormonal therapy affects quality of life.

Psychologists at our institution have conducted studies of sleep disorders and depression associated with hormonal manipulation. Since bicalutamide has fewer of these side effects than LHRH agonists, I offer it to patients.

Dr Fradet is a Professor and Chairman of the Department of Surgery at the Université Laval and CHUQ, L’Hôtel-Dieu de Québec in Québec, Canada.
Strategies to reduce bicalutamide-associated gynecomastia

Of the patients treated with bicalutamide 150 milligrams, 75 percent will have significant gynecomastia. I usually propose pretreatment radiation therapy to the breast, which has been shown to reduce breast enlargement by at least 50 percent. Because bicalutamide blocks the peripheral action of testosterone, the feedback mechanism is blocked and a slight increase in testosterone occurs. The excess testosterone is transformed into estrogen.

In men, estrogen is not counterbalanced at the breast by testosterone, which leads to gynecomastia. Hence, the mechanism for gynecomastia seems to be an excess estrogen effect with an absence of testosterone effect on the breast. The addition of tamoxifen, which blocks estrogen, might prevent bicalutamide-associated gynecomastia.

Two studies have shown that tamoxifen can reduce bicalutamide-associated gynecomastia by almost 85 percent. However, one study suggested tamoxifen might affect the efficacy of bicalutamide 150 milligrams. I’m the principal investigator of an international study that will determine whether tamoxifen reduces the incidence of gynecomastia in men with high-risk prostate cancer who are being treated with bicalutamide 150 milligrams.

We’re evaluating different doses of tamoxifen (10 or 20 milligrams) combined with bicalutamide 150 milligrams. After one year, tamoxifen is discontinued, bicalutamide is continued, and the PSA is monitored. One trial with an aromatase inhibitor has been conducted (1.2), but that strategy was not as effective and has been abandoned in favor of tamoxifen.

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Role of prostatectomy in men with high-risk disease

In the United States, many men with high-risk prostate cancer are guided toward some therapy other than surgery. In my opinion, the opposite should occur. I believe that in patients with higher-grade and higher-risk cancer, surgery as a primary treatment adds to the chance of survival quite significantly. The surgical morbidity in a man with higher-risk cancer is not different from the surgical morbidity in a man with lower-risk cancer. I have a very different attitude than many American doctors.

Our results in these men with high-risk disease (Gleason ≥7, PSA ≥10 or 20 ng/mL depending on the Gleason score, and a clinically palpable tumor) are quite spectacular. Patients we have treated with prostatectomy have a 90 percent 10-year survival rate, compared to patients treated with radiation therapy who typically have a 10-year survival rate of about 50 percent. A few studies, mostly from the Mayo Clinic, suggest that long-term survival may be better when using surgery as the primary treatment and adjuvant radiation therapy or hormonal therapy (or both) if the PSA fails — about 15 percent of those cases.

The only randomized trial comparing radiation therapy and surgery was a small series from Japan that was published in Urology in 1999. In that trial, patients with stage B2 and C cancers were treated with hormone therapy and then randomly assigned to surgery or radiation therapy. Although the radiation therapy doses administered were lower than those used today, patients treated with surgery showed a 10 percent difference in cancer mortality at five years. Hence, growing evidence suggests that even in high-risk cancer, treatment of the primary tumor makes a difference in survival.

Select publications


Boccardo F et al. Tamoxifen (T) is more effective than anastrozole (A) in preventing gynecomastia induced by bicalutamide (B) monotherapy in prostate cancer (pca) patients (pts). *Proc ASCO* 2003; Abstract 1608.


Iversen P et al. Casodex (bicalutamide) 150-mg monotherapy compared with castration in patients with previously untreated nonmetastatic prostate cancer: Results from two multicenter randomized trials at a median follow-up of 4 years. *Urology* 1998;51(3):389-96. Abstract


See WA et al. Bicalutamide 150 mg alone or as adjuvant to standard care significantly improves progression-free survival in patients with early, non-metastatic prostate cancer (median 5.4 years’ follow-up). Program and abstracts of the 99th Annual Meeting of the American Urological Association 2004; Abstract 810.

See WA et al. Bicalutamide 150 mg in addition to standard care significantly improves prostate specific antigen progression-free survival in patients with early, non-metastatic prostate cancer: Median 5.4 years’ follow-up. *J Urol* 2004; Abstract 1316.


See WA et al; Casodex Early Prostate Cancer Trialist Group. Bicalutamide as immediate therapy either alone or as adjuvant to standard care of patients with localized or locally advanced prostate cancer: First analysis of the early prostate cancer program. *J Urol* 2002;168(2):429-35. Abstract


Case 1: A 52-year-old man with Gleason 7 prostate cancer

History
This young executive had a normal digital rectal exam and a PSA that was on the higher side of normal, but less than 4 ng/mL. His primary care doctor was concerned and sent him to a urologist for a biopsy. His prostate volume was only 18 cc, and all eight cores were positive for cancer with a Gleason score of 4 + 3, which automatically put him in a high-risk category. His urologist recommended a radical prostatectomy, and he was a good surgical candidate.

Discussion
I usually spend about 30 to 45 minutes with patients like this because I not only review the surgical technique, but also the patient’s “prostate profile” — his age, medical condition, pathology, total volume of disease, PSA and rectal examination. This patient’s actuarial survival was 86 years of age, which meant he had 34 more years to live — but he had high-volume and high-risk disease with every core positive.

This man had been divorced for two or three years and was now involved with a woman whom he was going to marry in six months. Because his sexual function and quality of life were of paramount importance to him, and he wanted to have his nerves spared, I told him, “You have high-risk bilateral disease. If a surgeon tries to ‘peel off’ the nerves, they’re going to leave cancer behind. You need a wide excision. I know you don’t want to hear it, but that’s what I’m going to recommend.”

Other options included external beam radiation therapy, radioactive seeds or a combination. However, patients with high-risk and high-volume disease do not do well. He also had a small prostate; hence, radiation could interfere with his bladder and rectum more than if he had a bigger prostate. Additionally, if he were to have a PSA recurrence two years from now, we would not be able to operate because the tissue would have been radiated.
Managing patients with a PSA relapse

PSA relapse is not unusual — even patients with negative margins can have up to a 20 to 30 percent risk depending on the extent of capsular penetration. I have had patients whose PSA was negative for 10 or 11 years; then, all of a sudden, it crept up to 0.1, 0.2, 0.4 ng/mL, and two years later it was 1.0 ng/mL or more.

Prostatectomy for patients with high-risk disease

Currently, we treat patients with high-risk disease differently than we did one or two years ago. Now we do a wide-excision prostatectomy, removing the nerves and the surrounding tissue. Then we would check the PSA at six and 12 weeks. If the PSA is negative and the lymph nodes are negative, we recommend participation in SWOG-S9921 (2.1). In that trial, patients with high-risk disease are randomly assigned to receive hormonal ablation for two years with or without chemotherapy. In patients with high-risk disease who do not enroll in SWOG-S9921, we use leuprolide or goserelin in combination with bicalutamide for a period of 12 to 24 months.

In patients with high-risk disease, postprostatectomy PSAs at six and 12 weeks that are not zero signify that the patient already has systemic disease and should receive total androgen ablation — bicalutamide and an LHRH analog — for a two-year period.

2.1 Phase III Adjuvant Study of Androgen Deprivation with or without Mitoxantrone Plus Prednisone

Protocol IDs: SWOG-S9921, CALGB-99904, CTSU
Target Accrual: 1,360 (Open)

Eligibility:
High-risk adenocarcinoma of the prostate s/p radical prostatectomy

Goserelin sq q12wk and bicalutamide po qd x 2 years
(Goserelin sq q12wk and bicalutamide po qd x 2 years) + (mitoxantrone IV on day 1 + prednisone po bid on days 1-21) q3wk x 6

Study Lead Organizations:
Southwest Oncology Group
L. Michael Glode, MD, Protocol Chair
Tel: 720-848-0170, 1-800-473-2288


Managing patients with a PSA relapse

PSA relapse is not unusual — even patients with negative margins can have up to a 20 to 30 percent risk depending on the extent of capsular penetration. I have had patients whose PSA was negative for 10 or 11 years; then, all of a sudden, it crept up to 0.1, 0.2, 0.4 ng/mL, and two years later it was 1.0 ng/mL or more.
More common, however, are the patients with negative margins who have a PSA recurrence after one or two years. The management of these patients is more of a challenge; we don’t jump right away to treat them. If their PSA has gone from zero to 0.1 or 0.2 ng/mL, we tend to check another PSA to determine the PSA velocity. Three months later, if the PSA has gone from 0.2 to 0.8 ng/mL, we have a problem. If, instead, the PSA has gone from 0.2 to 0.3 ng/mL, it’s less worrisome.

The data indicate that these patients need to be treated by the time their PSA is 1.0 ng/mL. Previously, we would wait until the patient was symptomatic to start treatment. Now, early androgen ablation is recommended, but it all depends on the patient. I tell them, “I don’t want your PSA to go above one. So, sometime between now and then, I would like to give you external beam radiation therapy.” Usually, we send them for external beam radiation therapy to the prostatic bed. If the rise in PSA is rapid, radiation therapy may not be sufficient, in which case we use androgen ablation with or without radiation therapy. When the radiation is complete, we discontinue the hormonal ablation and evaluate the PSA.

**Select publications**


Case 2: A 50-year-old man presenting with metastatic prostate cancer at initial diagnosis

**History**
This man presented to his local physician with a chief complaint of intermittent back pain. He was managed for several months on a variety of nonsteroidal anti-inflammatory agents. Suddenly, he developed acute urinary retention and was seen by his local urologist, who detected a very large prostate that he thought was related to benign prostatic hyperplasia. The patient did well after his catheter was removed, and a transurethral resection of the prostate was discussed. A few more months passed, and during this entire time the patient’s PSA had not been checked.

Approximately eight to 10 months after the initial incidence he developed back pain again. The primary care physician finally ordered an X-ray, which didn’t reveal a compression fracture or any major pathology; however, the bone appeared a little opacified and was suggestive of metastatic disease. A bone scan revealed widespread metastatic disease. The PSA at diagnosis was 230 ng/mL and the prostate biopsy revealed Gleason 4 + 5 cancer.

**Discussion**
This man was in the poor-risk category; he had a high Gleason score, a high PSA and a large prostatic mass. He was referred to us for possible enrollment in early treatment trials. Unfortunately, he had already started hormonal therapy — bicalutamide and leuprolide — and that excluded him from the protocols. If he had not been treated with hormones and did not have metastatic disease, he would have been eligible for neoadjuvant treatment (docetaxel and estramustine; or paclitaxel, estramustine and carboplatin followed by radiation therapy).

Because he had been on hormonal therapy for two to three months with no improvement in quality of life and a very slowly declining PSA, he was treated with docetaxel and estramustine in addition to hormonal therapy. His family...

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*Dr Slovin is an Assistant Member of Genitourinary Oncology Service at Memorial Sloan-Kettering Cancer Center in New York, New York.*
was devastated and he was convinced death was around the corner because his urologist had told him that he would probably be dead within a year. I find this very disconcerting, because for every Gleason grade the outcome can be variable. Some patients with Gleason 9 cancer live for 10 years before their disease progresses, and other patients with Gleason 8, 9 or 10 cancer can have a demise within two years. Even with metastatic disease, some patients with high-grade lesions seem to progress more rapidly than others.

If this patient had presented to me without having received hormonal therapy and was not eligible or didn’t want to participate in a study, I would have discussed the standard of care, the relative merits and deficits of hormonal therapy and the likelihood that his disease would not go into remission. I would have started him on an LHRH analog with or without an antiandrogen. Strong data do not exist to support the use of combined androgen blockade. We use it because we learned many years ago that the addition of an antiandrogen provides a seven-month survival benefit. Nevertheless, several meta-analyses and reviews have supported the use of monotherapy with an LHRH analog. As a rule, however, I use combined androgen blockade despite what the data show.

We are seeing more younger men who, at initial diagnosis, have metastatic disease. We don’t know why this is occurring. Are physicians reluctant to check PSAs in their younger patients because it’s not considered the standard of care or allowed by some insurance companies? We do not know.

Case 3: A 62-year-old man treated with bicalutamide monotherapy for prostate cancer recurrence

History
Several years after prostatectomy, this patient was started on bicalutamide 50 milligrams daily for biopsy-proven recurrent prostate cancer in a palpable inguinal lymph node. He was married to a woman who was about 25 years his junior, and sexual potency was an important issue. He had asked me about bicalutamide 150 milligrams, and we discussed the rationale for using leuprolide as the standard of care and the risks of not being on an LHRH analog. We also talked about investigational trials, but he did not wish to sacrifice potency at any cost. He wanted to try bicalutamide.

We tried intermittent bicalutamide 50 milligrams for about a year and a half, and he did very well. Then, several other lymph nodes evolved in the groin and retroperitoneum. I was ready to initiate leuprolide, but he did not want it. He was comfortable with bicalutamide, so we increased the dose to 150 milligrams. For two years, the lymph nodes regressed and he did wonderfully. While he was on bicalutamide 150 milligrams, he maintained his libido and had no complaints other than significant gynecomastia, which was tolerable. More recently, the lymph nodes grew to 50 percent of their previous size and his PSA started to rise. We have stopped the bicalutamide and we’re starting leuprolide.
Discussion

The only data evaluating monotherapy with bicalutamide 50 milligrams daily in patients with metastatic disease are from a study by Gerry Chodak. Because I have had several patients who didn’t want to receive leuprolide or an investigational treatment, I have used bicalutamide 50 milligrams daily on an intermittent basis. Usually these patients have only a rising PSA and not metastatic disease. If they do have metastatic disease, it’s a moderate amount of adenopathy in the retroperineum. I allow their PSAs to nadir to about 1 ng/mL because if I let them go beyond 1 ng/mL for a long period of time, the disease can become resistant. It takes about two or three months for the PSA to nadir at 1 ng/mL; then we stop the bicalutamide, allow the PSA to rise to whatever panic value that patient sets and then restart bicalutamide. Many of my patients have been following this strategy of intermittent bicalutamide for about three or four years.

Indications for chemotherapy

I have not utilized adjuvant chemotherapy in a nonprotocol setting and generally do not recommend chemotherapy in men with PSA relapse until they are resistant to hormones. Most clinical oncologists do not rush to administer chemotherapy in these settings. If the patient does not experience a durable response — less than six months — with hormonal therapy, then I’d immediately proceed to chemotherapy.

Select Publications


Docetaxel/estramustine plus bevacizumab in patients with hormone-refractory metastatic prostate cancer

We conducted a single-arm Phase II trial evaluating docetaxel/estramustine plus the humanized monoclonal antibody bevacizumab in patients with hormone refractory metastatic prostate cancer. Bevacizumab targets the vascular endothelial growth factor (VEGF) protein, which is thought to be one of the mediators of angiogenesis. The drug was developed several years ago and hit the press in a major way in colorectal cancer, where it actually prolonged survival when added to standard chemotherapy regimens.

We enrolled 72 patients in this trial and although we shouldn’t make too much of efficacy in a single-arm trial, I have been impressed by the high response rate. In our docetaxel/estramustine backbone trial we saw a response rate of 69 percent. Here we are seeing a response rate closer to 79 percent. Starting at a base of nearly 70 percent leaves little room for improvement. I believe any increase is impressive. We are also seeing that patients are staying on this therapy for a while and appear to have their disease under control.

With regard to toxicity, we saw some thrombotic problems, but the question is whether they were higher than what we would see with a drug such as estramustine, which is an estrogenic agent and causes thrombotic problems by itself. An ASCO poster suggested that about five to 10 percent of patients on estramustine have thrombotic problems. That’s approximately the same rate we saw in our trial. We also saw some hypertension, one fatal mesenteric vein thrombosis and one patient who clearly had a bowel perforation. We attributed that to a diverticulosis, although given previous bowel perforations observed in the colon cancer trial, I am not sure we can just write that off. We also saw the common toxicities you see with docetaxel/estramustine — nausea, vomiting, fatigue, hair loss, cytopenias — but nothing else that really stood out from our previous experience with chemotherapy.

I would like to see bevacizumab move forward into a randomized trial to really show if it has efficacy. The design of that type of trial is currently being debated nationally and internationally. A very simple trial would be docetaxel/estramus-
tine with or without bevacizumab. However, that would be a fairly large trial, and before we make such a commitment, we need to consider whether it would be worth doing to see a 10 percent improvement. Others have suggested a trial of docetaxel/bevacizumab versus docetaxel/estramustine. I think estramustine adds a lot of toxicity. If bevacizumab is truly an active drug it might be a good substitute with greater tolerability.

Case 4: A 62-year-old man with a rising PSA
One of the patients I saw today in my clinic was a 62-year-old retired railroad worker who was a participant in our bevacizumab trial. He was first diagnosed in 1997 with high-risk disease. He had a prostatectomy and was given radiation therapy and hormonal therapy. When I first saw him, his PSA had just started to rise while he was on hormonal therapy, and his bone scan had become positive. Initially, we took him off bicalutamide and his PSA went down, he had no pain and the PSA stayed down for about six months.

However, after failing several antiandrogens, in 2002 he agreed to participate in our bevacizumab/docetaxel/estramustine study. At that time, his PSA was well over 100 ng/mL and he was experiencing considerable pain. He enrolled in the study and had a dramatic response. His pain was gone after his first dose of chemotherapy and his PSA dropped as low as 2 ng/mL. His bone scan improved dramatically and his CT scan looked normal. He no longer needed narcotics and was able to participate in activities that he had previously avoided because of the pain.

Aside from alopecia, fatigue and neutropenia, he tolerated the therapy very well and received nine cycles over six months. However, toward the end of that time, his PSA began to rise and he was increasingly fatigued. We stopped all therapy in March 2003. He did well for about eight to 12 weeks and then his PSA went up from 6 to 10 to 50 ng/mL within a few months, and he began to have pain again.

Because of his fatigue from docetaxel and some residual neuropathy, we had a long discussion and decided to use mitoxantrone and low doses of prednisone in accordance with the FDA-approved indication. He again responded well: the pain went away and the PSA went down to a very low level. He had no side effects from the mitoxantrone, but we were concerned about the cumulative possibility of cardiotoxicity so we stopped therapy after about six cycles thinking that we had achieved a good response.

Three weeks ago his pain returned and he went back on oxycodone and a lot of short-acting narcotics, and he restarted mitoxantrone. When I saw him today he had completely stopped his short-acting narcotics, and we are starting to taper his oxycodone. I think he is a good example of somebody with chemosensitive disease. He does well as long as he is on chemotherapy; however, whenever we stop his chemotherapy, his disease progresses and his quality of life and his performance status deteriorate along with it.

Select publication
Picus J et al. The use of bevacizumab (B) with docetaxel (D) and estramustine (E) in hormone refractory prostate cancer (HRPC): Initial results of CALGB 90006. Proc ASCO 2003;Abstract 1578.
1. A Phase II trial evaluating docetaxel/estramustine plus bevacizumab demonstrated a response rate approximately _________ percent higher than an earlier study of docetaxel/estramustine.
   a. Zero  
   b. Three  
   c. Seven  
   d. 10

2. The Early Prostate Cancer Trials are evaluating _________ as adjuvant therapy.
   a. Goserelin  
   b. Bicalutamide 150 milligrams  
   c. Docetaxel  
   d. All of the above  
   e. None of the above

3. A randomized trial demonstrated that survival is equivalent for patients with MO disease who are treated with either an LHRH agonist or bicalutamide 150 milligrams.
   a. True  
   b. False

4. Which of the following strategies have been evaluated for the prevention of bicalutamide-associated gynecomastia?
   a. Radiation therapy to the breast  
   b. Tamoxifen  
   c. An aromatase inhibitor  
   d. All of the above  
   e. None of the above

5. In patients with high-risk prostate cancer, several randomized clinical trials have proven that those treated with prostatectomy have a better survival outcome than those treated with radiation therapy.
   a. True  
   b. False

6. Which of the following factors should be considered when discussing primary therapy with a patient who is newly diagnosed with prostate cancer?
   a. Age  
   b. Volume of disease  
   c. Pathology  
   d. PSA  
   e. All of the above

7. SWOG-S9921 randomly assigns patients with high-risk prostate cancer after prostatectomy to:
   a. Hormonal ablation for two years  
   b. Hormonal ablation for two years plus chemotherapy  
   c. Chemotherapy alone  
   d. Either a or b  
   e. All of the above

8. The PSA doubling time can be used to determine the urgency to initiate treatment for a patient with a PSA recurrence.
   a. True  
   b. False

9. Chemotherapy is considered the standard of care for the initial treatment of metastatic prostate cancer.
   a. True  
   b. False

10. The Japanese randomized trial by Akakura comparing radiation therapy and surgery in patients with Stage B2 and C prostate cancer demonstrated no difference in five-year mortality between the treatments.
    a. True  
    b. False
Evaluation Form:
Prostate Cancer Update — Issue 3, 2004

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Please answer the following questions by circling the appropriate rating:

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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. .......................... 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
- Offer patients information regarding their prognosis with and without various therapeutic options. .......................... 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
- Discuss chemotherapy and biologic therapy options in the treatment of prostate cancer. .......................... 5 4 3 2 1 N/A

EFFECTIVENESS OF THE INDIVIDUAL FACULTY MEMBERS

<table>
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<tr>
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<td>Raju Thomas, MD, FACS, MHA</td>
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<td>Susan F Slovin, MD, PhD</td>
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<td>Joel Picus, MD</td>
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OVERALL EFFECTIVENESS OF THE ACTIVITY

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Related to my practice needs .......................... 5 4 3 2 1
Will influence how I practice .......................... 5 4 3 2 1
Will help me improve patient care .......................... 5 4 3 2 1
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Conversations with Urologic Oncology Leaders
Bridging the Gap between Research and Patient Care

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Prostate Cancer
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