PCU2 | 2002

Prostate Cancer™

U P D A T E

Conversations with Urologic Oncology Leaders

Bridging the Gap between Research and Patient Care

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2 audio tapes

2 audio CDs

Monograph

CME Certified

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Prostate Cancer Update: A CME Audio Series and Activity

Statement of Need /Target Audience

Prostate cancer is one of the most rapidly evolving fields in urology. Published results from clinical trials lead to the emergence of new surgical and radiation therapy techniques as well as 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 must be well-informed of these advances.

To bridge the gap between research and patient care, Prostate Cancer Update utilizes one-on-one discussions with leading urologic oncology investigators. By providing access to the latest research developments and expert perspectives, this CME program assists physicians in the formulation of up-to-date clinical management strategies.

Issue 2, 2002 of Prostate Cancer Update consists of discussions with four research leaders on a variety of important issues, including postoperative management of erectile dysfunction, evaluation and management of PSA recurrence, micrometastases in patients with prostate cancer, early versus delayed hormonal therapy and state-of-the-art radiation therapy.

Educational Objectives

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

- Discuss the evaluation and management of a PSA recurrence following local therapy in a man with prostate cancer.
- Describe the natural history of a PSA recurrence postprostatectomy.
- Compare and contrast traditional and nontraditional hormonal therapy for prostate cancer.
- Evaluate the efficacy and long-term compliance associated with the available treatments for erectile dysfunction in men with prostate cancer.
- Describe a penile rehabilitation program for postprostatectomy patients.
- Discuss the role of hormonal therapy in combination with radiation therapy for prostate cancer.
- Examine the potential for PSA doubling time to serve as a surrogate for cancer specific survival.
- Understand the role of the androgen receptor in prostate cancer.
- Assess the efficacy and tolerability of bicalutamide 150 mg monotherapy relative to castration in patients with nonmetastatic locally advanced prostate cancer.

Accreditation Statement

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of the Postgraduate Institute for Medicine and NL Communications, Inc. The Postgraduate Institute for Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Designation Statement

The Postgraduate Institute for Medicine designates this educational activity for a maximum of 3 hours in category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the activity.

Faculty Disclosure Statements

The Postgraduate Institute for Medicine has a conflict of interest policy that requires course faculty to disclose any real or apparent commercial financial affiliations related to the content of their presentations/materials. It is not assumed that these financial interests or affiliations will have an adverse impact on faculty presentations; they are simply noted in this supplement to fully inform participants.

Prostate Cancer™ UPDATE

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How to use this supplement

This monograph supplements the audio program and contains edited comments, clinical trial schemas, graphics and references. Prostatecancerupdate.net includes a full transcription of the audio program and an easy-to-use representation of each page of this booklet, allowing users to link immediately to relevant full-text articles, abstracts, trial information and other web resources indicated throughout this guide in red underlined text.

Editor's Note

"The Talk"

> *"I usually have 'the talk' with men when their PSA goes above 0.2 ng/mL after radical prostatectomy. We discuss the fact that we probably have not completely cured the cancer, may need secondary treatment and should start thinking about our options. I dread this as a clinician. We go into the surgery expecting a cure and usually the PSA is undetectable after surgery. The moment the PSA rises represents a point of major frustration for both the patient and the doctor."*
>
> **— Judd W Moul, MD**

Nothing in medical school adequately prepares us for the daunting task of informing a patient that a therapy with significant morbidity has been unsuccessful, and that the disease is now life-threatening. Like all oncologists, I have had these "talks" many more times than I care to remember.

Because of our ability to monitor PSA, prostate cancer is very unusual and these "talks" often occur years before the disease becomes clinically symptomatic. However, the emotional toll of this situation can be enormous. While the biologic and clinical implications of this relatively new phenomenon are still being defined, patients and doctors — already faced with morbidity from the local therapy — struggle with decisions about embarking on additional treatments with their own toxicities.

In the enclosed program, Dr Moul sorts through his approach to patients with a PSA-only relapse. I noticed with great interest how often he uses the word "we" in describing his shared decision-making with the patient. Prostate cancer management has always involved difficult treatment choices, particularly with respect to optimal local therapy. Dr Moul outlines a logical, patient-centered, decision-making approach to the more recent phenomenon of PSA-only relapse.

The dilemma of PSA-only relapse has become so important in clinical practice that the topic also surfaced in the other three interviews in this issue of Prostate Cancer Update. Dr Craig Zippe notes that PSA screening has resulted in the earlier diagnosis of prostate cancer, which allows more frequent preservation of potency after radical prostatectomy. Therefore, the impact of castration on quality of life for a patient with a PSA relapse is a major issue. Dr Zippe remarks that potency-sparing alternatives, such as antiandrogen monotherapy, may be important options for these patients.

Dr Anthony D'Amico comments on the rapid evolution of clinical research in men with PSA-only relapse, and he reviews the use of factors, such as PSA

doubling time, to identify men at an increased risk of death from prostate cancer. Dr D'Amico points out that the ability to identify patients with a poor prognosis is not only important for current patient care but also for clinical research. Surrogate endpoints, like PSA doubling time, may allow investigators to answer key clinical questions more quickly in randomized clinical trials.

Dr Anna Ferrari provides an interesting biologic perspective relevant to how PSA-only relapse fits into the continuum of metastatic prostate cancer. Dr Ferrari's research suggests that approximately 30% of prostate cancer patients with pathologically negative lymph nodes have evidence of micrometastatic disease, detected by RT-PCR, in their lymph nodes.

She notes that clinical research in breast cancer has clearly demonstrated that systemic therapy is more effective for micrometastatic disease than for clinically evident metastases. While a comparable database does not exist in prostate cancer, available evidence suggests that early endocrine intervention may improve long-term outcome.

The first issue of Prostate Cancer Update included an interview with urologist and prostate cancer research leader, Dr Paul Schellhammer, whose own recent struggle with the disease includes a PSA-only relapse. Dr Schellhammer related how his perspective on the risks and benefits of intervention has changed as a result of living personally with prostate cancer.

Similarly, after his interview, Dr Moul shared with me his experience with his father-in-law who died from prostate cancer some years ago. When I asked Dr Moul how this experience affected his approach to patient care, he said, "In addition to being as empathetic as I can with the patient, I try to be as compassionate as possible with families. I try to get as many family members involved who want to be involved or whom the patient will allow to be involved."

Management of the patient with PSA-only relapse is a complex biopsychosocial challenge. As noted by Dr Ferrari, the potentially long natural history of prostate cancer suggests that a chronic disease management model is appropriate, like diabetes. From that perspective, "the talk" must be viewed as the beginning of a long and often complex series of clinical interventions with the ultimate goal of maximizing quantity as well as quality of life.

— Neil Love, MD

Judd W Moul, MD

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Edited comments by Dr Moul

Evaluation and management of a PSA recurrence

Proper counseling is essential, and I block an hour off my schedule to spend the time going through the options.

For a prostatectomy patient, the first option to consider is salvage radiation therapy to the prostatic bed if we think the disease is localized. I may do a ProstaScint scan to determine if there is occult systemic disease in the lymph nodes, either in the pelvis or the retroperitoneum. If the man has a positive ProstaScint scan, showing pelvic or retroperitoneal adenopathy, I will not offer radiation therapy, because he probably has systemic disease.

I believe about 70% of the patients with a PSA recurrence have systemic occult prostate cancer. They will either be on watchful waiting to monitor how quickly their PSA is rising or go on systemic therapy if they are very nervous about the PSA recurrence. If they decide to go on systemic therapy, the mainstay is hormonal therapy. We counsel them about traditional hormonal therapy (i.e., an LHRH agonist or complete androgen blockade) or nontraditional hormonal therapy. Because of some of the newer data, I think the current favorite approach in terms of nontraditional therapy would be bicalutamide 150 mg.

Natural history of a PSA recurrence following radical prostatectomy

Charles Pound, MD, from the Johns Hopkins group, published in *JAMA* in 1999 the best data on the natural history of a PSA recurrence postprostatectomy. Their data suggest that once the PSA rises to 0.2 ng/mL, it takes about eight years before patients develop a positive bone scan if they receive no other therapy. After the patients develop a positive bone scan and receive hormonal therapy, the median survival is another five years.

I use the Pound paper extensively in counseling patients. We have the figures and tables from the paper laminated and available in our exam room. The good news is — that approach appears to result in about a 13-year survival. The bad news is — that is not very reassuring for individual patients, particularly younger ones. Using that article, many more men select early treatment, rather than watchful waiting, when they have those specific time lines to apply to their individual life.

Three prognostic factors emerged from the Pound paper — a PSA doubling time less than 10 months, a pathologic Gleason score of 8-10 and a PSA recurrence within the first two years. Those were all poor prognostic factors that moved the eight-year time to a positive bone scan down to the four- or five-year range. Clearly, more of those men will take active treatment.

METASTATIC DISEASE-FREE SURVIVAL AFTER PSA-RELAPSE: JOHNS HOPKINS SERIES

	% Probability (95% CI)		
	3 years	5 years	7 years
All patients (n=304)	78% (73-84)	63% (56-70)	52% (44-60)
Gleason 5-7			
PSA recurrence > 2 yrs (n=124)	89% (81-94)	82% (71-94)	77% (65-86)
PSA recurrence ≤ 2 yrs (n=83)	80% (68-88)	62% (49-73)	47% (33-60)
Gleason 8-10			
PSA recurrence > 2 yrs (n=44)	77% (55-89)	60% (33-79)	47% (17-72)
PSA recurrence ≤ 2 yrs (n=53)	53% (39-66)	31% (17-45)	21% (9-35)

Derived from Pound CR et al. *JAMA* 1999;281(17):1591-97. **Abstract**

Timing of hormonal therapy

In a man with a rising PSA after surgery or radiation, I take into account his age, overall health status and psychological makeup. I try to gauge his feelings about a rising PSA and his understanding of the implications of a rising PSA. Then, we talk about treatment options.

In general, my philosophy is to favor early hormonal therapy in many of these men — particularly the younger, healthier men. If we follow these men expectantly and they develop a positive bone scan eight years later, most will still be quite healthy, vigorous and in good shape. Since we do not have a cure for metastatic prostate cancer, a positive bone scan essentially means a death sentence from prostate cancer. Traditional hormonal therapy works well, but typically patients with stage D2 disease have about a five-year survival. So, I am making an assumption that using earlier treatment to change the natural history is reasonable. If we increase the eight-year time to metastases, hopefully we can extend the time to death to 15, 17 or 19 years. Then, we can be more assured that the man will die of some other cause.

Center for Prostate Disease Research (CPDR) database

In the next couple of years, we will have important data on this question from the Center for Prostate Disease Research (CPDR) database, a Department of Defense-funded initiative that includes nine major military medical centers throughout the United States collecting data on prostate cancer patients. The CPDR database has enrolled about 15,000 patients.

The database will give further insight into the controversy over early versus delayed hormonal therapy for PSA recurrence. At the American Urological Association 2002 Annual Meeting, CPDR presented data suggesting that early hormonal therapy delays the time to a recurrent rise in PSA. In 187 men with a postprostatectomy PSA recurrence, traditional hormonal therapy was started before the PSA reached a level of 3.0 ng/mL. These men in the database were followed for a mean of five years. On average, it took about ten and one-half years for the men to experience a further rise in PSA. So, hormonal therapy allows an average of 10-11 years before the PSA starts to rise again.

We do not know if that will change the natural history of a PSA recurrence as reported in the Pound paper. Will hormonal therapy change the time to a positive bone scan from eight years to a longer period? Beyond the time to a positive bone scan, what about the ultimate survival? We are not able to obtain that information yet.

Traditional versus nontraditional hormonal therapy

In a man with a rising PSA for whom I am considering hormonal therapy, first I counsel him about traditional hormonal therapy options — orchiectomy, LHRH agonists alone or in combination with an oral antiandrogen. Even though it is debatable, some men choose traditional hormonal therapy because they believe it offers the best chance of disease control and survival. Other men are reluctant to take traditional hormonal therapy because of the side effects — loss of libido, loss of sexual function, hot flashes, weight gain and osteoporosis. Those side effects are becoming more relevant in our younger and healthier men. But, it is important to counsel them about those options.

After discussing the traditional hormonal therapies, I counsel them about nontraditional hormonal therapy approaches — intermittent hormonal therapy, oral combination therapy (low-dose bicalutamide or flutamide with finasteride) and antiandrogen monotherapy. Recently in practice, I think we are seeing — as a result of the Early Prostate Cancer (EPC) trial comparing adjuvant bicalutamide 150 mg to placebo — more willingness to use that particular therapy for PSA recurrence.

An advantage to bicalutamide 150 mg is that, in nonmetastatic prostate cancer, it is equivalent to traditional hormonal therapy. The disadvantages

include the fact that we do not know about its efficacy beyond six years relative to traditional hormonal therapy. In a man with a rising PSA, there is uncertainty as to whether bicalutamide 150 mg is as effective as an LHRH agonist in the long term. But, there are fewer side effects associated with bicalutamide 150 mg than traditional hormonal therapy. Bicalutamide 150 mg does not cause weight gain, hot flashes or a loss of muscle mass. Patients on bicalutamide 150 mg are able to maintain their libido and sexual function, particularly if they had a nerve-sparing prostatectomy.

The one unique downside to antiandrogen monotherapy is gynecomastia and breast tenderness. In my own practice when I offer antiandrogen monotherapy, I strongly encourage patients to seek a radiation oncology consultation for prophylactic, low-dose breast irradiation to prevent the breast side effects.

Since the results from the Early Prostate Cancer trial were presented, we have become more comfortable offering bicalutamide 150 mg to patients with a PSA recurrence. I have personally treated about three or four men in the last several months who have elected bicalutamide 150 mg for a PSA recurrence.

Adjuvant hormonal therapy

When combining all 8,000 patients in the EPC trial, there is an irrefutable positive result. Bicalutamide 150 mg decreases the number of bone scan events compared to placebo. When the patients are stratified by risk, the benefits from two years of adjuvant bicalutamide are less in patients with low-risk disease and greater in patients with high-risk disease. I certainly have a greater comfort level offering bicalutamide 150 mg to high-risk individuals whom I believe are going to benefit even in the short term, rather than to low-risk individuals who have a greater likelihood of being cured by the primary therapy. However, that may change with time.

Urologists have been "behind the eight ball" with regard to considering multiple treatment options and multiple prognostic factors. In the last decade, urologists have begun to think about different treatment options for localized disease. We are getting better at teaching patients about surgery, radiation and brachytherapy. Last year at the AUA meeting, there was a lot of buzz with regard to risk assessment.

Since the Partin tables were developed for staging, more urologists are thinking about multiple factors to predict risk. This will translate into thinking about risk assessment and realizing that monotherapy will not cure these high-risk patients. Over the next five years, there will be a further understanding of risk assessment and adjuvant therapy options.

Until recently, urologists believed that many patients had localized disease. Now there is recognition that a lot more patients have micrometastatic disease than we originally thought. The only adjuvant therapy that urologists

thought about was traditional hormonal therapy. As surgeons, we pride ourselves in diagnosing these men early and performing nerve-sparing prostatectomies to maintain sexual function. We do not want to compromise sexual function. Since we know traditional hormonal therapy will impact on their sexual function, we are reluctant to recommend it. We need to start thinking about other hormonal therapy options that may not have as much of an effect on sexual function.

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Craig D Zippe, MD

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Edited comments by Dr Zippe

Postprostatectomy erectile dysfunction

I believe the average urologist, performing 50 or more bilateral nerve-sparing procedures, has a 30 to 50% potency rate with at least 15 or 20% of that being medically assisted with Viagra® (sildenafil). The long-term efficacy of sildenafil in maintaining erections, in our study, was very good. About 70% of the patients, who responded to sildenafil at one year, were still obtaining a good response at three years. The best predictor of response to sildenafil is the quality of the initial nerve-sparing prostatectomy, measured by some partial function following surgery. Partial function would be reflected by an International Index of Erectile Function (IIEF) abridged score of at least 15. The other predictive factors for a response to sildenafil include bilateral compared to unilateral nerve-sparing surgery and, of course, age.

Nerve-sparing radical prostatectomy

I perform bilateral nerve-sparing prostatectomy in 90% of my patients. In the community three or four years ago, ten percent of the prostatectomies were nerve-sparing and 90% were non-nerve-sparing. That ratio is slowly changing.

We have looked at whether our positive margin rates were higher with bilateral nerve-sparing prostatectomy. I initially thought so when I was more inexperienced. But the more experienced one becomes, the easier it is to do bilateral nerve-sparing surgery with most tumors.

Technical caveats when performing a nerve-sparing prostatectomy include achieving excellent hemostasis of the dorsal vein and obtaining precise visualization at the apex. I have improved my vision by wearing 2.5 magnification loops, which help me see a little better. However, the ability to control hemostasis allows perfection of the nerve-sparing technique. The

actual handling of the nerve bundle is also very important. Many nerves are dysfunctional not because you cut them, but because you traumatize them. We should be operating more like neurosurgeons, compared to urologists or pelvic surgeons.

Postoperative management of erectile function

I am very aggressive with penile rehabilitation. Typically in the past, there was a neuropraxia period after surgery that lasted nine to 12 months — where patients were not getting nocturnal erections. We used to just let this period endure. After one year, we would then become aggressive and start treatment.

My current practice is very different than that. Now two weeks after surgery, patients start either oral sildenafil with a vacuum constriction device (VCD) or an early injection program with papaverine and phentolamine without any PGE1. We are using sildenafil to both prime the vasculature and try to induce erections. I have patients take it an hour or two before they use their VCD. Those men who are sexually active feel the sildenafil enhances the sexual experience from the VCD.

The year after prostatectomy is very important to these men in terms of keeping a relationship with their spouse. One of the advantages to an early rehabilitation program is that no physical or emotional separation occurs between the couple. It is really hard for many couples to re-establish physical intimacy 12 to 18 months after surgery. That physical and emotional separation may be a reason many of these patients are not interested in becoming sexually active again.

I have a nurse who specializes in sexual dysfunction who works with the patients. I also spend a lot of time discussing sexual function both before and after surgery. One to two years after surgery, most of us become impotence doctors. One year after surgery, 90% of my patients have an undetectable PSA and are continent without pads. Meanwhile, we are dealing with 75 or 80% of the patients who are still unhappy with their erections.

Therapeutic options for erectile dysfunction

Initially, I give patients all the options. In the same visit, I typically ask patients to come for injection training as well as prescribe a VCD and MUSE® (alprostadil). In any patient, the efficacy or long-term compliance with each option is not predictable. The long-term compliance with many of these options is only 50%. However, 50% of the men are happy with them. So, I give patients all the options as early as possible. Each individual patient — or couple, I should say, because the wife has to be satisfied as well — will narrow down what they prefer.

Sildenafil has been a marvelous addition to our armamentarium. Two other new drugs with at least equal, if not greater, efficacy are vardenafil by Bayer

and Cialis® (tadalafil) by ICOS-Lily. These new drugs need to be compared to sildenafil and evaluated for their side-effect potential. It is an exciting time, because we will have more options when these new oral treatments are approved. However, these drugs only work with good neurovascular preservation.

Each of us who performs prostate cancer surgery, especially on younger patients, must continue to work on our nerve-preservation techniques. However, we still try sildenafil in patients with nonnerve-sparing surgery, because about 10% of them will respond.

There are several university centers in the United States using sural nerve grafts. This procedure is slowly growing throughout the country. In sexually active young patients who require resection of both neurovascular bundles, we perform sural nerve grafting. Since two nerves are always better than one, especially when you consider the response to sildenafil, we have also started using it when we take out one nerve. The nerve grafts appear to respond to oral therapy as well as the native nerves. It takes 18 to 24 months to see a response from the transplanted nerve. Usually, a plastic surgeon helps to harvest the nerve and also sutures the nerve graft.

LOCAL TREATMENTS FOR ERECTILE DYSFUNCTION

Treatment	Efficacy	Discontinuation Rate
Intracavernous injection therapy	75-87%	31-58% at 1-3 years
Vacuum Control Device (VCD)	55-79%	20-44% at 1 year
Intraurethral alprostadil (PGE1)	32-58%	40-80% at 1-2 years
Sildenafil	30 to >80%*	10%

* Dependent upon patient age and postoperative potency. Sildenafil is often used in combination with the above local therapies with increased efficacy and patient satisfaction.

Source: Presentation by Dr Zippe, 2002

Evaluation of erectile function

In the past, good measures for erectile function were not available. Physician-assisted data collection was highly biased and probably inaccurate. Great strides were made with the implementation of validated questionnaires. Some of the earlier questionnaires were too complicated; they required the patient take them home and a statistician to input the data into a computer. I think the best questionnaire is the five-question Sexual Health Inventory for Men (SHIM). It consists of five questions that quantitate frequency of erections, maintenance of erections and sexual satisfaction. The SHIM is easy to complete and put in the patient's chart. In my clinic, men fill out the SHIM in the waiting room. It is reproducible and should probably be the gold standard for any specialty evaluating sexual function outcomes. To compare

perineal and laparoscopic prostatectomy with retropubic prostatectomy, we all need to use the same instrument to assess erectile function. There are no reports in the radiation therapy literature using the SHIM questionnaire.

Challenging Case 1: 76-year-old man in excellent health with Gleason 7 prostate cancer in 2/10 core biopsy

Clinical history

This very active and healthy man, with a history of diverticulitis and rectal polyp removal, presented with a PSA of 10.5 ng/mL. Two years earlier, his PSA was 4.3 ng/mL, and a biopsy was not performed. On physical exam, there were no palpable nodules, and he seemed to have a fairly large prostate (approximately 60 grams).

A 10-core biopsy revealed that the left side was normal, but the right side had two positive cores with Gleason 7 (3+4) adenocarcinoma. His bone scan was negative, and a CAT scan was not done. He did not want to receive any form of radiation. At the same time, he did not want to be observed.

Key management question

Which hormonal therapy options should be presented to this man?

Follow-up

The patient elected bicalutamide 150 mg monotherapy. He has been on it for nearly three years, and he is very happy with his treatment plan. His PSA is stable around 1.4 to 1.6 ng/mL. He has not experienced any toxicity, such as gynecomastia or hot flashes.

Case discussion

While I-125 seeds might have been an option, this patient did not want to have any radiation. At the same time, he did not want to be observed either. In a situation like this, a 76-year-old man with a Gleason 7 tumor probably has an 89% chance of survival at ten years with observation. However, he also has a 42% chance of developing metastatic disease with observation.

Healthy 76-year-old men will not accept observation with that kind of risk of developing metastatic disease. They will usually elect treatment. Most of my patients do not choose observation when presented with the statistics about the risk of developing metastatic disease.

So, we discussed hormonal options. One option was combined androgen ablation, which I think was too aggressive for this patient's tumor. The other hormonal therapy options included intermittent LHRH agonist therapy and bicalutamide monotherapy. I believed his tumor could be controlled without

much androgen deprivation, and that he did not need castration or to suffer from its side effects.

He chose bicalutamide monotherapy. The mean decrease in PSA with bicalutamide monotherapy is around 76 to 80%. Although about 30% of patients may become refractory to bicalutamide in two years, according to our small series of patients, this man did not. In our series, we have been able to use an LHRH agonist to rescue all of the patients with antiandrogen-refractory PSAs. I am comfortable with bicalutamide monotherapy in delaying PSA progression. This patient's quality of life was not compromised by treatment.

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Edited Comments by Dr D'Amico

Brachytherapy

If quality-assured, brachytherapy offers low-risk patients the opportunity to escalate the radiation dose and spare much of the toxicity. Acutely, patients have more urethral symptoms. Long term, impotence is no better, but radiation proctitis may be improved with brachytherapy compared to external beam radiation. The quality assurance for brachytherapy should include CT-based postimplantation dosimetry. For intermediate-risk patients, many believe brachytherapy should be combined with external beam radiation. Only the Seattle group believes implants alone can be used in intermediate-risk patients. We use MRI-based implants, which are a little more precise. For the most part, ultrasound-based implants are fine as long as there is quality assurance afterwards.

Adjuvant hormonal therapy

For T3-4 disease, there is no argument that the standard of care should include long-term hormonal blockade. RTOG and EORTC consider two and three years of hormonal therapy, respectively, to be long-term. Two years is most commonly used.

In localized disease, I would recommend the addition of hormonal therapy for a high-risk patient or an intermediate-risk patient who has unfavorable features (i.e., Gleason score ≥ 4+3 or PSA > 10 ng/mL and more than half of the biopsy cores positive). These patients are more likely to have a systemic, as opposed to a local-only, pattern of failure. I would use six months of hormonal therapy — two months before, two months during and two months after radiation therapy.

Higher radiation doses

Since men receiving hormonal therapy are also at risk for local failure, do they need higher radiation doses? This question remains unanswered. I am conducting a clinical trial at our institution using a higher radiation dose in combination with six months of hormonal therapy. We protect the rectum by using a 3-D conformal technique and inserting an intrarectal balloon for either the first or the last three weeks of radiation. I obtain a lateral port film to see the balloon, set my posterior border so the rectum is almost completely excluded and then treat. That is the only way I feel comfortable using high-dose radiation and hormones.

I am convinced that rectal toxicity is lower with 3-D conformal radiation therapy, as suggested by a number of phase II studies. I think 3-D conformal radiation therapy is key from a quality-of-life perspective. A Foley catheter and a rectal tube should no longer be used to locate the prostate. A CT-based simulation or at least a CT scan to transfer onto bony anatomy should define our target. Dose-escalations beyond 72 Gy without a conformal approach are dangerous, because one does not know the location of the rectum. The conformal technique is a technical advance with quality-of-life improvements.

The Surgical Prostatectomy versus Interstitial Radiation Intervention Trial (SPIRIT)

The SPIRIT trial, conducted by the American College of Surgeons, will compare two treatment modalities in patients with low-risk prostate cancer. Patients will be randomized to either radical prostatectomy or brachytherapy. This trial is particularly important because it will help to define both quality of life and cancer control outcomes in a disease state — low-risk prostate cancer — that has become the most prevalent as a result of PSA-based screening.

Hormonal therapy in combination with radiation therapy

There have been a number of studies, conducted primarily by the RTOG and the Europeans, evaluating the role of hormonal therapy in combination with radiation therapy. The main study, published by Bolla in the New England Journal of Medicine in 1997, was the EORTC trial. This trial, which changed practice patterns, added three years of hormonal therapy both during and following radiation therapy in patients with locally advanced prostate cancer. Since that trial was published, the standard of care for patients with T3-4 prostate cancer has become radiation and hormonal therapy.

In patients with localized prostate cancer, three trials have been completed and await follow-up. RTOG 9408 compared four months of hormonal therapy (two months prior and two months during radiation therapy) to radiation therapy alone in patients with T1-2 disease, PSA < 20 ng/mL and any

Gleason score. A second trial, conducted at Dana-Farber Cancer Institute, randomized patients with intermediate- and high-risk prostate cancer to radiation with or without six months of hormonal therapy (two months prior, two months during and two months after radiation therapy). The final study, by the Europeans, also compares six months of hormonal therapy to no hormonal therapy in radiation-managed patients with localized prostate cancer.

These studies will determine whether the addition of hormonal therapy can improve survival in patients with localized disease who are treated with radiation therapy. Currently, most radiation oncologists in the United States are adding hormonal therapy to radiation therapy in patients with localized prostate cancer and a PSA > 10 ng/mL or a Gleason score ≥ 7. The regimen is short term, usually anywhere from four to six months. However, we are awaiting these trial results to answer this localized prostate cancer question definitively.

Standard hormonal therapy consists of complete androgen blockade with an LHRH agonist and a nonsteroidal antiandrogen. A study is currently being planned to compare bicalutamide 150 milligrams to complete androgen blockade. Until results from that trial are available, we have not moved to using high-dose bicalutamide alone. However, instead of using no hormonal therapy in patients refusing an LHRH agonist — maybe because of quality-of-life issues — we may offer them high-dose bicalutamide monotherapy.

Patients with low-risk prostate cancer

In patients with low-risk prostate cancer, current radiation doses may be inadequate. An abstract presented at the AUA meeting, suggests that conventional radiation therapy doses (70 Gy) are not as effective as radical prostatectomy after eight years of follow-up in low-risk or low-volume, intermediate-risk patients. Radiation therapy is less effective than radical prostatectomy in otherwise low-risk prostate cancer patients, because the radiation doses used are ineffective to sterilize one or two cubic centimeters of adenocarcinoma. There are no other sites in the body where we can completely sterilize two cubic centimeters of adenocarcinoma with radiation doses of 70 to 85 Gy. The exceptions are head and neck or gynecologic cancers, but those are predominantly squamous cell.

According to the Bolla trial, hormonal therapy in combination with radiation therapy provides some synergy that seems to improve patient outcomes. RTOG 9413 asked, “Is hormonal therapy better when given before and during than after radiation therapy?” Radiation therapy given concurrently with hormonal therapy was the superior regimen in that study in terms of progression-free survival — overall survival cannot be determined yet. RTOG 9413 and the Bolla trial indicate that some type of synergy occurs in terms of tumor cell kill when radiation and hormonal therapy are combined

synchronously. In patients with low-risk prostate cancer, there are two approaches: one is to increase the radiation dose, and the other is to add hormonal therapy to the standard radiation dose.

Managing PSA recurrence after radiation therapy

A retrospective study that will be published this summer shows that when hormonal therapy is started before the bone scan becomes positive in the postradiation therapy setting, the duration of response and survival is longer. It is a retrospective study, so it is not randomized. Therefore, it is not a conclusion, but a hypothesis.

However, based on this data, my policy has been to not wait much beyond a PSA of 10 ng/mL to treat the patient. Around a PSA level of 10 ng/mL, bone scans start to become positive. In several hundred patients with a rising PSA after radiation that had not yet reached 10 ng/mL, we did not find a single positive bone scan. Once the PSA got above 10 ng/mL, bone scans started to become positive. Above 20 ng/mL, then most of the bone scans were positive.

Early versus delayed hormonal therapy

Three studies in the literature support early, rather than delayed, hormonal therapy. The Bolla trial essentially compares adjuvant and delayed hormonal therapy in patients with T3-4 disease. The Messing trial compares immediate and delayed hormonal therapy in node-positive patients treated by radical prostatectomy. The Medical Research Council trial compares early and delayed hormonal therapy in patients with metastatic or T3-4 disease. All of those trials can be criticized for various reasons, but they all, as a group, support the concept of early hormonal therapy.

Initiating hormonal therapy at PSA recurrence

I either offer patients with PSA elevation a clinical trial or immediate hormonal therapy, if they wish. If they do not want treatment, I say, "Okay. I'm comfortable waiting until your PSA is 10 ng/mL, not beyond that because of the positive bone scan issue."

Bicalutamide monotherapy may be more appealing to a patient with a biochemical relapse who does not want to be treated with castration. But, we do not know whether combined hormonal blockade and high-dose bicalutamide are equally effective. Some patients have accepted high-dose bicalutamide as an alternative. Since they are getting some therapy, but not experiencing the full repertoire of side effects, many of them are happy with it as a compromise. In terms of the quality of life for bicalutamide monotherapy compared to an LHRH agonist, patients need prophylactic irradiation up front for the gynecomastia; they do not get as anemic and are

not as fatigued; they do not have the same degree of hot flashes; and they maintain their libido. Overall, for a man in his fifties or sixties, it definitely provides an improvement in quality of life. But, we do not know the cancer-control outcome.

Bone mineral density is also decreased with hormonal therapy. A recent New England Journal of Medicine article by Matthew Smith suggests that the bone density loss can be reversed by the addition of a bisphosphonate during hormonal therapy. While there is no proven cancer-control benefit, it may very well be down the road. Bisphosphonates appear, in terms of bone density, likely to impact on the risk of developing a pathologic fracture in the future.

PSA doubling time as a predictor of survival

There are six studies in the literature — three in surgical and three in radiation therapy patients — which have evaluated a number of parameters in terms of their ability to predict the time to bone scan progression and death from prostate cancer after the initiation of hormonal therapy. All six studies have one factor in common — the rate at which the PSA rises following local therapy. If the PSA doubles within 6 to 12 months after local therapy, the patient is likely to develop a positive bone scan and subsequently die of the disease sooner.

In a group of 381 men managed with 70 Gy of radiation for T1-2 disease, we looked at prostate cancer-specific and overall survival. On a multivariate analysis, a PSA doubling time of less than a year was the most important predictor of time to prostate cancer death following the PSA failure. When we plotted cancer-specific survival and overall survival and stratified by PSA doubling time, we found that cancer-specific survival and overall survival for patients whose PSA doubling time was less than a year was essentially equal.

This meant that if a man with a PSA doubling time less than a year following radiation died, he died of prostate cancer. Possibly, a doubling time of less than year may be a surrogate for prostate cancer-specific death. Since the median age at diagnosis was 73 and the men had comorbid illnesses, these results are particularly intriguing.

In patients with a PSA doubling time greater than a year, cancer-specific survival five years following PSA failure was 95%. Our results mimic the Pound paper from Johns Hopkins, which found that it took on average eight years to go from PSA failure to distant failure and another five years to die — a total of 13 years until death. This indicates that the Johns Hopkins group is well selected for low- to intermediate-risk patients. Therefore, they do not have patients with a fast PSA doubling time. In our study, the patients with a PSA doubling time of less than a year had a five-year median survival from PSA failure to death.

I am looking at larger databases to validate whether or not a PSA doubling time less than a year is a surrogate for cancer-specific survival. If it is, this

may have an enormous impact on clinical trial design. If we had a surrogate end point for cancer-specific survival (i.e., PSA doubling time less than a year), the number of patients required to answer a question in a phase III trial would decrease markedly, the follow-up period would also decrease markedly and answers would be available more quickly.

Select publications

The Medical Research Council Prostate Cancer Working Party Investigator Group. **Immediate versus deferred treatment for advanced prostatic cancer: Initial results of the Medical Research Council trial.** *Br J Urol* 1997;79:235-246. **Abstract**

Bolla M et al. **Improved survival in patients with locally advanced prostate cancer treated with radiotherapy and goserelin.** *N Engl J Med* 1997;337:295-300. **Abstract**

D'Amico A. **Radiation and hormonal therapy for locally advanced and clinically localized prostate cancer.** *Urology* 2001;58(2 Suppl 1):78-82. **Abstract**

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

Messing EM et al. **Immediate hormonal therapy compared with observation after radical prostatectomy and pelvic lymphadenectomy in men with node-positive prostate cancer.** *New Engl J Med* 1999;341:1781-1. **Abstract**

Pound CR et al. **Natural history of progression after PSA elevation following radical prostatectomy.** *JAMA* 1999;281:1591-7. **Abstract**

Roach III M et al. **Neoadjuvant hormonal therapy (NHT) with whole-pelvic (WP) radiotherapy (RT) improves progression-free survival (PFS): RTOG (Radiation Therapy Oncology Group) 9413, a phase III randomized trial.** *Proc ASCO* 2002;**Abstract 711.**

Smith MR et al. **Pamidronate to prevent bone loss during androgen-deprivation therapy for prostate cancer.** *N Engl J Med* 2001;345:948-55. **Abstract**

Soloway MS et al. **Neoadjuvant androgen ablation before radical prostatectomy in cT2bNxMo prostate cancer: 5-year results.** *J Urol* 2002; 167:112-6. **Abstract**

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Edited comments by Dr Ferrari

Lymph node micrometastases in patients with prostate cancer

In an ongoing trial that will accrue 315 patients, so far out of 180 cases analyzed, we found the incidence of pathologically positive pelvic lymph nodes to be about 2 to 3%. In the patients with pathologically negative lymph nodes, roughly 30% had evidence of micrometastatic disease by PSA reverse transcription-polymerase chain reaction (RT-PCR). This indicates the presence of metastatic cells. I have also analyzed lymph nodes from 60 men without prostate cancer, and I found no PSA expression by RT-PCR.

PSA recurrence – local or systemic disease?

Patients fail local therapy with radical prostatectomy and radiation therapy. In our series with Nelson Stone and Richard Stock, prostate biopsies were taken in patients with high-risk prostate cancer. The prostate biopsies were negative for recurrence. Therefore, the disease recurred distantly. However, it may take time to see the recurrence on a bone scan or a CT scan.

There is no question, in the case of prostate cancer, that PSA is a relatively good marker, but the more undifferentiated the tumor, then the more androgen-independent and the less PSA produced. It is not unusual for a patient to have an almost undetectable PSA one day, and soon after, they can be riddled with metastases. Does that tell you the cancer cells multiplied fast? No, the cancer cells have been there all along. They may just produce less PSA relative to their parental cells in the prostate. Additionally, some cells do not produce PSA at all. Although PSA is an excellent tool, it does not tell us the entire story.

Androgen receptor signaling in androgen-refractory prostate cancer.

Grossmann ME et al. *J Natl Cancer Inst* 2001;93:1687-97.

This review paper recognizes that the androgen receptor, like the estrogen receptor in breast cancer, plays a major role in the control of prostate cancer. To some extent, this has been ignored in the general prostate cancer literature. Initially, the androgen receptor uses testosterone and dihydrotestosterone to drive cell proliferation, differentiation and death. This is why treatment with hormonal suppression is so successful. Later on when androgen is suppressed, the androgen receptor, rather than shutting off and disappearing, remains present and increases its activity several fold.

The androgen receptor also becomes "promiscuous." In the absence of androgens, it will use any other available steroid hormones (i.e., estrogen, progesterone and glucocorticoids). Additionally, the androgen receptor can be activated by other growth factors (i.e., epidermal growth factor and vascular endothelial growth factor), which normal cells use to shuffle signals from the environment. These growth factors can continue to drive prostate cancer cell survival and proliferation.

Over time, the androgen receptor can develop mutations. These mutations can turn an androgen receptor antagonist into an agonist. Many therapies are being developed that actually target the androgen receptor itself. This paper highlights the significance and implications of the many different ligands that use the androgen receptor to drive the progression of the disease. By attacking all the different signaling pathways and the androgen receptor itself, we may achieve more. An overexpressed androgen receptor present in prostate cancer cells, but not normal cells, gives us a window of opportunity whereby those cells may be targeted more easily. They may be more sensitive, perhaps, to our interventions. This opens up a whole host of new therapeutic options that may be developed.

Evidence for the differential expression of a variant EGF receptor in human prostate cancer.

Olapade-Olaopa EO et al. *Br J Cancer* 2000;82:185-94.

As prostate cancer progresses, epidermal growth factor receptor expression in androgen-independent cells is universally and prevalently expressed. This paper reports on a mutant form of these epidermal growth factor receptors that are constitutively active. There are various mechanisms by which receptors can be detrimental. First, there could be too many of them, and they could be associating when they should not, like HER2 in breast cancer. In other cases, they can have a mutation, which keeps them activated and proliferating.

Since there is evidence that the epidermal growth factor receptor keeps the androgen receptor active, therapies targeting the epidermal growth factor

receptor would be positive. There are two molecules that are collaborating to sustain androgen-dependent progression. Therefore, interrupting anywhere along that pathway would be a promising approach. Obviously, this requires testing in clinical trials.

There are agents that might be available clinically in the next couple of years. Various companies are developing epidermal growth factor receptor antagonists and small molecules that target the epidermal growth factor pathway more downstream. Iressa® is one of those molecules. There are the antivascular endothelial growth factor and the COX-2 inhibitors, as well.

Bicalutamide monotherapy compared with castration in patients with nonmetastatic locally advanced prostate cancer: 6.3 years of follow-up.

Iversen P et al. *J Urol* 2000;164:1579-82.

This paper reports on the long-term results from two randomized trials that compared bicalutamide 150 mg monotherapy to castration in 480 patients with locally advanced prostate cancer that was nonmetastatic. The goal was to determine if there was equivalency between these two treatments. One offers androgen-sparing therapy, and the other suppresses testosterone completely.

At the end of 6.3 years, 56% of the patients, who did not receive any form of local therapy and were only managed with hormonal manipulation, had died. There was no statistically significant difference in survival or time to progression between groups. This study essentially demonstrated that with 6.3 years of follow-up, the two treatments were equivalent.

The results were quite remarkable with respect to quality of life and tolerability. In terms of sexual interest or libido, there was a highly statistically significant benefit for the group receiving bicalutamide monotherapy. There was also a significant difference in the ability to sustain intercourse.

However, the number of patients who participated in this part of the study was very small. It is difficult to predict if this will hold up in a larger patient population, but it makes biologic sense. There were other significant differences related to quality of life, particularly physical capacity in terms of well-being, ability to perform sports, sexual interest, hot flashes and other activities.

The downsides associated with bicalutamide monotherapy were breast tenderness and gynecomastia, which are generally not observed with an LHRH agonist or orchiectomy. The quality of life issues become very important, particularly in those who will not be able to receive local therapy. Those patients will receive androgen deprivation for prolonged periods of time and/or intermittent androgen suppression. Monotherapy really offers, in my view, a number of quality-of-life improvements. Not just for men in their fifties or sixties; I have patients in their eighties who switch to bicalutamide monotherapy, once they learn about it.

QUALITY OF LIFE COMPARISON BETWEEN BICALUTAMIDE 150 MG AND CASTRATION AFTER 12 MONTHS OF TREATMENT

Key findings

Bicalutamide more favorable versus castration:

- Sexual interest (p=0.029)
  - * fewer declines in sexual function relative to baseline (18% versus 37%)
- Physical capacity (walking, climbing stairs, sports, etc) (p=0.046)
- Hot flashes (13% versus 50%)
- Bone mineral density

Toxicities of bicalutamide:

- Bicalutamide resulted in gynecomastia/breast pain in 40-50% of patients, with 1.3% withdrawing from the study due to these side effects

Derived from: Iversen P et al. *J Urol* 2000;164;1579-82. **Abstract**

Challenging Case 2: 61-year-old professional dancer with Gleason 8, hormone-independent, prostate cancer

Clinical history

In 1991, this 61-year-old black male, professional dancer was diagnosed with Gleason 8, prostate adenocarcinoma. He was treated with external beam radiation therapy. Subsequently, he had a rising PSA and was treated with an LHRH analog and an antiandrogen for four years. Then, he developed metastases to the iliac bone with some pain. He was referred for evaluation and further treatment. His main concern was that chemotherapy would interfere with his quality of life and ability to perform.

Key management question

What treatment options are available to this man?

Follow-up

He had a second hormonal manipulation, antiandrogen withdrawal, which was not effective. Then, he had a third hormonal manipulation, another antiandrogen, which worked for a brief period of time. His PSA continued to rise to 56 ng/mL.

At that point in 1995, he reluctantly started chemotherapy. He entered a clinical trial with paclitaxel and estramustine. Since he was one of the first patients on the trial, he got a very low dose and, therefore, did not respond well. Then, his doses were increased, and he had a 50% PSA response. Through all of this, he continued to perform and dance. After 1998, his disease continued to progress, and he was switched to mitoxantrone-prednisone. He did not have a response in his PSA, but he did have a symptomatic response in his pelvic pain.

He then went off therapy completely for a number of years. His PSA ranged anywhere between 170 to 200 ng/mL. When his PSA jumped to 250 ng/mL, he enrolled on an arsenic trioxide phase II trial. He had a 50% PSA response, completed the regimen and then went on to progress. Up until then (February 2000), he continued his normal activity — besides being a dancer, he had a full-time job. After that, he retired and was off all therapy. Finally, he developed disseminated intravascular coagulation from bone metastases, had a subdural hematoma and died.

Case discussion

Since this patient had received extensive pelvic radiation for his prostate cancer, he could not receive further radiation to the pelvic bone for his pain. After a second and third hormonal manipulation, he reluctantly decided to start chemotherapy. He had a preconceived notion that he would be nauseous, vomiting, in the hospital and not able to lead his life.

However, he was fully active, lived by himself, never needed home assistance, never had any type of medical support and was only admitted once to the hospital. From 1995 to 2002 — for seven years, he lived a full life on chemotherapy, but he adapted to the idea that he had a chronic disease. He lived with androgen-independent metastatic prostate cancer for seven years with various chemotherapy manipulations. Once he lost the fear of chemotherapy and realized that his quality of life would not be impaired, he was willing to take any therapy. This illustrates how much we have advanced in the management of metastatic prostate cancer. It is not unusual to see this kind of course in patients like this.

Once patients enter the phase of androgen-independent, hormone-refractory prostate cancer, they can compare it to having diabetes and requiring insulin. Sometimes, they can remain on the same dose for a long time, but sometimes it does not work. They may have to change the type of insulin, the insulin schedule and/or the type of agent. Oncologists and patients must be willing to change therapies. One has to move on in the process, not let the process dominate. If the PSA rises with one regimen, it does not mean it will not respond to the next.

Select publications

Ferrari AC et al. **Prospective analysis of prostate-specific markers in pelvic lymph nodes of patients with high-risk prostate cancer.** *J Natl Cancer Inst* 1997;89:1471-3. **Abstract**

Grossmann ME et al. **Androgen receptor signaling in androgen-refractory prostate cancer.** *J Natl Cancer Inst* 2001;93:1687-97. **Abstract**

Iversen P et al. **Bicalutamide monotherapy compared with castration in patients with nonmetastatic locally advanced prostate cancer: 6.3 years of follow-up.** *J Urol* 2000;164:1579-82. **Abstract**

Olapade-Olaopa EO et al. **Evidence for the differential expression of a variant EGF receptor in human prostate cancer.** *Br J Cancer* 2000;82:85-94. **Abstract**

Pharmaceutical agents discussed in this program

GENERIC	TRADE	MANUFACTURER
alprostadil	Muse®	Vivus, Inc.
arsenic trioxide	Trisenox®	Cell Therapeutics, Inc.
bicalutamide	Casodex®	AstraZeneca Pharmaceuticals, LP
finasteride	Proscar®	Merck & Co., Inc.
goserelin	Zoladex®	AstraZeneca Pharmaceuticals, LP
mitoxantrone	Novantrone®	Immunex Corporation
paclitaxel	Taxol®	Bristol-Myers Oncology
pamidronate	Aredia®	Novartis Pharmaceuticals
prednisone	—	Various
sildenafil	Viagra®	Pfizer Labs
vardenafil	Nuviva®	Bayer Corporation
tadalafil	Cialis®	ICOS-Lilly

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Speakers' Bureau: Bristol-Meyers, Aventis Pharmaceuticals

Questions ***(please circle answer)***

1. Which of the following best describes the American Society for Therapeutic Radiology and Oncology (ASTRO) definition for PSA recurrence?

a. Three consecutive rises in PSA after the nadir
b. Two consecutive rises in PSA after the nadir
c. Any PSA over 0.5 ng/mL
d. b and c
e. None of the above

2. The Pound paper, published in *JAMA 1999*, suggests that once the PSA rises to 0.2 ng/mL, it takes about eight years before patients develop a positive bone scan if they receive no other therapy. Which of the following is not one of the three prognostic factors that emerged from the Pound paper?

a. PSA doubling time less than 10 months
b. Patient age
c. Pathologic Gleason score of 8-10
d. PSA recurrence within the first two years
e. None of the above

3. The nontraditional hormonal therapies include:

a. Intermittent hormonal therapy
b. Orchiectomy
c. Antiandrogen monotherapy
d. All of the above
e. a and c

4. What percentage of postprostatectomy patients who responded to sildenafil at one year will still respond at three years?

a. 100% b. 70% c. 40% d. 10% e. 0%

5. Which of the following options are currently available for the treatment of erectile dysfunction?

a. Tadalafil b. Sildenafil c. Alprostadil d. a and b e. b and c

6. The Sexual Health Inventory for Men (SHIM) quantitates:

a. The frequency of erections
b. The maintenance of erections
c. Sexual satisfaction
d. All of the above
e. a and b

7. Which of the following statements is true about the role of hormonal therapy in combination with radiation therapy?

a. It is routinely used for all patients with T3-4 prostate cancer.
b. It is routinely used for all patients with localized prostate cancer.
c. It is routinely used for patients with localized prostate cancer and a PSA > 10 ng/mL or a Gleason score ≥ 7.
d. a and b
e. a and c

8. True/False: According to a retrospective study, when hormonal therapy is started before the bone scan becomes positive in the postradiation therapy setting, the duration of response and survival is longer.

9. **True/False:** The rate at which the PSA rises following local therapy may predict the time to bone scan progression and death from prostate cancer.

10. What were the results from the trial comparing bicalutamide 150 mg monotherapy to castration in patients with nonmetastatic locally advanced prostate cancer?
    a. Bicalutamide 150 mg monotherapy was better than castration in terms of survival.
    b. Bicalutamide 150 mg monotherapy was comparable to castration in terms of survival.
    c. Bicalutamide 150 mg monotherapy was better than castration in terms of quality of life.
    d. a and c
    e. b and c

Post-test Answer Key: 1. *a,* 2. *b,* 3. *e,* 4. *b,* 5. *e,* 6. *d,* 7. *e,* 8. *True,* 9. *True,* 10. *e*

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5 = ***Outstanding*** 4 = ***Good*** 3 = ***Satisfactory*** 2 = ***Fair*** 1 = ***Poor***

Extent to which program activities met the identified objectives

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

- Discuss the evaluation and management of a PSA recurrence following local therapy in a man with prostate cancer. 5 4 3 2 1
- Describe the natural history of a PSA recurrence postprostatectomy. 5 4 3 2 1
- Compare and contrast traditional and nontraditional hormonal therapy for prostate cancer 5 4 3 2 1
- Evaluate the efficacy and long-term compliance associated with the available treatments for erectile dysfunction in men with prostate cancer. 5 4 3 2 1
- Describe a penile rehabilitation program for postprostatectomy patients. 5 4 3 2 1
- Discuss the role of hormonal therapy in combination with radiation therapy for prostate cancer 5 4 3 2 1
- Examine the potential for PSA doubling time to serve as a surrogate for cancer specific survival. 5 4 3 2 1
- Identify the role of the androgen receptor in prostate cancer 5 4 3 2 1
- Assess the efficacy and tolerability of bicalutamide 150 mg monotherapy relative to castration in patients with nonmetastatic locally advanced prostate cancer. 5 4 3 2 1

Overall effectiveness of the activity

Objectives were related to overall purpose/goal(s) of activity 5 4 3 2 1

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

Stimulated my intellectual curiosity 5 4 3 2 1

Overall quality of material 5 4 3 2 1

Overall, the activity met my expectations 5 4 3 2 1

Avoided commercial bias or influence 5 4 3 2 1

Will the information presented cause you to make any changes in your practice?

___Yes ___No

If Yes, please describe any change(s) you plan to make in your practice as a result of this activity.

_____

_____

Degree:

☐ MD ☐ DO ☐ PharmD ☐ RN ☐ NP ☐ PA ☐ BS ☐ Other _____