



PCRI's "Town Hall Meeting" Involves Advanced PC Patients

On Saturday, April 8, 2006, forty-one advanced prostate cancer patients and their wives met with six prostate cancer specialists in the Los Angeles Ballroom of the LAX Hilton for a unique program that the PCRI has named a "Town Hall Meeting." The meeting, which was underwritten by an educational grant from Abbott Laboratories, was developed from a pilot program produced by the PCRI at the 2005 National Conference on Prostate Cancer in Washington D.C. The meeting was structured to allow advanced PC patients an opportunity to discuss the latest



PCRI's Town Hall Meeting in Los Angeles drew advanced PC patients from as far away as the Midwest, the Southeast, and even Brazil, to hear much needed information directly from PC physicians.

advances in treatment with a panel of experts.

"With the advent of PSA testing in the 1980s, the incidence of advanced PC has decreased precipitously," explains the PCRI's Program Director, Harry Pinchot, who has organized both Town Hall meetings. "Even so, our ability to prevent or delay advanced PC progression is still limited. However, progress is being made, and the benefits of secondary hormonal therapies, chemotherapy,

and biologic, immune, and other novel therapies are being further understood and investigated.

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Chemotherapy for Prostate Cancer: Why Bother? (Page 2)

Brad Guess, PA-C, Executive Director, PCRI

Until recently, the use of chemotherapy for men with advanced prostate cancer was considered to be of no benefit and too toxic. However, this thinking has changed, based on the results of two large randomized clinical trials, which concluded that the chemotherapy drug docetaxel (Taxotere®) offers patients 2 to 2½ months longer survival compared to the conventional chemotherapy drug mitoxantrone. After reading this, some medical practitioners and patients may conclude "why bother for 2 to 2½ more months of life?" In this article the author warns that "this conclusion should be avoided, since survival analysis is very easily misinterpreted, often in the direction of underestimating hope." He concludes that "a closer look at survival analysis and the other benefits incurred by chemotherapy, such as a reduction in pain

and improved quality of life, necessitate the need for considering chemotherapy in men with advanced prostate cancer. The use of neoadjuvant or adjuvant chemotherapy in high-risk, PSA relapse and HRPC patients also needs to be considered, based on early clinical studies and its use in other solid tumors. Lastly, the combination of chemotherapy with novel cancer agents is a logical and exciting next step in the development of better treatment for men with advanced prostate cancer."

The Changing Role of the Urological Oncologist (Page 4)

Ralph deVere White, MD and Arline Detich, PhD

This article posits a significant change in the treatment of prostate cancer. The authors state that "Prostate Cancer is a disease that until recently was left to urologists and radiation oncologists to manage. This is no longer true." They point out that most laboratory-based prostate cancer is no

longer directed by urologists. If a urologist wants to become an independent, competitive researcher, he or she must probably devote a minimum of three or four days a week to laboratory research after spending years as a fellow. It is nearly impossible to do this while continuing to develop surgical skills. The authors suggest a number of alternative options to overcome this obstacle, and they conclude by stating that as specialists, urologists clearly face choices. At the basic research level, they cannot compete in a meaningful way. They have to compete at the level of correlative, translational, and clinical science. Since they are relatively few in number, there must be total involvement of both academic and community urologists for this to be meaningful. If urologists continue to focus merely on the type of incision to be made, or whether it is best to remove prostates surgically or to radiate them, they will continue to become marginalized in finding better treatments for our patients.

Chemotherapy for Prostate Cancer: “Why Bother?”

by Brad W. Guess, PA-C Executive Director, PCRI

Introduction

I recently had the opportunity to sit in on a prostate cancer (PC) journal club meeting attended by PC experts from a multitude of medical specialties. The focus of this meeting was the use of chemotherapy in PC, specifically docetaxel (Taxotere®), a drug recently approved by the Food and Drug Administration (FDA) for metastatic hormone-refractory prostate cancer. One participant at the meeting, an eleven year advanced PC survivor, patient advocate and lay expert, raised an important and challenging question about the results of the two large phase III clinical trials that led the FDA to approve the drug.

“I speak to guys with advanced disease every day,” he said. “They read these studies, and they say to me, ‘You’ve gotta be kidding me; if I do chemotherapy I’m going to live 2 to 2½ months longer. Why bother?’” In this article, I will attempt to answer this question, as well as discuss the use of docetaxel in earlier stages of PC, and introduce some novel drugs in clinical development for advanced PC, many of which are being combined with chemotherapy.

The First Chemotherapy Drug to Increase Survival in Metastatic Hormone-Refractory Prostate Cancer

Prior to the approval of docetaxel in May 2004, the only other FDA-approved chemotherapy for advanced PC was mitoxantrone. Even though mitoxantrone showed no evidence of a survival benefit in two large randomized phase III clinical trials (in 1996 and

1999), the FDA approved it because it demonstrated that approximately one-third of symptomatic patients experienced improvement in pain.^{1,2}

Then in October 2004, the *New England Journal of Medicine* reported on two studies using docetaxel in advanced PC. The first was TAX 327, which randomized 1006 men to docetaxel plus prednisone or mitoxantrone plus prednisone. After completion of the study, the median survival of all patients treated with docetaxel was 18.2 months compared with 16.4 months for those treated with mitoxantrone.³ The second study was SWOG 9916, which randomized 770 men to docetaxel and estramustine compared with mitoxantrone and prednisone. In this study, overall survival favored docetaxel (18.9 months compared with 16 months for mitoxantrone).⁴

Why Bother?

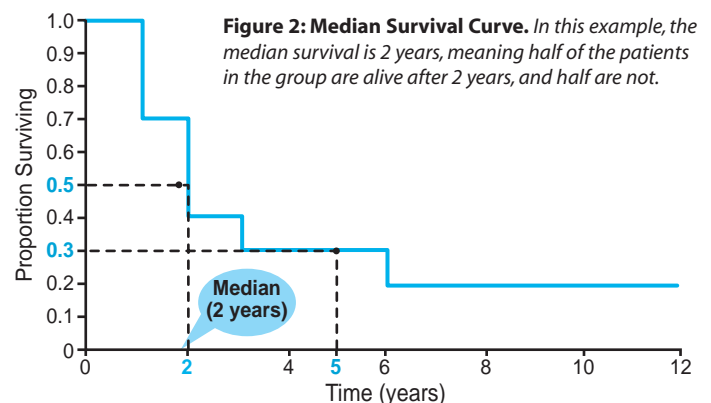
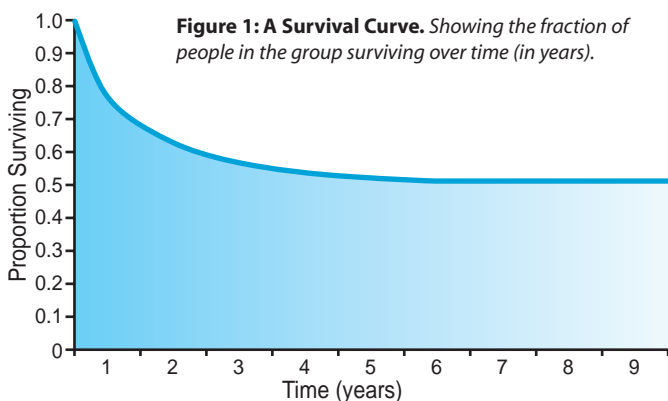
Mark Twain’s (sometimes attributed to Disraeli) famous quip about the practice of lying, identified three types, each worse than the one before – lies, damned lies, and statistics. “Survival analysis” with the production of “survival curves” (see Figure 1) is the most common statistical method used to determine the effectiveness of a new drug in cancer patients, for the purposes of FDA approval. This type of analysis compares the “median survival” of one group of patients treated with a new drug or treatment to the median survival of those patients who were treated with a conventional drug (or placebo if no conventional drug exists). Median survival (see Figure 2) is the time at which half of the patients have died, or to say more optimistically, the time at which the per-

centage surviving is 50%. In the two previously mentioned docetaxel studies, it was an increase in the median survival of men treated with docetaxel compared to the conventional drug mitoxantrone that led to FDA approval. Considering that docetaxel compared to mitoxantrone (a treatment which offered no improvement in survival) increased median survival by only 2 to 2½ months, it is no surprise that many medical practitioners and informed patients ask the question “Why bother for 2 to 2½ more months?” However, this conclusion should be avoided, since survival analysis is very easily misinterpreted, often in the direction of underestimating hope.

Survival Analysis

Several points should be made about the survival analysis in these studies. First, both studies crossed over (to docetaxel) men who initially received mitoxantrone and did not respond. In other words, some men who were treated with mitoxantrone eventually received docetaxel (the better treatment), but only after a considerable delay. This cross over skewed the differences in survival between the two treatment groups by improving the survival of some of the mitoxantrone treated men.

Second, survival analysis that is done by comparing median survival of two groups obscures an improvement in survival when less than half the men treated have their lives prolonged. This is because such analysis includes all patients, not only those who respond, but also those that do not respond. Additionally, the survival of any one individual may be much longer (in some cases sev-



eral years) than that of the median of the study population.

The third point to consider is that median survival analysis says little about patients on the right side of the survival curve (the men who respond to treatment, despite a poor prognosis). In a study of the data of 217,573 patients with breast, colorectal, lung, and prostate cancer, Kato et al analyzed **conditional median survival**.⁵ Conditional median survival can be defined as a survival rate conditioned on having survived x years (for example, a 5-year rate for individuals having already survived 2.5-years). To say it another way, the prognosis of people with common cancers who had metastatic disease at the time of their initial diagnosis changed as a result of their continued survival. The existence of a small group of survivors far past the “median” point, even in cancers with a dire prognosis such as advanced PC, should provide real hope even when the prognosis is bleak.

Lastly, and on a more practical note, when men who are not a part of a clinical trial are treated with chemotherapy and are not responding, their treatment is quickly changed, and they go on to other potentially beneficial treatments, which may also have the potential to extend life. These facts are not taken into consideration in survival analyses. (For a much more comprehensive and articulate handling of the statistics of survival and other related topics, see Steve Dunn’s excellent website www.cancerguide.org.)

A Closer Look at the Benefits of Docetaxel for Men with Advanced Prostate Cancer

In addition to survival, two other important benefits (which should not be overlooked) were seen in men treated with docetaxel. The first benefit was that pain was reduced more frequently among men receiving docetaxel compared to those treated with mitoxantrone. Anyone who has experienced or taken care of a man with bone pain from advanced PC understands the significance of this benefit. The second benefit seen with the use of docetaxel compared to mitoxantrone in men with advanced PC, was an improvement in quality of life. The greatest benefit in

the docetaxel group with regard to quality of life was in the area of weight loss, appetite, pain, physical comfort, and bowel and genitourinary function. It is well known that if untreated, advancing PC will ruin the quality of life of a man, often for many months or even years, before he succumbs.

What About Chemotherapy in Earlier Stages of PC?

With the benefit of a docetaxel-based therapy in advanced PC now well established, its potential role in earlier-stage PC becomes a much more important question. There are several groups of earlier-stage PC patients to be considered. The first group is men who have been newly diagnosed with “high-risk” PC. Generally speaking, high-risk PC is defined as having a PSA > 20 or a Gleason score of 8 or higher or a Clinical Stage of T3 or higher determined by a digital rectal exam (tumor is already extending outside of the prostate gland). Men with high-risk PC have a high chance (usually > 50%) of disease recurrence even after definitive local therapy such as surgery, radiation or cryotherapy. The primary reason for this is the presence of microscopic disease outside the prostate and beyond the reach of the local prostate treatment. Clinicians and patients are now better able to identify those men at high risk through the use of nomograms (see Dr. Glenn Tisman’s article “Using Nomograms to Predict PC Treatment Outcomes” in *PCRI Insights* Nov 2005 Vol. 8, No. 4).

The use of chemotherapy in high-risk patients takes place in a “neoadjuvant” or “adjuvant” setting. (Neoadjuvant chemotherapy is the use of chemotherapy prior to any other treatment such as surgery or radiation. Adjuvant chemotherapy takes place at the same time as one or multiple other therapies.) Recently, pre-clinical data evaluating the optimal timing and combination of chemotherapy and hormone blockade supports the use of simultaneous therapy.⁶ Numerous small phase II trials using neoadjuvant and adjuvant chemotherapy in men with high-risk PC have been performed, with encouraging results.⁷ A small but interesting trial, and one which makes an argument for early chemotherapy in high-risk men, was performed by Wang et al.⁸ They randomly

assigned 96 men with high-risk PC or advanced metastatic PC to mitoxantrone plus combined hormone blockade (CHB) versus CHB alone. In the 38 patients without metastatic disease treated with mitoxantrone and CHB, the median survival was significantly better (80 months compared to 36 months for patients treated with CHB alone). In contrast, no survival advantage was seen with the combination of mitoxantrone and CHB in men with metastatic disease. Several large randomized phase III clinical trials are ongoing or are planned and should give us better answers to the question of whether adding chemotherapy to the treatment of men with high-risk PC is effective.

The second study in which men are being treated with early chemotherapy focuses on men with a rising PSA after local therapy (commonly called a “PSA relapse”), especially men with a fast PSA doubling time (< 6 months), and risk of shortened survival.⁹ Hussain et al studied 39 men (7 with clinical metastasis and 32 without) with a rising PSA of > 4 ng/mL after surgery or radiation, treated with docetaxel followed by CHB for 12-20 months. The most interesting finding in the study was that five of the men treated with the combination maintained a low and stable PSA at 0.1ng/mL for a median of 18.9 months after therapy. Three of these five men had soft tissue metastasis at entry but remained in a complete remission.¹⁰

A third group consist of men with hormone-refractory prostate cancer (HRPC). HRPC is commonly defined as a rising PSA despite castrate (≤ 20 ng/dL) levels of testosterone, but no visible cancer outside the prostate, such as in the bones or lymph nodes. Men who develop HRPC have a high likelihood of developing visible metastatic disease (in approximately nine months, according to one analysis¹¹), especially if they do not achieve a PSA nadir of less than 0.05 ng/mL anytime after the initiation of CHB.¹² The argument that chemotherapy should be utilized as soon as HRPC is diagnosed is suggested by experience and proven benefits reported in other solid tumors such as breast and colorectal cancer, where adjuvant chemotherapy is considered standard.¹³

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The Changing Role of the Urological Oncologist

Ralph deVere White, MD and Arline Deitch, PhD UC Davis Cancer Center, Department of Urology

The future role of the urological oncologist in managing urological cancer patients is uncertain. Formerly, these specialists played major roles in making treatment decisions for patients with urological cancers. However, we are in the midst of a paradigm shift affecting cancer treatment options for these patients. I believe that if the urological community does not support treatment changes, the future will see these diseases largely being managed by medical oncologists.

For testicular cancer, largely due to the work of Drs. Donohue, Skinner and the group at Memorial Sloan Kettering, integrated care was established between the urologist and the medical oncologist, with the surgeon playing a major role in patient management. This remains true in the United States today. In Europe, however, this disease has become the province of the medical oncologist, a fate that might be just around the corner in the U.S. Clearly, for patients having residual tumor masses after chemotherapy, surgery remains a necessary part of treatment. However, for patients for whom there is a legitimate choice among observation, chemotherapy and surgery, who will drive these treatment choices? Will it be the urological oncologist or the medical oncologist? In Europe, the answer definitely is the medical oncologist.

Two decades ago, surgery was the only choice of treatment for kidney cancer. The use of CT scans and ultrasound in the initial workup of anyone presenting with abdominal pain had not yet arrived. Chemo- and immuno-therapy were used solely for patients having metastatic disease. The basic tenet was that if the contralateral kidney was normal, the tumor-bearing kidney was removed, regardless of the size of the tumor. Today, treatment options for this disease have changed. Open surgery has given way to laparoscopic surgery, and partial removal of a tumor-bearing kidney is carried out when possible. As smaller tumors are detected, there are continuing efforts to treat them percutaneously utilizing cryotherapy or radio frequency ablation. There is a move by

interventional radiologists to take over the management of these cases. Since our interventional colleagues are in competition for control of vascular cases, they will look for other outlets including kidney cancer cases.

Among urological cancers, the treatment of bladder cancer has changed the least during the past two decades. The standard therapy for muscle-invasive disease remains

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surgical excision with or without neo-adjuvant or adjuvant chemotherapy. On the other hand, treatment of prostate cancer (PC) has undergone the most changes. PC is a disease that until recently was left to urologists and radiation oncologists to manage. This is no longer true. With the advent of the PSA era, PC received a large amount of publicity. This was based on our ability to detect this cancer earlier and on our assertions that early treatment will improve patient survival.

Since the response of these tumors to chemotherapy was extremely poor, the importance of early detection and treatment was obvious. In cases of advanced PC, tumor response to chemotherapy was so poor that urologists often retained management of these patients even when they failed androgen deprivation. They felt that chemotherapy merely decreased quality of life without giving meaningful palliation or increased longevity. Moreover, busy medical oncologists were not particularly anxious to treat sick, elderly patients with toxic agents that resulted in extremely poor response rates.

In many ways, the changing role of the medical oncologist is the result of the public attention now given to PC. Much publicity followed Michael Milken's treatment for his PC and his subsequent creation of the CapCure Foundation for funding research in this field. Attention to PC also increased as the result of the publicity given to Senator Robert Dole's PC and the erectile dysfunction

he experienced after treatment. Both issues were discussed freely by Senator Dole in multiple appearances in person and on television. He also has appeared in many advertisements on television and in the press. With increased public awareness of PC and with the help of the CapCure Foundation, the National Cancer Institute, and the Department of Defense, money rapidly became available for basic, clinical and translational research in PC. This has greatly benefited our patients. Hope for finding a cure for PC is now equal to that for any other type of solid tumor.

Dwindling Research Opportunities

We must recognize, however, that most laboratory-based PC research is no longer directed by urologists. It has become more and more difficult for urologists to compete for basic science R01 funding while remaining clinically active. This funding problem is general and is not specific to urology. In fact, we are doing as well as many other surgical subspecialties and even better than many.

With decreased funding, increased competition for grant money and decreased clinical reimbursement, it is nearly impossible for a young urological surgeon to develop an independent laboratory-based research program. If a urologist wants to become an independent, competitive researcher, he or she must probably devote a minimum of three or four days a week to laboratory research after spending years as a fellow. It is nearly impossible to do this while continuing to develop surgical skills.

A better option would be to follow a different path, one that medical oncologists have been very successful in adopting. Young urological oncologists can apply for career development awards. Rather than trying to personally acquire the skills necessary to

Most laboratory-based prostate cancer research is no longer directed by urologists.

seek basic science funding, they can spend a year or more participating in laboratory research in order to gain a firm understanding and empathy for what occurs in carrying out basic research. They can participate in NIH-based K30 grants to understand all aspects of clinical and translational research. They can join national clinical trial groups and become involved in integrated institutional tumor boards. Using NIH-based translational research initiatives related to clinical trials, they can become funded and cooperate with a Cancer Center's shared resource program that can perform the necessary basic science research. These activities can be supported through NIH-sponsored R21 or R01 grants. With multiple private investigators now being permitted to head NIH-based R01 grants, there will be even further opportunities for clinical scientists who do not head their own laboratories to participate in basic research. If urologists do not follow these avenues, we are in danger of becoming marginalized in determining future research directions and the management of urological diseases.

At the clinical level, medical oncologists have done a superb job of advertising to the public that they are in charge of cancer patients. It is they whom patients see prior to making the decisions about how their cancers will be treated, regardless of who will deliver the treatment. Medical oncologists greatly outnumber urological oncologists, so if we accept a passive role in this decision-making process, we are in danger of becoming purely surgical technicians.

While we tend to discuss issues that interest urologists, these issues do not appear to capture public attention. For instance, we often refer to the truly remarkable 15-year survival of many patients treated for localized PC without capturing much lay attention. Yet medical oncologists have received tremendous publicity for the fact that after 40 years of using different chemotherapeutic regimens to treat hormonally-resistant PC, they now report that docetaxel regimes offer these patients two to two and a half months longer life compared to using mitozantrone

and prednisone. Considering that in previous studies mitozantrone offered no survival advantage over the use of a placebo, this is tantamount to saying that the docetaxel regime is better than a placebo by a median survival of two to two and half months.

While we can be pleased that over the past two decades there is increased public awareness of urological cancers and increased funding for research in this field, we must recognize the fact that most of the basic science and an ever-increasing amount of the clinical research is being conducted by non-urologists. Clearly, without a change in our approach, we will lose further ground in the years to come.

Prostate Cancer Issues

A discussion of PC will illustrate some of the issues facing us as a profession. With the advent of PSA testing, the number of patients being diagnosed with early-stage PC has increased and may continue to increase. In the 1980s, stage T1c cancers only accounted for approximately 10% of the prostate cancers being diagnosed. Now, close to 90% of diagnosed cases are stage T1c. The adoption of widespread PSA testing has resulted in stage migration. Decreased numbers of patients now have positive lymph nodes or positive surgical margins, and there is a concomitant decrease in the percentage of those having metastases to bone.

The outcome for prostate surgery was greatly enhanced by the introduction of nerve-sparing radical retropubic prostatectomy. Public interest has also been stirred by the adoption of robotic devices during surgery. In the past, every PC meeting held a major debate between those advocating surgery and those endorsing radiation therapy for treatment of localized PC. Today, these debates have shifted to discussing whether the prostate should be removed by open incision or by endoscopy. Understandably, there are also concerns about the appropriateness of the increasing number of operations being performed for low-volume PC.

Questions are also being raised concerning whether all surgeons perform the operation equally well. Behind debates centering on details of surgical performance is this underlying thought: if one could guarantee the best possible outcome with minimal side effects, it would make this operation more acceptable to patients who may not wish to undergo surgery.

Selecting a Surgeon

So, the question is, do all urologists perform this operation equally well? If it were only a matter of the urologists having to perform a certain number of surgeries and passing the appropriate qualifying tests, the answer would be yes. However, we know that within the urological community there are certain surgical "stars" who outperform the large majority. In an analogy to professional golf, we know that to get on a PGA tour requires a lot of practice and qualifying tests from all the contestants, yet only one player wins on a Sunday.

Since there are no longer any bad urology programs in this country, and since urologists also go through much practice and qualifying tests, we have to recognize that each newly-qualified urologist brings different technical skills to surgical practice. Therefore, we can ask whether all urologists should be permitted to perform radical prostate surgery. If not, how can we judge fairly who should and who should not? One frequently made assumption is that **high-volume hospitals** have better results. While this appears to be intuitively correct, it is evidently not always true. Ellison et al¹ recently reported outcomes for 22,635 men who had radical retropubic prostatectomies performed at hospitals hav-

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There were no differences in the overall ten-year survival or in the ten-year cause-specific survival among prostatectomy patients in three groups of hospitals.

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Table 1. Selected Novel New Agents in Early Clinical Trials
(many in combination with chemotherapy) **for Metastatic Hormone Refractory Prostate Cancer**

Target	Agent(s)
Microtubule	Epotholones, halichondrin, B analog, SB 715992
VEGF, VEGFR, Integrine	Bevacizumab, EMD121974, PTK787, SU11248
Histone deacetylase	SAHA, aplidine
EGFR, PDGF, HER-2	Sorefanib, imatinib, trastuzumab
AKT, mTOR	CCI779, RAD001
Endothelin receptor	Atrasentan
Immune modulation	Vaccines (GVAX, APC8105), lenalidomide, Revamid, Prostavac-VF, Provenge
Apoptotic pathway	Gossypol, Bcl-2 antisense, anti-clusterin
Proteasome Inhibition	bortezomib
Antiangiogenic	thalidomide

Combining Chemotherapy with Novel Agents in Advanced Prostate Cancer

An important consideration when deciding on treatment for metastatic HRPC is the heterogeneity of the disease. Heterogeneity in advanced PC simply means that there are several or multiple forms or clones of PC cells existing within one patient. Therefore, the combination of chemotherapy with a novel or innovative agent takes advantage of our evolving understanding of advanced PC biology.

Table 1 contains a list of novel agents being studied individually or in combination with docetaxel in advanced PC. One of the more exciting of these novel agents for advanced PC is bevacizumab (Avastin®) which has already been approved by the FDA for kidney cancer. Bevacizumab is an anti-vascular endothelial growth factor (VEGF) antibody, and works by inhibiting the blood supply to tumors (antiangiogenesis). In a phase II study of 79 men with advanced PC, the combination of docetaxel, estramustine and bevacizumab resulted in a PSA decline in 81% of patients, a median time to disease progression of 9.7 months, and an overall median survival of 21 months.¹⁴

Another antiangiogenic agent, thalidomide, has been evaluated in phase II studies both alone and in combination with docetaxel in men with advanced PC.¹⁵ When thalidomide was combined with docetaxel, the response rates were better than with doc-

etaxel alone, and survival was improved. Recently, the use of the triple combination of docetaxel, thalidomide and bevacizumab in advanced PC was reported.¹⁶ Early results of this phase II trial of 60 patients show PSA response rates of 86% and significant improvement in measurable disease in many of the patients.

Another novel agent, DN-101, a high dose form of calcitriol, which is a biologically active form of vitamin D, has shown encouraging results when combined with docetaxel in advanced PC. Beer et al recently reported early results from the AIPC Study of Calcitriol Enhancing Taxotere (ASCENT).¹⁷ These results suggest an improved survival advantage with the combination versus docetaxel alone; however analysis is ongoing and larger studies are planned for the future. Interestingly, the addition of DN-101 appears to protect against side effects of chemotherapy, such as a loss of energy, gastrointestinal and thromboembolic events. (A full discussion of the side effects of chemotherapy will be presented in an article in an upcoming issue of *Insights*.)

Radiopharmaceutical agents, namely strontium-89 and samarium-159 have been shown to relieve bone pain in men with metastatic PC.^{18,19} (This was described in Oliver Sartor's article, "Newer Concepts in the Treatment of HRPC with Bone Metastases" in PCRI *Insights* May 2005 Vol. 8, No. 2.) It is thought that by releasing short-range radiation, these agents may kill PC cells in bone, leading to relief of pain. Data from a

small phase I study combining samarium and docetaxel has shown impressive results with a decrease in PSA of > 80% in 4 of 6 patients.²⁰ Further studies are ongoing.

Conclusion

With the benefit of docetaxel-based therapy in advanced PC now well established, more men are likely to be offered chemotherapy in advanced disease. The conclusion that the only benefit one can expect is 2 to 2½ months increased median survival is deceptive. This small time period is a watered-down average that includes all the men who did not respond as well as men who were treated with mitoxantrone but subsequently were treated with docetaxel. Other benefits received by chemotherapy in this group of men, such as a reduction in pain and general overall improved quality of life also needs to be pointed out. In all likelihood the use of neoadjuvant or adjuvant chemotherapy in high-risk, PSA relapse and HRPC patients is going to be utilized with increased frequency. Lastly, the combination of docetaxel with novel cancer agents is a logical extension, and exciting responses are occurring that in the past would have never been thought possible. ■

References

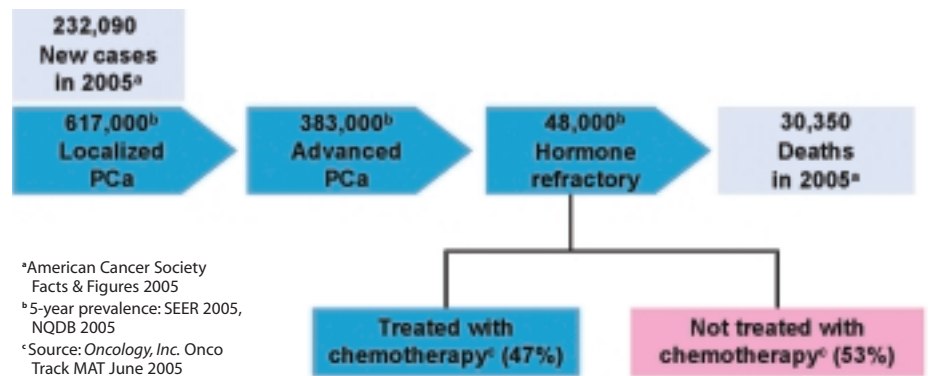
1. Tannock IF, et al: Chemotherapy with mitoxantrone plus prednisone or prednisone alone for symptomatic hormone-resistant prostate cancer: A Canadian randomized trial with palliative endpoint. *J Clin Oncol* 14:1756-1764, 1996.
2. Kantoff PW, et al: Hydrocortisone with or without mitoxantrone in hormone-refractory prostate cancer: results of the Cancer and Leukemia Group B 9182 study. *J Clin Oncol* 17:2506-2513, 1999.
3. Tannock IF, et al: Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. *N Engl J Med* 351:1502-1512, 2004.
4. Petrylak DP, et al: Docetaxel and estramustine compared with mitoxantrone and prednisone for advanced refractory prostate cancer. *N Engl J Med* 351:1513-1520, 2004.
5. Kato I, et al: Conditional median survival of patients with advanced carcinoma: Surveillance, epidemiology, and end results data. *Cancer* 92(8):2211-19, 2001.
6. Eigel B, et al: Timing is everything: Pre-clinical evidence supporting simultaneous rather than sequential chemo-hormonal therapy for prostate cancer. *Clin Cancer Res* 11:4905-4911, 2005.
7. Gleave M, et al: High-Risk localized prostate cancer: A case for early chemotherapy. *J Clin Oncol* 23(32):8186-8191, 2005.
8. Wang J, et al: Adjuvant mitoxantrone chemotherapy in advanced prostate cancer. *BJU Int* 86:675-680, 2000.
9. D'Amico AV, et al: Prostate specific antigen failure and mortality. *Prostate Cancer Sym (suppl; abstr 204:195)* 2006.
10. Hussain A, et al: Docetaxel followed by hormone therapy in men experiencing increasing prostate-specific antigen after primary local treatment for prostate cancer. *J Clin Oncol* 23(12):2789-2796, 2005.

References continued on page 9

Raising a Voice for Advanced Prostate Cancer

By Jim O'Hara PCRI Educational Facilitator

Awareness of prostate cancer (PC) and early detection of the disease are increasing but most of the media attention ignores the facts graphically shown in the adjacent figure. More than 30,000 men in the United States died of this disease during 2005, and there are currently 48,000 men dealing with hormone-refractory prostate cancer (HRPC). For these men, there are few treatment options available. Even treatments in the late stages of development offer little measure of hope. The outlook appears even darker when you consider the impending impact of the "baby-boomers."



“We are vastly under-treating advanced prostate cancer. Let’s get all of the drugs that are out there for advanced cancers and try to find out on a group of patients, if there is anything here to give them hope.”

The combination of limited research money, low public awareness, and an ultra-conservative approval process by the FDA has contributed to effectively shutting down the pipeline of FDA-approved drugs targeted for advanced PC where the need for new treatments is most dire. Clearly something should be done about these interrelated fund-

ing, public awareness, and drug approval limitations. And as the HIV/AIDS community has proved, something can be done. Recently, a promising step forward was made when leaders of several PC nonprofits convened in an unprecedented roundtable meeting to discuss opportunities for our community to better work together and to identify core issues in “advanced prostate cancer.”

The **Advanced Prostate Cancer Advocacy Meeting**, sponsored by an unrestricted grant from Abbott Laboratories, was held February 23, 2006 in San Francisco before the *2006 Prostate Cancer Symposium*. There were attendees from organizations including the **Prostate Cancer Research Institute (PCRI)**, UsTOO International, Prostate Cancer Foundation, The Prostate

Net, National Alliance of State Prostate Cancer Coalitions, California Prostate Cancer Coalition, Prostate Cancer Coalition of Michigan, and American Prostate Health Initiative, plus PC experts Dr. Donald Coffey and Dr. Stephen B. Strum.

The meeting was structured to first listen to advocates for other diseases describe advocacy efforts that have significantly helped improve patient care. Marty Delaney and Brenda Lein of the HIV/AIDS advocacy organization **Project Inform** and Ellen Coleman of **CancerCare** discussed best practices and key achievements. They shared some key lessons learned in their advocacy movements with HIV/AIDS, breast cancer, lung cancer and multiple myeloma. For example:

- ✓ **Organizations must work together** in a coordinated effort and agree on specific direction. “The enemy is the disease, not each other.”
- ✓ **Partnerships are important**, not only with each other, but also with government (NIH, NCI, FDA, Congress and the Administration), with academia, the pharmaceutical industry, the media and the public. Relationships must be developed with the key people to get results.
- ✓ **Advocacy requires sponsors** to provide funds to support paid professionals, activism and media campaigns.
- ✓ **There is a need for activism** to build grass roots support and gain media attention to the message and get it on the evening news.

- ✓ **Advanced PC patients and their caregivers must be convinced that they deserve to receive better options.**

Our guest advocates also suggested ways to make PC advocacy successful:

- ✓ **Men with advanced PC and their loved ones must be heavily involved** in PC advocacy issues.
- ✓ **Advocates must be recruited and trained** in both advocacy and the science of the disease.
- ✓ **Advocates must be members of the committees** that review new developments. They must stay on top of the latest research to be credible.
- ✓ **Advocates must seek out opportunities** to be heard at professional and scientific conferences.

Next we heard from a few of our own experts regarding current issues facing PC.

- ✓ For men, PC remains second only to lung cancer in deaths and second to skin cancer in incidence (30,350 deaths and 232,090 new cases for 2005).
- ✓ While media attention has increased, most of the stories, especially in the “big” media, focus on early detection and local treatment options. This gives the public the impression that PC is not a life-threatening illness. **“The world does not even know that advanced prostate cancer exists.”**

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ing case volumes ranging from low to high. In this study, low case volume was defined as 1 to 33 cases, moderate case volumes as 34 to 61 cases and high case volumes as over 103 cases performed during a four year period. There were no differences in the overall ten-year survival or in the ten-year cause-specific survival among prostatectomy patients in these three groups of hospitals. Furthermore, there were only minor differences in the number of patients in these groups who received adjuvant therapy for recurrent PC. This was 37% for patients at low case volume hospitals and 33% for patients at high-volume centers. I agree with the author's conclusion that these data do not support restricting this surgical procedure to high-volume centers.

Ellison et al suggested that it might be reasonable to recommend **minimum case volume** standards to urologists who wish to perform radical prostatectomies. This issue was also discussed by Bianco and his colleagues² who reported on 159 surgeons, all considered by them to be high-volume surgeons. Between them, these surgeons performed 5,238 radical retropubic prostatectomies in four years. By the criterion adopted by Bianco et al, a surgeon doing four to five cases a year was classified as a high volume-surgeon. It is hard to believe that if a surgeon does three radical prostatectomies a year rather than four, this will lead to a difference

might consider using robotic surgery and performing *simulated* radical prostatectomies, much as airline pilots now undergo testing using flight simulators.

Surgery vs. Secondary Prevention

While the debate flourishes, increasing numbers of PC patients are being diagnosed with less aggressive disease. If we cannot currently select surgeons on the basis of their case loads, can we at least identify the patients with aggressive tumors that should be treated with immediate intervention, be it by surgery or radiation therapy? Do the results of randomized clinical trials permit us to justify our choice of therapy? Unfortunately, for localized PC in this country, the answer is no. Recently, the Southwest Oncology Group (SWOG) spent four years putting together a trial to compare radiation therapy and radical prostatectomy for localized PC. During 18 months, only four patients were enrolled in this trial, and it was therefore closed. The only slight consolation we have is that radiation therapists were as reluctant as urologists to randomize patients to this trial. A recently completed Scandinavian trial supported surgery over watchful waiting for localized PC. This would seem to be helpful in eliminating one treatment option, but the Scandinavian trial was conducted in a patient group that had far more advanced disease at presentation than we see today in United States. Ten percent of the Scandinavian patients had stage T1c disease as compared to close to 90% of the patients presenting with this disease stage in the United States. It is therefore difficult to extrapolate these results to our group of patients.³

Urologists need to take the lead in addressing these questions. The mortality from PC has dropped over the past ten years due to PSA screening. If we take the position that patients should continue PSA screening in every case where PC is found, and if we agree that definitive therapy, be it radiation therapy or surgery, should be given, I believe that we will lose our leadership role in managing these patients. We can legitimately

argue that in the appropriate cases, patients should be screened with PSA tests so that these cancers can be detected. However, once diagnosed, we must find a way to determine which cancers truly need immediate intervention. We also need to be able to select the appropriate treatment for individual patients based on tumor characteristics and on clinical factors.

There are now studies in a number of parts of the world looking at what can be accomplished using primary prevention of PC or, after its diagnosis, secondary prevention to reduce the need for surgery or radiation therapy. Secondary prevention would in some cases postpone treatment indefinitely; in other cases it would safely postpone therapy so patients would only have to undergo the expense and side effects of treatment when it was clear that their tumors posed a more immediate threat. The obvious problem is that the methods available to make this determination are not perfect. We currently rely on PSA levels and doubling time, Gleason grading and disease volume at diagnosis for these decisions. Admittedly, these are imperfect predictors. Our future studies need to be directed at trying to find better serum markers as

well as molecular markers of tumor biopsies to answer these questions. If, however, all these patients receive the same treatment, whether radical prostatectomy or radiation therapy, it will be impossible to evaluate the true benefits of these markers. Furthermore, patients would certainly appreciate knowing the reliability of any new markers before they receive definitive treatment rather than afterward. The only way to accomplish this is by placing our patients on well-controlled randomized clinical trials.

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These studies suggest that judgments about who should do this operation will probably have to be made on an individual basis.

in outcome. The authors examined modeling to try and predict surgical outcome and this did not work. For example, while the model predicted that the incontinence rate should be negligible for a given group of 11 surgeons, it was in fact 40%. Bianco et al expressed their surprise that they found considerable variation in outcome among high-volume surgeons. These studies suggest that judgments about who should do this operation will probably have to be made on an individual basis. Therefore, to test for competence we

continued at right

- ✓ Older advanced PC patients tend to accept their disease and have proven to be poor advocates for their own cause, while men diagnosed at a younger age may keep their disease secret because it could put their careers in jeopardy.
- ✓ There has not been a major new treatment modality for advanced PC in 70 years and there are few options to offer to men who fail to respond to androgen deprivation (hormone) therapy.

Drs. Strum and Coffey both addressed this last point. Dr. Strum reiterated the plea that he and Bill Blair made at the 2005 PCRI National Conference on Prostate Cancer that *“there are a number of things in development or being used for other cancers that look very exciting but have not been made available to men with advanced prostate cancer.”* Dr. Coffey forcefully concurred, stating that *“We are vastly under-treating advanced prostate cancer. Let’s get all of the drugs that are out there for advanced cancers and try to find out on a group of patients, if there is anything here to give them hope.”*

Attendees passionately discussed the current “invisibility” of advanced PC patients, their lack of voice, and the relatively low media coverage the topic currently receives. This roundtable advocacy meeting was an important step toward presenting a more united front on the specific issues facing advanced PC patients. Attendees identified two priority issues:

- ✓ Impacting FDA approval procedures that will lead to a meaningful change in treatments and tools available for advanced PC patients.
- ✓ Raising public and media awareness of the needs of advanced PC patients.

The organizations represented agreed to vigorously pursue these two issues. By far, the greatest task will be to energize the PC patient and caregiver community to carry this advocacy banner forward. *If you would like to join an ad hoc group of advocates in Raising a Voice for Advanced Prostate Cancer, send an email with your name, address and phone number to: raiseavoice@pcri.org.* ■

11. Bianco FJ, et al: Duration of response to androgen deprivation therapy and survival after subsequent biochemical relapse in men initially treated with radical prostatectomy. *J Clin Oncol* 22:394s, (suppl; abstr 4552), 2005.
12. Scholz, et al: Ultra-sensitive PSA nadir on testosterone-inactivating pharmaceutical accurately predicts early prostate cancer progression. *Prostate Cancer Sym* (suppl; abst 40:113), 2006.
13. Ryan CJ, et al: Chemotherapy for hormone-refractory prostate cancer: Now it’s a question of “when?” *J Clin Oncol* 23(32):8242-8246, 2005.
14. Picus J, et al: The use of bevacizumab with docetaxel and estramustine in hormone refractory prostate cancer: Initial results of CALGB 90006. *Proc Am Soc Clin Oncol* (suppl; abst 1578) 2003.
15. Salimchokami M, et al: Combining angiogenesis with cytotoxic chemotherapy enhances PSA response in hormone refractory prostate cancer: a randomized study of weekly docetaxel alone or in combination with thalidomide. *Proc Am Soc Clin Oncol* (suppl; abst 1725) 2003.
16. Ning, YM, et al: A phase II trial of docetaxel, thalidomide, bevacizumab, and prednisone in patients with metastatic androgen-independent prostate cancer. *Prostate Cancer Sym* (suppl; abst 224:205) 2006.
17. Beer TM, et al: “ASCENT: A double-blinded randomized study of DN-101 plus docetaxel vs. placebo plus docetaxel in androgen independent prostate cancer (AIPC)”. *ECCO* (abst 811), 2005.
18. Oosterhof GO, et al: Strontium-89 versus palliative local field radiotherapy in patients with hormonal escaped prostate cancer: A phase III study. *Eur Urol* 44:519-526, 2003.
19. Sartor O, et al: Samarium-153 for treatment of painful bone metastases in hormone-refractory prostate cancer. *Urology* 63:940-945, 2004.
20. Widmark A, et al: Optimizing the time of co-administration of docetaxel and samarium-153 for advanced androgen independent carcinoma of the prostate [abstract]. *Proc Am Soc Clin Oncol* 22:433, 2003.

At the other end of the disease spectrum, it is now accepted that for metastatic disease, docetaxel treatment does offer patients a median of two to two and a half months extra survival time compared to employing a placebo. While it can be argued that this is not a great improvement for patients with metastatic disease, nevertheless it furnishes evidence that docetaxel is an effective agent against PC. It therefore raises the question, would docetaxel be even more effective if it were used **earlier** in high-risk patients? Small clinical trials have already been performed and larger trials are about to be initiated to examine using docetaxel in high-risk patients prior to radical prostatectomy. Another trial using docetaxel for patients having elevated PSA levels after radical prostatectomy is also about to be performed. Since most urological oncologists

do not administer chemotherapy, this will introduce the medical oncologist even earlier into the treatment decision process in PC patients.⁴ Urological oncologists must participate actively in all phases of these trials from conception, to recruitment, to reporting results. Recruitment cannot be left just to major cancer centers. Most PC patients are treated in community hospitals. Therefore, community urologists must remain involved, otherwise the medical oncologists will truly become the arbiters of patient treatment for patients with early PC.

Conclusions

As specialists, urologists clearly face choices. At the basic research level, we cannot compete in a meaningful way. We have to do so at the level of correlative, translational, and clinical science. Since we are

relatively few in number, there must be total involvement of both academic and community urologists for this to be meaningful. If we continue to focus merely on the type of incision to be made, or whether it is best to remove prostates surgically or to radiate them, we will continue to become marginalized in finding better treatments for our patients. ■

References

1. Ellison LM, Trock BJ, Poe NR, et al: The Effect of Hospital Volume on Cancer Control After Radical Prostatectomy. *J Urol* 173: 2094, 2005.
2. Bianco FJ, Reidel ER, Begg CB, et al: Variations Among High Volume Surgeons in the Rate of Complications After Radical Prostatectomy: Further Evidence That Technique Matters. *J Urol* 173: 2099, 2005.
3. Bill-Axelsson A, Holmberg L, Ruutu M, et al: Radical Prostatectomy Versus Watchful Waiting in Early Prostate Cancer. *J Urol* 352: 19, 2005.
4. Carducci MA: What is More Exciting? The Activity of Docetaxel in Early Prostate Cancer or the Successful Collaboration Between Urologists and Medical Oncologists to Complete a Study in Early Prostate Cancer? *J Clin Oncol* 23: 15, 2005.

pants with PSAs approaching 50 ng/mL and Clinical Stage T2 to participate, it is clear that many in the WW group were not good candidates for WW and warranted earlier treatment.

Dr. Leonard Klotz of the University of Toronto described a study with different participant qualifications and quite different results. His study consisted of 299 patients followed with active surveillance with selective delayed intervention. "Patients under age 70 were required to have a PSA less than or equal to 10 and Gleason 6 or less. Patients over 70 were eligible if their PSA was less than 15, and Gleason 7 or less (3+4)... Patients were followed with active surveillance until they met specific criteria defining rapid or clinically significant progression" [PSA doubling time (PSADT) of < 2-3 years]. With a median follow-up of 72 months, 65% off the patients have remained on surveillance. At nine years, only two of the 299 patients have died of PC. Dr. Klotz concluded that "The approach of active surveillance with selective delayed intervention based on PSADT represents a practical compromise between radical therapy for all... and watchful waiting with palliative therapy only."

Dr. Anthony V. D'Amico of the Dana Farber Cancer Institute reported from his study of 206 men with a median age of 75 that "death from prostate cancer was not observed in men who experienced PSADT greater than 12 months and who had salvage [ADT] initiated at a PSA of about 10 ng/mL," and that "in the setting of salvage [ADT] initiation at a PSA level of 10 ng/mL, PSA failure did not shorten survival unless the PSADT was less than six months." He concluded from this study that "Men with a PSADT greater than 12 months could be considered for entry in a prospective randomized study evaluating the effect on survival of initiating [ADT] at a PSA level of 10 ng/mL versus at the time of bone, visceral, or lymph node metastases."

PCRI co-founder Mark Scholz, MD led a team that did a retrospective chart

review of 154 PC patients with negative bone scans and PSAs < 100 who had started on ADT before January 2000. The study team evaluated the predictive value of Gleason score, initial PSA, PSA doubling time, clinical stage, and ultra-sensitive PSA nadir for their ability to predict early progression to bone metastases within 72 months of starting an anti-androgen and an LHRH agonist. The report described the finding that "Ultra-sensitive PSA nadir (≤ 0.5 ng/ml) is a more accurate indicator of early progression to bone metastases (90%) than Gleason score (75%) as well as being more sensitive and specific 72% vs. 37% and 95% vs. 86%, respectively." Moreover, the report concluded, this prognostic information provided by PSA nadir is obtainable within the first eight months of starting ADT in 97% of the patients.

Hormone Refractory Prostate Cancer Treatment

Dr. Cora Sternberg of San Camillo and Florlanini Hospitals in Rome recommended when and how to treat hormone-refractory disease with chemotherapy. She pointed out that both TAX 327 and SWOG 9916 clinical studies demonstrated that a docetaxel regimen can reduce the risk of death by 20-24%. She also mentioned the SPARC trial under way, which will compare satraplatin plus prednisone to prednisone alone. She concluded that "Chemotherapy is clearly indicated for patients who have symptomatic metastatic hormone-refractory prostate cancer. However, only a few small Phase II trials have addressed the optimal sequencing of therapy trials regarding the timing of chemotherapy. Taxotere works after mitoxantrone; mitoxantrone is less effective after docetaxel; and docetaxel is now being combined with several newer biologic and targeted therapeutic agents. Newer approaches and better drugs are clearly needed."

Dr. Maha Hussain of the University of Michigan described a new generation of clinical trials commencing to evaluate a variety of new agents against traditional targets as well as against entirely new biologic

targets as shown below. However, she cautioned, "It is too soon to assess what roles these agents will play in the treatment of hormone-refractory disease, either as single agents or in novel biotherapy-chemotherapy combinations with more traditional cytotoxic agents such as docetaxel. (For a listing of novel agents being studied in advanced PC, see Table 1 of "Chemotherapy for Prostate Cancer" which appears on page 6 of this issue of *Insights*.)

Dr. Eric Small of UC San Francisco presented a talk on the rationale for Immunotherapy in PC to induce antibody and/or T-lymphocyte immune responses targeted at cancer cells. He discussed G-VAX, Provenge and CTLA-4 Blockade-based Immunotherapy, all of which have exciting possibilities. He stated that the overall survival benefit seen with Provenge seemed to be significant. There were other papers covering other targets arising out of epigenetics and modification of proteins. EGFR and HER-2 were discussed as potential therapeutic targets. He concluded that "Most emerging immunotherapeutic approaches have been tested in patients with advanced prostate cancer. These patients, however, possess a high frequency of underlying immune suppression, so testing patients with less advanced disease will be important. Additionally, combining various treatment modalities (e.g. antigen presentation together with an immunostimulatory approach) will likely be necessary."

ASCO Special Lectureship by Dr. Donald Coffey

In his own inimitable way, Dr. Coffey gave a provocative presentation that asked WHY some treatments work – citing Lance Armstrong as an example. The talk ranged widely, and included self-organization, chaos, and how hyperthermia increases the effect of chemotherapy and radiation. Since cancer cells are sensitive to heat, heat can kill them before it damages normal cells. If you direct the hyperthermia directly to the tumor, you can enhance immunology, radical prostatectomy, and chemotherapy. ■

“While treatment options are expanding and new therapies are on the horizon for advanced PC, there remains a large gap between these men, whose need is urgent, and the experts in the field who have extensive first-hand experience and knowledge of the latest advancements. The Town Hall meetings are an attempt to bridge that gap.”

Unique Meeting Format

The Los Angeles Town Hall meeting brought advanced PC patients and their wives into direct contact with urologist Dr. Stanley Brosman (Pacific Urology Institute, Pacific Clinical Research, Santa Monica, CA) and medical oncologists Drs. Mitchell Gross (Louis Warschaw Prostate Cancer Center, Cedars-Sinai Medical Center, Los Angeles, CA), Jacek Pinski (USC/Norris Comprehensive Cancer Center, Los Angeles, CA), Glenn Tisman (Whittier, CA), and Mark Scholz and Richard Lam (Prostate Oncology Specialists, Marina del Rey, CA). Attendees had submitted questions in advance, and physicians on the panel addressed them one by one, thereby supplying the information that was most urgently needed by the attendees. A case study was also presented that offered numerous opportunities for expanding on this information.

In addition, at the opening continental breakfast, the mid-morning break, and the post-meeting luncheon, there was a great deal of one-on-one interaction between the attendees and members of the panel. Attendees, who came from as far away as the Midwest, the Southeast, and even Brazil, responded to this flow of needed information with uniformly favorable comments.

Subsequent Town Hall Meetings Planned

“Since the response to these meetings has been so positive and because of a generous educational grant from Abbott Laboratories, we were encouraged to stage another meeting in Chicago this June,” announced PCRI Executive Director Brad Guess.

As with the successful Los Angeles meeting, the Chicago meeting will provide a forum for men with advanced PC to receive information they may badly need about treatment options, emerging therapies, and

supportive care from experts in this field. Again, pre-screened questions submitted in advance from participants will enable the moderator to facilitate discussion on a wide range of topics and avoid conversations specific to any one individual’s case.

The PCRI videotaped the Los Angeles Town Hall meeting, and DVDs will soon be available and distributed at no charge to individuals and support groups that so request via the PCRI website (www.pcri.org) or the PCRI Helpline (310-743-2110). ■

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Highlights of the 2006 Prostate Cancer Symposium

The 2006 Prostate Cancer Symposium, held in San Francisco February 24-26, was a unique and noteworthy event. Accurately subtitled “A **Multidisciplinary Approach**”, the three-day symposium brought together “leading experts in the fields of urology and medical, radiation, and surgical oncology...with the goal of increasing the understanding of the diagnostic and therapeutic strategies that can be used in the multimodality treatment of patients with prostate cancer.”

In all, 364 abstracts of papers were presented. Of particular interest were the following subjects that attracted abstracts from several speakers.

1. Obesity and Prostate Cancer
2. Cancer Epidemiology, Google, and the promise of a Global Biospecimen Network
3. Active Surveillance (Watchful Waiting)
4. HRPC Treatment

Editor's Note: *In this issue, we have two excellent articles. One, by Dr. Ralph deVere White, is an expose of sorts on the changing role of the urological oncologist in the future treatment of PC. The other, by PCRI Executive Director Brad Guess, is a review of the potential benefits of docetaxel in the treatment of advanced PC. What becomes apparent to the observant reader of both articles is the differing enthusiasm for the use of docetaxel in men with advanced PC, specifically with regard to the interpretation of the survival benefits seen in the two large studies that lead to the FDA approval of docetaxel in advanced PC. This conflict in the interpretation of the benefits of docetaxel for men with advanced PC is not new, and it highlights the importance of collaboration between the urology and oncology communities when deciding on the best treatment for men with advanced PC.*

Obesity and Prostate Cancer

Dr. Peter R. Carroll of the UC San Francisco Comprehensive Cancer Center reported that obese men are more likely to have positive surgical margins but that their risk of biochemical recurrence, second treatment and prostate-related death appeared to be no different than they are for the non-obese group. He also stated that although diet and supplements may reduce the risk of prostate cancer (PC), it is unknown whether they have an effect in men already diagnosed.

Dr. Stephen J. Freedland of the Duke University School of Medicine reported that Duke researchers have found that “the association between obesity and the risk of being diagnosed with prostate cancer is less clear. Whereas some older studies – particularly those out of Europe – suggested obesity was associated with the risk of being diagnosed with prostate cancer, more recent studies from the United States suggest that obesity may actually be associated with a lower risk of being diagnosed with prostate cancer among certain subsets of men.” (There may be other barriers to diagnosis.)

Cancer Epidemiology, Google, and the Promise of a Global Biospecimen Network

Clinton Leaf of *Fortune* magazine expanded on his provocative article, “Deadly Caution”, in which he wrote, “[o]ur regulators have fallen prey to a deadly caution. Simply put, the need for certainty in drug approval is killing people. Excessive caution is delaying the availability of potentially

helpful treatments for cancer, multiple sclerosis, Parkinson's, and a host of other ailments; it's slowing the absorption of new knowledge and diagnostic tools into medical practice; and it's discouraging the pursuit of vaccines and next-generation antibiotics that could save tens of millions of lives.” In his talk at the symposium, he described the need for a data management system for cancer researchers that would link the millions of data points relevant to their work. He concluded that the perfect model for such a global information system already exists: **Google**.

Active Surveillance (Watchful Waiting)

A number of papers were delivered on this subject. In the first, Dr. Anna Bill-Axelsson of the Scandinavian Prostate Cancer Group described a ten-year study from 1989 to 1999. A total of 695 men, 75 or younger, with newly diagnosed PC were randomly assigned to receive either radical prostatectomy (RP) or watchful waiting (WW). Follow-up included PSA testing every six months and a bone scan annually. End points were death, occurrence of distant metastases, and occurrence of local progression. Systemic hormone treatment was recommended if metastases were observed. By the end of 2003, no men in the RP arm had died of PC, compared to 50 in the WW arm. However, since the study allowed partici-

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