WRNMMC Us TOO, Inc.
A PROSTATE CANCER SUPPORT GROUP
SPONSORED BY
WALTER REED NATIONAL MILITARY MEDICAL CENTER
NEWSLETTER

VOLUME 21 **NUMBER 4** **NOVEMBER 2012**

♦ PROSTATE CANCER FACTS AND FIGURES - 2012 ♦

New Cases: An estimated 241,740 new cases of prostate cancer will occur in the US during 2012. For reasons that remain unclear, incidence rates are significantly higher in African Americans than in whites. Overall, incidence rates for prostate cancer have changed substantially since the mid-1980s, in large part reflecting changes in prostate cancer screening with the PSA blood test. Since 2004, incidence rates have decreased by 2.7% per year among men 65 years of age and older and have remained stable among men younger than 65 years.

Deaths. With an estimated 28,170 deaths, prostate cancer is the second-leading cause of cancer death in men. Prostate cancer death rates have been decreasing since the early 1990s in both African Americans and whites, although rates in African Americans remain more than twice as high as those in whites.

Risk Factors. The only well-established risk factors for prostate cancer are increasing age, African ancestry, and family history of the disease. About 60% of all prostate cancer cases are diagnosed in men 65 years of age and older. Recent studies suggest that a diet high in processed meat or dairy foods may be a risk factor, and obesity appears to increase the risk of more aggressive prostate cancer.

Early Detection. At this time there are insufficient data to recommend for or against routine testing for early detection with the PSA test. The American Cancer Society recommends that beginning at age 50, men at average risk for prostate cancer and having a life expectancy of at least 10 years receive information about the potential benefits and known limitations associated with testing in order to make informed decisions about testing.

Treatment. Treatment options vary depending on age, stage, and grade of the cancer, as well as other medical conditions. The grade assigned to the tumor (Gleason score) indicates the likely aggressiveness of the cancer. Surgery, external bean radiation, and brachytherapy may be used to treat early stage disease. Data show similar survival rates for patients with early stage disease with any of these methods, and there is no current evidence supporting a "best" treatment for prostate cancer. Adjuvant hormonal therapy may be indicated in some cases. Hormonal therapy, chemotherapy, radiation, and a combination of these treatments are used to treat more advanced disease. Hormone treatment may control advanced prostate cancer for long periods by shrinking the size or limiting the growth of the cancer. Men whose advanced cancer is not responding to hormones may benefit from the cancer vaccine called Provenge. Another option for these men is Abiraterone, recently approved for the treatment of metastatic disease that is resistant to hormone and chemotherapy.

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♦ *INSIDE THIS ISSUE* ♦

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♦ FROM THE EDITOR'S DESK ♦

We are always looking for ideas for topics for our quarterly meetings held on the first Thursday of February, May, August, and November. Let me know if you have any topics to recommend, or even a specific local speaker whom you have heard elsewhere.

We also solicit first-person articles about your personal experiences in dealing with prostate cancer. If you have an interesting tale to tell, contact me so we can talk about it.

♦ AUGUST SPEAKER'S REMARKS ♦

Our August program featured Dr. Nancy Dawson, an internationally-recognized genitourinary cancer expert who is Director of Clinical Research and attending oncologist at the Lombardi Comprehensive Cancer Center, Georgetown University Hospital. Her topic was "Dealing with Advanced Prostate Cancer" which emphasized the latest developments in medical oncology for the treatment of advanced prostate cancer. A summary of her presentation begins on page 10.

♦ MEETING SCHEDULE FOR NOVEMBER 1, 2012 ♦

Our speaker for Thursday, November 1, 2012, is Clesson E. Turner, MD. Dr. Turner is a graduate of the University of Vermont's College of Medicine. His board certifications include: Diplomate, American Board of Medical Genetics and Fellow, American College of Medical Genetics. **DR. TURNER'S TOPIC IS "FAMILIAL CANCER"** wherein he presents basic genetic considerations regarding cancer, especially prostate cancer. This should be of particular interest to African American men and diagnosed men who have first degree male relatives who may be vulnerable to the disease. Now serving within WRNMMC, Dr. Turner has had two tours of duty in Afghanistan with the 82d Airborne Division. Come join us at 7:00 PM, Thursday, November 1, 2012. Your family members and friends are always welcome.

SEE THE BACK PAGE OF THIS NEWSLETTER FOR IMPORTANT INFORMATION ABOUT THIS MEETING.

Radium-223 Benefits. Radium-223, a novel investigational medication, improves overall survival and time to first skeletal-related event, with a highly favorable safety profile, in castration-resistant prostate cancer (CRPC) patients with bone metastases, according to findings presented at the European Society for Medical Oncology 2012 Congress. Moreover, radium-223 preserves quality of life (QOL), with better functioning and well-being, compared with placebo.

Radium-223 targets bone metastases with high-energy, very short range alpha particles. The interim analysis showed that the drug improved overall survival by 3.6 months with a 30.5% reduction in risk of death. Moreover, radium-223 was better at preserving quality of life compared with placebo.

The updated analysis looked at 921 patients (614 treated with radium-223 chloride and 307 who received placebo). The mean age of the patients was 70 years and 94% were Caucasian. Eligible patients in this trial had previously received or refused docetaxel or were docetaxel-ineligible. Investigators randomized patients to receive radium-223 or a placebo every four weeks for six weeks.

Parker, et al., The Royal Marsden NHS Foundation Trust, Sutton, United Kingdom said that “Given that most men with metastatic CRPC die within a few years, maintaining a good quality of life is extremely important.” (Source: *Renal & Urology News,* October 8, 2012)

Prostate Cancer and Masculinity. Men with prostate cancer often experience erectile dysfunction as a side effect of their treatment, and many find this to be upsetting to the point where it undermines their wellbeing. Moreover, men's distress about ED often does not improve over time — in some men, it worsens. A new study sheds light on the causes of this prolonged distress. While some researchers have thought that the severity of a man's ED is linked with how distressed he feels, the new findings show that regardless of men's ED severity, they are much more likely to be distressed when they feel they've lost their masculinity as a result of treatment.

Not all men experience this feeling of lost masculinity, said study researcher Talia Zaider, a clinical psychologist at Memorial Sloan-Kettering Cancer Center in New York City. But those who do are most at risk of feeling deeply troubled, embarrassed or ashamed about their ED. A feeling of lost masculinity is an aspect of prostate cancer treatment that's not often talked about. "Gender norms work against men," and can keep them from discussing it, she said.

In the study, about one-third of men who had been treated for prostate cancer in the last year reported feeling their masculinity was diminished, and that they had lost a vital part of their identity. A better understanding of how men respond to their sense of a change in their identity could help find better ways to assist men in recovery, the researchers said. More than 9 in 10 prostate cancers are diagnosed in early stages, and these men are likely to live for a long time after treatment. This optimistic outlook on survival means that researchers are looking closely at factors affecting men's quality of life after the treatment.

The researchers interviewed 75 men, whose average age was 60, and who had received prostate cancer treatment in the previous year. The men answered questions about their level of erectile function, how happy they were with their sex lives, the degree to which they felt a loss of masculinity, and the amount of "marital affection" they felt in their relationship (all men in the study were living with a spouse or partner). The men's spouses were also interviewed.

The researchers also found that among men who felt a loss of their masculinity, those in

relationships with a high degree of affection were less likely to feel distress over their ED.

Women do not always understand their husbands' feelings. When the man talks about how upset he is about his loss of erectile function, the wife might say "but you're alive, and we're OK." For men, it's not just about their function — it signifies a loss of who they are. There are feelings of incompleteness, say the researchers.

The findings make a case for involving men's partners in interventions aimed at helping men cope with their distress. The researchers have begun a trial to test the effectiveness of such an intervention (Source: *Journal of Sexual Medicine*, September 18, 2012, via *Zero*, October 15, 2012)

Laser Prostatectomy for BPH On the Rise. Studies suggest that laser prostatectomy may be associated with shorter hospital stays and catheterization time, and a decreased risk of clot retention compared with TURP. Laser prostatectomy use has increased substantially as a treatment for benign prostatic hyperplasia (BPH) at the expense of transurethral resection of the prostate (TURP), a study found. Schroeck, et al., University of Michigan, Ann Arbor, identified 54,399 TURP and 29,457 laser prostatectomy procedures that took place during the study period (2001 to 2009). Although the overall rates of transurethral surgery for BPH remained stable during the study period, laser prostatectomy use increased 400% from 25 to 114 procedures per 100,000 men during that same period, replacing about half of all TURPs. Older and sicker patients are less likely to undergo laser prostatectomy. Compared with patients without comorbidities, those who had one and two or more comorbidities were, respectively, 21% and 52% less likely to undergo laser prostatectomy.

The researchers found that most of the variation in laser prostatectomy use was determined by the urologist seen by the patient, “implying that who the patient sees is a major determinant of which type of surgery is performed.” They also said that given the potential advantages of laser prostatectomy, the study results raise concern about possible underuse of this new technology among elderly and infirm patients.

In a discussion of study limitations, the researchers noted that they were unable to elicit which type of laser or TURP equipment was used in a specific procedure. Nevertheless, they felt that this shortcoming did not bias the results of the study. (Source: *Renal & Urology News*, September 26, 2012)

Second Pill for Prostate Cancer Also Prolongs Survival. Enzalutamide (formerly known as MDV3100), a once-daily oral therapy, significantly prolongs survival in men with metastatic castration-resistant prostate cancer after chemotherapy, according to a study published in the September 27 issue of the *New England Journal of Medicine*.

The median overall survival was 18.4 months for men who received the drug and 13.6 months in the placebo group, a 4.8 month improvement, according to Scher, et al., Memorial Sloan-Kettering Cancer Center, New York. Enzalutamide was approved for the treatment of metastatic castration-resistant prostate cancer by the FDA in August. It became the second oral therapy to be approved in this setting. Abiraterone acetate was approved in 2011. With abiraterone, survival was prolonged 4.6 months, which is comparable to the 4.8 months seen with enzalutamide.

According to one expert, enzalutamide adds to the treatment that can be offered to patients with advanced prostate cancer. It can be used sequentially with other active agents, such as docetaxel, abiraterone, cabazitaxel, radium-223, and immunotherapy.

The effectiveness of enzalutamide in patients who previously received abiraterone is unknown, but the agents are theoretically not cross-resistant because they have different mechanisms of action. Ennzalutamide works differently than abiraterone, which inhibits androgen synthesis and lowers testosterone levels to nearly undetectable levels.

An expert explains that enzalutamide is likely to be active in all patients with metastatic castration-resistant prostate cancer in whom the androgen receptor is still driving the disease. Unfortunately, there is currently no method to clinically assess which patients have active androgen receptors. However, there is some promising research on a biomarker that might eventually translate into a clinical tool.

Notably, in this study, prostate-specific antigen (PSA) levels increased in a majority of patients who had disease progression while receiving enzalutamide. This suggests the tumors remained driven by androgen and androgen receptors.

The overall survival benefit was consistent across all subgroups, including age, baseline pain intensity, geographic region, and type of disease progression at entry, the authors report. The superiority of enzalutamide over placebo was shown for all secondary end points.

The benefits of enzalutamide were observed even though a greater proportion of patients in the placebo group received subsequent systemic therapies for prostate cancer. For example, 42% of enzalutamide patients went on to receive abiraterone or another therapy, compared with 61% of placebo patients. (Source: *N Engl J Med*. 2012;367:1187-1197, 1256-1257, via Medscape Medical News ©, September 27, 2012, WebMD)

More About PSA Testing. Prostate cancer survival rates in the United States have improved since the introduction of prostate-specific antigen (PSA) testing, researchers report. (PSA is a protein released into the body by the prostate gland. PSA screening involves measuring the amount of PSA in a man's blood. The higher the PSA level, the more likely it is that a man has prostate cancer.)

The new study, published August 23, 2012, in *The Journal of Urology*, found that routine use of PSA testing for prostate cancer screening and monitoring has resulted in earlier and more sensitive detection of the disease. This has led to improved survival for patients with newly diagnosed prostate cancer that has spread to the bones or other parts of the body.

In addition, the survival rate for black patients has improved and is now about the same as for whites, the investigators found.

For the study, researchers analyzed data from three clinical trials conducted over the last three decades that evaluated patient survival after androgen (hormone)-deprivation treatment for prostate cancer. Two of the clinical trials were conducted before the introduction of PSA screening, and one took place after.

Median survival was 30 months in the first trial (conducted from 1985 to 1986), 33 months in the second trial (conducted from 1989 to 1994), and 49 months in the third trial (conducted from 1995 to 2009). Patients in the most recent trial also had a 30 percent decreased risk of death, the study found.

Among black patients, median survival was 27 months in the first trial and 48 months in the third trial, which is close to that of white patients, the study authors noted in a journal news release. This improvement in black patients' survival may be due to greater awareness of prostate cancer and increased likelihood that they will seek health care, suggested Thompson, et al., University of Texas Health Science Center, San Antonio.

However, the researchers noted that black men have a twofold to threefold greater incidence of newly diagnosed metastatic prostate cancer than white men, which contributes to a similarly higher death rate. This shows the need for a greater effort to eliminate disparities in prostate cancer, they said.

While not all of the improvements in prostate cancer survival can be attributed strictly to PSA testing, the researchers concluded that undoubtedly PSA testing played a role in extending many lives.

PSA testing has been controversial. In May, the U.S. Preventive Services Task Force recommended against routine PSA screening, saying too many non-dangerous cancers were

being treated aggressively and resulting in unnecessary harm. But a July study in the journal *Cancer* found that not screening American men would triple the number developing advanced cancer, and the American Society of Clinical Oncology recommended that men with a life expectancy of more than 10 years talk with their doctors about getting the test.

While the new study uncovered an association between routine PSA testing and improved rates of prostate cancer survival, it did not prove a cause-and-effect relationship. (Source: *The Journal of Urology*, news release, August 23, 2012, via HealthDay News, August 23, 2012)

Outcome Disparities. Black men needing surgery for advanced prostate cancer seem to have worse outcomes than white men, according to a new study. Based on data collected from hospitals in three states, black men who had their prostates removed were more likely to need blood transfusions, stay in the hospital longer and die while hospitalized compared to white men. The study also suggested they also had lower quality of care.

Compared to whites, black men were 27 percent less likely to have their surgery at a hospital that routinely removes prostates and 33 percent less likely to be seen by a surgeon experienced in the procedure.

According to the American Cancer Society, over 241,000 men will be diagnosed with prostate cancer in the U.S. in 2012, and over 28,000 will die from it. Black men seem to be disproportionately represented in both of those numbers. They are 59 percent more likely to develop prostate cancer and more than twice as likely to die from it compared to white men, according to earlier research.

Barocas, et al., Vanderbilt University, Nashville, TN, say that some event seems to happens after diagnosis that leads to worse outcomes. The study sought to identify any such event(s) by studying information on 105,972 adult men who had their prostates removed because of cancer at hospitals in Florida, Maryland and New York between 1996 and 2007. Of those, 81,112 patients were white and 14,006 were black.

Because the number of surgeries performed at a hospital or by a surgeon can be used as a measure of procedure quality, the researchers compared the experience level of the hospitals and doctors that treated white and black men. For this study, a hospital was considered "high volume" if it did about two surgeries per month or more, while surgeons were considered experienced if they did about one per month.

The researchers found that 59 percent of black men in the study went to a high-volume surgeon, compared to 70 percent of white men. And 66 percent of black men were treated at experienced hospitals, versus 74 percent of white men. The researchers write that while the worse outcomes weren't directly tied to the hospitals or surgeons, black men who went to high-volume hospitals and surgeons seemed less likely to have complications than those who went to less experienced ones.

But, they noted that black men in the study who went to the high-volume hospitals and surgeons were still at greater risk of complications than white men. They suspected that the situations they found were based on access issues and economic issues. (Source *The Journal of Urology*, online August 17, 2012, via Reuters Health)

Candidates for Active Surveillance. Dr. Gerald Chodak, Medscape, commented on a recent article in *European Urology* regarding the current status of active surveillance for men with clinically localized prostate cancer. It involved men within PRIAS study who are participating in active surveillance on the basis of very strict criteria. Those include men who have a Gleason score of 6, only 2 positive cores, a prostate-specific antigen (PSA) level less than 10 ng/mL, and clinically localized disease.

About 450 men in this protocol are prospectively being monitored. If they meet certain criteria, they are advised to undergo radical prostatectomy, and those criteria also are very strict. Those patients have to have a PSA doubling time of less than 3 years, or more than 2

positive cores, or a Gleason score that goes above 6. Thus far, with a follow-up of less than 2 years, about one quarter of the men have been advised to undergo radical prostatectomy.

Dr. Chodak is concerned that 29% of the men actually had unfavorable pathology on the radical specimen. That means they had a Gleason score of 4+3, or they had grade T3/ T4 disease (locally advanced disease). On the basis of this study, it would appear that many of the men who are being followed very carefully have unfavorable characteristics for inclusion as good candidates for active surveillance. It creates the impression that active surveillance is still a very dangerous thing to do, because the patient has a 29% risk of having unfavorable pathology should he delay his radical specimen.

Dr. Chodak referred to the recent PIVOT trial which compared radical prostatectomy vs watchful waiting for men with clinically localized prostate cancer. In that study, men who had a Gleason score below 7 who were randomized to the watchful waiting approach were considered to have low-risk disease. At the end of 12 years, the difference in cancer mortality was only 3.6%. For those men who had a PSA below 10 ng/mL at the time of their enrollment in the randomized trial, the difference in cancer mortality at 12 years was only 0.6%, far different from the 29% with unfavorable pathology found in the PRIAS study.

This leads to the following questions. First, are we really doing a good enough job at selecting men for active surveillance, or are we being too strict? Second, are we also being too strict in deciding which patients should stay on active surveillance as opposed to going on to local therapy? It would appear that using the criteria currently available, we are telling too many men to proceed on to therapy.

Finally, if the difference in cancer mortality is so small at 12 years, it must mean that having extracapsular disease or having a Gleason score of 7 on your pathology cannot be the most critical determinant of aggressive treatment or the need for aggressive treatment, because having those pathologic findings is not translating into a very poor outcome, at least at 12 years.

Perhaps with longer follow-up, outcomes will change. But for the moment, Dr. Chodak believes that the way we conduct active surveillance is a long way from being optimal, and it still appears that far too many men are going to receive aggressive therapy using the criteria that we currently have available. (Source: Medscape Medical News, September 4, 2012)

Prostatectomy vs. Observation for Prostate Cancer: PIVOT. Until now, no randomized trial has been designed to compare surgery with "watchful waiting" in patients with primarily PSA-detected, localized prostate cancer. PIVOT (Prostate Cancer Intervention versus Observation Trial), conducted in the U.S., fills this gap.

The participants included 731 men with localized prostate cancer and life expectancy of at least 10 years who were randomized to radical prostatectomy or observation. Three quarters of cases were diagnosed through PSA screening, two thirds of men had PSA levels ≤10 ng/mL, and two thirds had Gleason scores <7. During the study, 10% of men in the observation group crossed over to prostatectomy.

At median follow-up of 10 years, neither all-cause mortality nor prostate cancer–specific mortality was significantly lower in the prostatectomy group than in the observation group. However, among men with PSA levels >10 ng/mL, mortality was lower with prostatectomy. Subgroups with higher-risk cancers (defined by criteria incorporating PSA levels, Gleason scores, and tumor staging) also showed trends toward lower mortality with surgery. Bone metastases occurred in 4.7% of prostatectomy patients and in 10.6% of observation patients.

Interpretation of these results likely will depend on one's preconceptions. Clinicians predisposed to no intervention will emphasize the overall results, which suggest low probability of benefiting from radical prostatectomy. Clinicians predisposed to aggressive intervention will note that prostatectomy was associated with significantly lower 10-year mortality in prespecified subgroups. Some will argue that PIVOT was underpowered; indeed, it fell short of its original

enrollment goal of 2000 participants. Nevertheless, these findings comprise the best available data and should be used by urologists, oncologists, and primary care physicians to guide clinical decision making. Finally, given that surgery was ineffective for men with PSA levels ≤10 ng/mL, it will be interesting to see whether PSA screening supporters will revise upward their favored PSA thresholds for triggering biopsy. (Source: Massachusetts Medical Society, *Journal Watch*, August10, 2012)

Questionable Data and Provenge. In Dendreon Corp's most important clinical trial for the controversial cancer therapy Provenge (sipuleucel-T), researchers analyzed some of the data differently from how the company told U.S. regulators they would, according to documents reviewed by Reuters.

That not only was a departure from scientific norms, but also artificially inflated the apparent benefit of the prostate cancer therapy when the results were revealed to doctors and investors through a 2010 paper in the New England Journal of Medicine, according to experts in biostatistics and clinical trials.

Dendreon said the discrepancy is immaterial and that Provenge is safe and effective. The U.S. Food and Drug Administration also stood by its April 2010 decision to approve the treatment.

The disclosure could mark another setback for Dendreon, whose market value has tumbled over 70% in the past eight months after disappointing sales of Provenge. The company also faces at least five lawsuits accusing management of insider trading and misleading shareholders about the treatment's prospects.

According to a copy of Dendreon's Statistical Analysis Plan (SAP) submitted to the FDA in early 2008 and reviewed by Reuters, the company said its key trial would look first at whether patients who received Provenge survived longer than patients who received a placebo. The company also said it would analyze whether the therapy affected patients differently depending on whether they were younger than 65, or 65 and over. But when it published the results of the IMPACT trial in July 2010, the cut-point for that age-based analysis was 71 years, not 65.

Dendreon denies that it manipulated the data. The company's chief medical officer, Dr. Mark Frohlich, said FDA guidelines require using 65 as a dividing line, but trial researchers later determined that 71 made more sense biologically, since it represented the median age of patients in the trial.

A spokeswoman for the FDA said that it approved Provenge based on the reported effect for all patients, regardless of age, and the agency stood by that decision. The FDA would not address queries by Reuters on whether the age-related discrepancies in the effects of Provenge cast doubt on the overall value of the treatment.

Data from the IMPACT trial showed that patients who received Provenge lived 4.1 months longer on average than men who received the placebo treatment. That benefit has been seized upon by doctors considering whether to prescribe the $93,000 therapy and by men deciding whether to undergo it. The IMPACT paper also reported that men older and younger than the age of 71 benefited from Provenge, though the younger men benefited slightly less. (Source: Reuters Health Information, October 11, 2012)

Proscar and Quality of Life. Proscar (finasteride), a drug used to treat an enlarged prostate, does not reduce the quality of life of men who use it for a prolonged period of time, according to a new study funded by the U.S. National Cancer Institute.

The research involved men aged 55 and older in a seven-year randomized clinical trial looking at the drug's possible use for prostate cancer prevention. Moinpour, et al., Fred Hutchinson Cancer Research Center, Seattle, examined three areas of patients' quality of life. Proscar did not significantly affect the men's physical functioning, mental health or vitality.

Participants completed questionnaires three months before the study and six months after the study began. They were also surveyed once a year for the next seven years. Men who smoked or had other health conditions saw more pronounced effects on their quality of life, particularly their physical functioning. The researchers said patients' lifestyles and other health problems should be considered when they are given treatments to prevent disease.

Other factors in the varied group of men made more of a difference than the drug. Diabetes and current smoking status had a greater clinically relevant impact on the physical functioning score then did finasteride treatment, according to the authors. (Source: *Journal of the National Cancer Institute*, news release, September 12, 2012)

Intermittent HDT. Stop-and-start hormone-deprivation therapy for localized prostate cancer doesn't shorten overall survival compared to continuous treatments, and yields fewer side effects such as impotence and hot flashes, a large new study suggests.

A team of Canadian, British and American researchers found that intermittent hormone treatments -- which suppress circulating male hormones such as testosterone that "feed" prostate tumors -- don't increase the risk of disease progression. Intermittent treatment also doesn't increase the chances that patients whose prostate-specific antigen (PSA) levels are slowly rising will eventually die from prostate cancer.

Nearly 1,400 patients whose localized prostate cancer was treated with surgery and/or radiation were split into two groups. One set received continuous hormone-deprivation therapy -- a mainstay treatment for prostate cancer that has spread -- while the rest were treated in eight-month cycles punctuated by months-long "breaks" depending on their PSA levels.

Slowly rising PSA levels may indicate the progression of prostate cancer, even if no evidence of the disease shows up on other tests such as MRI and CT scans. Study participants on stop-and-start hormone-deprivation treatments were placed back on therapy if their PSA scores grew to 10 or higher, or they experienced clinical symptoms of disease progression. After a follow-up of nearly seven years, only 14.2 percent of all participants had died from prostate cancer, with an overall survival of 8.8 years in the intermittent-therapy group and 9.1 years in the continuous-therapy set.

Side effects associated with hormone-deprivation therapy, such as erectile dysfunction, hot flashes, bone loss and depression, were less common among the intermittent treatment group. Even if they didn't regain erectile function, they had less fatigue and improved urinary function, which are very important quality of life issues.

The researchers noted that those on intermittent therapy had one-third of the treatments of the continuous therapy group, resulting in a considerable cost saving, in addition to better quality of life and no overall loss of survival.

Now the research effort should focus on learning the optimal timing for initiation of intermittent hormonal therapy, the researchers say. Their study was not designed to answer that question, which could take many more years of research. Nevertheless, they contend that the current evidence demonstrates that intermittent hormone therapy can become the standard of care for patients like those studied. (Source: *New England Journal of Medicine,* September 5, 2012, via HealthDay News, September 6, 2012)

(Cancer Facts and Figures 2012 - Continued)

Survival. More than 90% of all prostate cancers are discovered in the local or regional stages, for which the 5-year relative survival rate approaches 100%. Over the past 25 years, the 5-year relative survival rate for all stages combined has increased from 68% to almost 100%. According to recent data, 10- and 15-year survival rates are 98% and 91%, respectively. Obesity and smoking are associated with an increased risk of dying from prostate cancer. (Source: Cancer Facts & Figures 2012, The American Cancer Society)

" Advanced Prostate Cancer – An Update"

by

Nancy A. Dawson, MD - Professor of Medicine
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(Summary of a presentation to the WRNMMC Prostate Cancer Support Group on August 2, 2012)

Introduction. Good evening. I am going to be talking tonight about advanced prostate cancer. As a background, prostate cancer is the most common cancer in men with over 240,000 new cases diagnosed in 2011. It is the second leading cause of cancer death in men. Most men don't die of prostate cancer. One out of six men will be diagnosed with prostate cancer, but only one in thirty-five will die from the disease. So it is a very common cancer and if you are African American, or if you have a first degree relative, e.g., a brother or a father, with the disease, your chance of getting prostate cancer doubles. Every year over 30,000 men die of prostate cancer, and if you progress to advanced prostate cancer, it is likely to be the cause of your death if you become resistant to hormonal therapy. By the way, approximately one-third of cases are locally advanced or metastatic at the time of diagnosis.

Treating the Disease. Prostate cancer is treated by disease stage, but co-morbidity and side effect potential are influential factors. About 40% of men newly diagnosed with organ-confined disease will have a recurrence of their prostate cancer despite having had primary therapy such as surgery or radiation. Initially their PSA may simply rise, but eventually about eight years later they will develop metastatic disease, most likely in the bone or lymph nodes. At the outset these men would be hormone sensitive and would be treated with hormonal therapy, but eventually they will become what is called castrate-resistant. Lupron or Zoladex may keep the testosterone level very low, but the cancer progresses. These men may not have any symptoms initially, but eventually symptoms occur - the most common symptom is bone pain.

Gleason Score. After diagnosis and a biopsy, the resultant Gleason score is based on the first most common and second most common pattern of the cancer as determined by a pathologist (I hope everyone in this room knows what his Gleason score is!). The patterns are scored from one to five and so the total is going to be somewhere from 2 to 10. Your Gleason score is crucial in determining whether your cancer is likely to be cured by your primary therapy. The higher the Gleason score, the higher the chance your cancer will recur. Looking at this graph, you can see that men who don't have any 4 or 5s, so let's say their Gleason score was 6, then the chance that their cancer is going to recur is less than 5 percent. On the other hand, if most of a man's cancer has a Gleason score of 4 and 5, the chance that he will have a recurrence of cancer is more like 90 percent. So you can appreciate the role of the Gleason score in predicting recurrence.

Natural History of Prostate Cancer. This graph depicts what is called the natural history of prostate cancer. It also incorporates the newer therapies for dealing with advanced prostate cancer. This will be my primary focus tonight as we talk about new developments in the treatment of advanced prostate cancer. At this end of the curve we see surgery or radiation as initial therapies. Then we observe the rollercoaster effect caused by that forty percent of men with rising PSA because their cancer was not cured by either surgery or radiation. At some time along the way those men will be treated with androgen deprivation therapy, i.e., therapy intended to lower their testosterone levels by surgical removal of the testicles or by using a drug like Lupron. A large majority of those men, about 90 plus percent, will show initial improvement when the testosterone is removed. So if their PSA was rising and you treat them with what is commonly called hormonal therapy, their PSA in all likelihood will go back down as shown by this graph. Unfortu-

nately it eventually goes back up, and when it does, we will treat men with what are termed second-line hormone therapies. You should understand that prostate cancer does not become resistant to androgen, instead it becomes hypersensitive to androgen so when the testosterone is removed and the PSA starts to rise again, we need to start thinking of ways to target the other sources of androgens that are available to stimulate the cancer; those other androgens are coming from the adrenal glands that sit on top of the kidneys. The androgens also come from the cancer itself because the cancer learns to make androgen, enough androgen that it can stimulate itself. So the second thing we do is try to block, or at least lower, the adrenal androgens using anti-androgen drugs like Casodex and Flutamide. They do not lower testosterone, instead they block the adrenal androgen from stimulating the cancer. We also can lower the adrenal androgens with a drug like ketoconazale which is an anti-fungal drug. These drugs may work for a while.

There is a new drug called Abiraterone and I will talk more about it later. Abiraterone blocks not only the androgen that the testicles and the adrenal glands produce, but it also blocks the androgen that the cancer itself can make. In the meantime, the patient with advancing prostate cancer is on Casodex, or we might have tried ketoconazale. The patients likely are asymptomatic and they might not have metastatic disease, but eventually their cancer will spread, usually to the bone. In the meantime, we may resort to immunotherapy with drugs like Provenge when the person is still not having a lot of symptoms. This approach may work for a while, but when it stops working we may use chemotherapy drugs such as Taxotare or Cabazitaxel. Post-chemotherapy, there are several drugs under development now and they are reaching the stage where we soon may be able to use them. Abiraterone already has FDA approval for post-chemotherapy use, and it probably will soon be approved for pre-chemotherapy use. There is another drug called MDV3100 that promises to be a super anti-androgen. It could be approved in the next few of months at least for post-chemotherapy use.

There is a new therapy referred to as Radium-223 or alpharadin; it has not been approved yet, but it is part of the expanded access process that, under certain conditions, allows for early use of a trial drug prior to full FDA approval. There are some drugs that we are using right now in this expanded access process. In the first place, many of these drugs are FDA-approved for patients who already had chemotherapy, but they are also being tested for pre-chemotherapy use. The public is largely unaware that about 70 percent of drugs used in oncology are prescribed off-label, i.e., they are FDA-approved primarily for other purposes. Then we must contend with insurance companies who will only reimburse for FDA-approved drugs even when we know they are effective otherwise. It is a very complicated matter.

Hormonal Therapy. If you think about prostate cancer as a plant and testosterone as water, the idea is to stop watering the plant so that it slowly shrivels up and dies when it is denied what it needs to grow. Hormonal therapy, also termed androgen deprivation therapy, seeks to: blockade of the effect of testosterone on the prostate gland; suppress the production of adrenal androgens; and block androgen production by the cancer itself. All these manipulations of androgens result in what is called program cell death or apoptosis. It often takes a lot to kill the cancer, but at the outset, the cancer it is very sensitive to androgen manipulation, and the better job you do at blocking the androgen, the better control you have of the cancer. These are the different tools we have. Traditionally we treat advanced prostate cancer by orchiectomy which removes the testicles, thereby removing the androgens (testosterone) produced by the testicles. We also use a drug referred to as an LHRH (luteinizing hormone releasing hormone therapy) which centrally decreases LHRH levels and testosterone synthesis. Then again, we can use combined therapies. For example, if a person is on a drug like Lupron, an LHRH agonist, it can be combined with a drug like Casodex, an anti-androgen. It's what is referred to as combined androgen blockade.

(Dr. Dawson then presented and discussed several slides that depicted the action of LHRH analogs and nonsteroidal antiandrogens and listed the available hormonal agents.)

I want to mention Degarelix, the only approved GnRH receptor antagonist, and the outcome of a clinical trial involving 610 men who were randomized to Degarelix or Lupron. Degarelix-treated patients achieved a faster castrate level of testosterone and a more rapid PSA decline. Whether that pays off in increased longevity is not clear, but it does make the testosterone and the PSA go down faster. Degarelix also avoids any flare reaction. That would be a problem, for example, if a patient's disease had spread to the bone and it was sitting in the back near the spinal cord. That flare effect could actually have the cancer press on the spinal cord, thereby affecting mobility. Furthermore, a drug like Lupron could be combined serially with a drug like Casodex to block the flare effect, but Delgarelix avoids the flare all together. So if there is a real concern about a flare, Degarelix would be a better choice.

Hormonal therapy is best employed for early prostate cancer, but if you have a nice Gleason 6, an early, localized prostate cancer, you would not need hormonal therapy. But let's say you had a large prostate cancer and were not a good candidate for surgery. Your cancer was more locally advanced and radiation therapy was indicated. A major clinical trial in Europe studied men with prostate cancer who were not considered good surgery candidates. There were two groups. One group received radiation only, and the second group received radiation combined with three years of hormonal therapy.

As you can see from this slide, the patients who received the combined radiation and hormonal therapy had significantly better outcomes in terms of survivability. So if a patient has a more locally advanced prostate cancer and he is going to be radiated and you want to get that improved survival, you can really only do it with several years of hormonal therapy. If the patient has a less aggressive prostate cancer, say the Gleason score of 7, that is an intermediate prostate cancer, you can also achieve improved survivability by radiation therapy by adding on maybe four months of hormonal therapy. That is also associated with a better survival experience. Only the patients with low-risk disease do not benefit when you add hormonal therapy to radiation.

D1 disease is the now-obsolete term for when the prostate cancer has advanced into the lymph nodes. It is another situation wherein hormonal therapy has improved survivability. In an older study, men who had radical prostatectomies and who were found to have the disease in their lymph nodes were given immediate hormonal therapy while a second group received delayed hormonal therapy only when a problem occurred. After seven years only 4.3 percent of those receiving immediate hormonal therapy had died, compared to 31 percent of those who received delayed hormonal therapy. So early hormonal therapy in men with disease into the lymph nodes has been associated with improved survival.

Another European trial involved immediate versus delayed hormonal therapy in men who had more advanced disease or metastatic disease. Men who had immediate hormonal therapy had better outcomes in these categories: pathologic fracture, spinal cord compression, ureter obstruction, and extra-skeletal metastasis.

Some men are hesitant to begin hormonal therapy even when clearly indicated because they are concerned about side effects. Well, yes, there side effects. The most common are hot flashes, osteoporosis, anemia, diminished sexual function, feeling of weakness, and muscle wasting. The two side effects that men dislike the most are hot flashes and sexual problems.

Metastatic Prostate Cancer and Hormonal Therapy. Let's talk about metastatic prostate cancer and hormonal therapy. In the natural progress of the disease, the patient's disease is hormone sensitive at the outset and then it probably becomes hormone hypersensitive, and then finally hormone refractory. The time will come when the cancer is independent of androgen, but that is usually very late in the course of the disease. Initially the patient may start on hormonal therapy and his PSA goes down; he does well for a time, but then his PSA goes up again. There are second-line hormonal manipulations we can try. They include anti-androgen withdrawal, antiandrogen addition, estrogens, ketoconazole, aminoglutethimide, and corticosteroids. Prednisone by itself works to lower adrenal androgens; it can also be employed as a secondary hormonal manipulation.

The newer therapies developed because the oncology community realized that metastatic men were not resistant to androgens, they were hypersensitive to them. We really have to go after the androgen receptors which sit on all prostate cancers. Furthermore, we needed to deal with the androgens being made by the adrenal glands as well as the androgens produced by the tumor itself. One response to this new awareness led to Abiraterone, an androgen biosynthesis inhibitor, that suppresses the synthesis of androgen and blocks the androgen made by the testicles, the adrenal glands, and by the cancer itself.. Another drug, MDV-3100, is like a super antiandrogen that goes after the androgen receptors. It does not itself do any thing to lower the adrenal androgens. Instead it just blocks the androgen receptor and prevents the cancer from being stimulated by the androgen receptor**.**

(Dr. Dawson then showed and discussed series of technical slides depicting the processes just described.)

What survival benefit have we seen from these new developments? When I started treating this disease a man who had progressed through hormonal therapy lived about a year on average. Now each of these new therapies have added on about three or four months of survival, and when you add them consecutively the patients are living another couple of years longer. Incidentally, during the various trials the investigators looked at other considerations besides the survival end point. One noteworthy consideration was complications in the bones and the resultant pain. The patients who got the Abiraterone were less likely to have complications of their cancer being in the bone, and they were less likely as a group to have pain.

Chemotherapy for Prostate Cancer. OK, let's say you had a second line hormonal therapy as just described and you are doing reasonably well, eventually your oncologist will talk to you about chemotherapy. Chemotherapy does not mean that you are at the end of the line! I always hate it when people say that about chemotherapy! It is simply another therapy that is going to make you live longer and hopefully you will feel well while you are on it.

Mitoxantrone was the first of the chemotherapy drugs used to treat prostate cancer that was castrate-resistant and a 1996 study showed that it did not increase survival. In fact at that time there was no drug for prostate cancer that increased survival. But mitoxantrone did have a positive palliative response which means that the patient had less pain or did not have to use as much pain medication. About forty percent of the patients who got the mitoxantrone and twenty percent of people who got prednisone alone had improvement in their pain. FDA approved the drug because it lessened pain and was well-tolerated, not because it had a survival benefit. Now that we have drugs that enhance survival, you don't hear much about mitoxantrone any more, although it is still FDA-approved.

The first chemotherapy drug approved to enhance survival was docetaxel or Taxotere and it is still considered the first line chemotherapy drug. Docetaxel is the generic name and Taxotere is the trade name. This study compared docetaxal with mitoxantrone and it showed about a three-month improvement in survival in favor of docetaxel. This was the very first drug that improved survivability and later drugs showed even better outcomes. Docetaxel can be beneficial to men no matter their age, and no matter their pain level. My own experience with chemotherapy for my patients is that many of them do very well. Cabazitaxel was the second chemotherapy drug to be approved because it increased survivability. This study took the patients who had progressed on docetaxal and gave them either cabazitaxel or mitoxantrone. The people who got cabazitaxel had better survival as a group than those who got the mitoxantrone. Again we are talking about a 2 ½ month improvement. But as I said earlier, when you start adding the numbers together you realize the progress being made.

There are other targeted therapies in process or that have already been approved. One is Cabozantinib. When men are progressing on hormonal therapy, they have an overexpression of MET which facilitates tumor cell invasion and metastasis. Cabozantinib blocks MET and also blocks something called VEGFR which would otherwise facilitate undesirable angiogenesis, causing the cancer to progress. Look at these bone scans. They show dramatic

improvement after just three months using this therapy. The patients also experienced reduced pain. Overall, Cabozantinib showed substantial antitumor activity: 68% overall objective disease control at Week 12; 74% measurable disease regression; 76% complete or partial resolution of bone scans; 67% pain improvement in patients with pain at baseline; 29 weeks overall median progression free survival (PFS); and significant PFS improvement post-randomization. This drug is now in clinical trial including a site in our local area.

Radium-223 (alpharadin) is a bone-targeted therapy. Over 90% of patients with metastatic CRPC (castrate-resistant prostate cancer) have radiologic evidence of bone metastases. And bone metastases are a major cause of death, disability, decreased quality of life, and increased treatment cost. Hence the heightened interest in Radium-223. Radium-223 is a novel alpha-pharmaceutical that may provide a new standard of care for the treatment of CRPC patients with bone metastases. Radium-223 is excreted by the small intestine and it mimics calcium. It actually targets a bone or a bone metastases without much damage to adjacent normal tissue. It just kills the cancer cells in the bone. Again, this drug is only for patients who have metastasis to the bone. But, of course, 90 percent of CRPC men do. The early Norwegian study showed there was about a three-month improvement in overall survival. The study was recently updated and the overall survival improved to about 3.6 months. Radium-223 also delayed the onset of any skeletal-related event. So it did make patients live longer with less likely complications in their bone; and it was very well tolerated with basically no side effects.

Immunotherapy for Prostate Cancer. No doubt most of you here tonight are aware of Provenge (sipuleucel-T) as the result of the controversy associated with its development. Provenge is the first therapeutic cellular immunotherapy to demonstrate effectiveness in Phase III clinical trials by prolonging survival in patients who have advanced, late stage prostate cancer. Sipuleucel-T is produced by extracting the patient's own white blood cells (androgen presenting cells) which are sent off to be combined with prostatic acid phosphatase antigen and GM-CSF which is an immune stimulator. This activated blood product is returned for infusion into the patient. That is how Provenge is produced, you get your own cells turned into cancer-fighting cells.

There were three studies, but the so-called Phase III IMPACT trial got the therapy approved. It was for men with asymptomatic or minimally symptomatic metastatic castrate-resistant prostate cancer. There were two arms - one got Provenge and the other got a placebo. The design of the trial eventually allowed men who got the placebo to get Provenge and about 70 percent of those patients did so. The median survival time for sipuleucel-T patients was 25.8 months compared to 21.7 months for the placebo-treated patients, a difference of 4.1 months. There are other clinical trials now going on looking at Provenge earlier in the course of the disease or in combination with other drugs. I am involved in a trial in looking at Provenge in combination with alpharadin.

What the side effects of Provenge? The side effects are chills, fever, headache, and other flu-like symptoms that usually last 24 to 48 hours. We can pre-medicate people to try to prevent them.

So these are some of the therapies. Alpharadin, Taxotere, docetaxel, cabazitaxel, Provenge, abiraterone, and now MDV 3100 have all been reported to improve survival. Even though the reported improvements in survival seem modest, you must not overlook the cumulative effect on longevity. As you start adding the positive outcomes together, you begin to realize how we have changed the natural history of prostate cancer for men with the disease.

Circulating Tumor Cells. The last thing I want to mention is something called circulating tumor cells. Not every man with prostate cancer has circulating tumor cells, but men who have more advanced prostate cancer may have elevated levels of circulating tumor cells that actually can be detected in their blood. This slide shows a blood vessel with some cancer cells adjacent to it. Some of those cancer cells may creep through the blood vessel walls and start circulating in the blood stream. Eventually they actually escape out of the blood vessel

and land some place where they become metastatic. But while they are circulating, you can sometimes detect the circulating tumor cells. They have prognostic significance because the more of them in your blood, the worse the situation is likely to get. Let's say you have a patient who has been diagnosed with castrate-resistant prostate cancer and you check him for circulating tumor cells. If the circulating tumor cell level is more than 5, then that is associated with a shorter survival, say about 11.5 months. If it is less than 5, that is associated with a longer survival, say more like 22 months.

Many times when you start a new treatment and check the patient's PSA, sometimes the PSA goes down, sometimes it doesn't. The circulating tumor cells are independently able to predict survival outcome. Look at this slide of the Kaplan-Meier Plot that features 4 lines:

Line 1. The green line represents the favorable population showing those patients that had less than 5 CTCs at all blood draws throughout the study and whose Median Overall Survival was more than 26 months.

Line 2. Contrast this with the red line or unfavorable population which were patients with 5 or more CTCs at all blood draws and their Median Overall Survival was 6.8 months, which is more than a four-fold difference from the favorable population.

Line 3. Perhaps the most significant population is the blue line patients. These were those who had 5 or more CTCs at baseline, which would have placed them in the red unfavorable population, but they showed less than 5 CTCs at the last blood draw. The Median Overall Survival of this population was 21.3 months, which is a dramatic change and statistically suggests improvement from the red line or unfavorable population.

Line 4. Finally, the gold line represents patients who had less than 5 CTCs at an early draw but increased to 5 or more at the last draw. The Median Overall Survival of this population was 9.3 months, which is almost 3 times less than the favorable population and is clearly approaching the red unfavorable population.

The PSA is not a good predictor in the first month or two of your treatment, but the circulating tumor cells are. The circulating tumor cells can tell you whether the treatment is taking you in the right direction. CTCs can provide valuable information at baseline, however, the test is intended to be used for serial monitoring, so it is important to understand the significance of the impact of CTC counts as they change or remain the same. CTCs are getting incorporated more and more into the treatment schemes for men with prostate cancer. Certain specialized equipment if required, but Medicare will pay for it and they are useful in some patients.

Closing. I enjoyed being with you again tonight. I trust you are buoyed by the new developments in the treatment of advanced prostate cancer. Now I am ready for your questions.

Question: This question is about the quality of life of men whose prostate cancer is at an advanced stage. I know one man in particular who is 91 after being diagnosed 20 years ago. He seems to enjoy a decent life style. He is active and is not walking around with a "woe is me" attitude. So what are these people like who are dealing with these issues?

Answer: Men with advanced prostate cancer have different degrees of disability associated with their cancer. I know men who have been on chemotherapy for three years who still go on vacation. You would not pick them out in the waiting room and say "aha" that one is on chemotherapy or that one is doing well. There are plenty of men getting chemotherapy who have very good quality of life. Some drugs like abiraterone and MDV-3100 don't have a lot of side effects. Your quality of life depends upon which organs or physical locations are affected by the disease. Most men with advanced prostate disease feel relatively well even until they get close to the end of life. On the one hand, if your liver or kidneys are affected by the disease, your quality of life will be poor because vital functions will be affected. But on the other hand, if you have a couple of spots on your bones and they are not painful, your quality of life can be surprisingly good. You need your functioning liver and kidneys to filter the bad stuff, but all your bones do is hold you up! My

clinic is filled with people who travel, hike, etc. Of course, in the last stages of prostate cancer, i.e., the last few months of life, quality of life is bad. But early on, these persons are doing most of the things they would normally would do. The principal complaint probably is that they are more tired than previously, but then, again, so am I!

The natural history of prostate cancer goes like this: a man's prostate is removed or radiated; if his PSA rises, the average man has about eight years until the disease spreads to the bones; he then gets hormonal therapy which likely will be effective for 2 to 3 years, perhaps even longer if he responds well to the therapy; then he becomes hormonal refractory (at one time, this stage lasted one year, now it is probably more like 3 years). Some men do better, some men do worse during this natural history of prostate cancer. As for men who have a bad quality of life, I am talking about at the last 3 months of that natural history. I have a castrate-resistant patient on Provenge who is going mountain climbing with his grandson! So quality of life depends on where patient is in the natural course of the disease.

Question: For the man with newly diagnosed prostate cancer, are there any dietary considerations that might extend longevity?

Answer: I am a big fan of soy, fish oil, the Mediterranean diet, and pomegranate use that appear to slow PSA aggression. Longevity after PSA rise is partly determined by the PSA doubling time. So if you can slow the doubling time by a dietary intervention, that will be associated with a longer time before a more serious condition develops.

Question: If my PSA is rising, at what point should I seek treatment?

Answer: There may not be an absolute number because everybody's cancer makes a different amount of PSA. It depends upon the clinical state you are in. Let's say your PSA is going up after your prostate was removed, but a bone scan doesn't detect any cancer. Another patient's liver may have cancer throughout, but his PSA is only 3. Another patient could have a PSA of 40 and a scan might not reveal any prostate cancer. The absolute PSA number is not usually a trigger, you have investigate what other factors may be at work. So we don't usually just treat the PSA because a rising PSA is just one indicator and we do not resume treatment based on the PSA alone. We know that the average patient with detectable prostate cancer in the bone likely has a PSA of 40 when the condition is first detected. If your rising PSA reaches 40 but without evidence that the disease has actually spread to the bone, would I need to treat you? Would I start you on hormonal therapy under these circumstances? No, I would not. So the situation is more complex than simply considering the PSA number.

Every patient's baseline PSA is different. If your prostate was surgically removed, your baseline PSA in general should be zero. If radiation was your primary therapy, your baseline PSA in general should be 0.1 or even 0.15. As a practical matter, the higher your PSA, the more the disease you have, but each patient's average volume of disease is different. Every person in here would have a different story.

A recent clinical trial involved men with metastatic disease who were on hormonal therapy. One group got continuous hormonal therapy and the other group got intermittent hormonal therapy. The trigger for intermittent therapy was to have a PSA that declined to less than 4. Then a trigger was needed to deal with men on intermittent therapy whose PSA rose again. Initially, the investigators decided that as long as the PSA was under 20, the patients were probably OK on intermittent hormonal therapy, but based on further study, they reduced the PSA value to 10. So if you are now on intermittent hormonal therapy and your PSA rises to 10, it is time to consider resuming continuous hormonal therapy. In the final analysis, there is not an absolute answer to your question, it depends upon the scenario you are talking about.

Question: What common sense rule is there that provides guidance as to when to commence hormonal therapy?

Answer: Once you are metastatic, you should be on hormonal therapy. So the issue I just discussed applied to patients who are not metastatic - do they or don't they need to start hormonal therapy and if so when? There is no ab-

absolute PSA number that says this is the time to commence hormonal therapy, otherwise you are going to have a shorter life span. However, if you get to the point where you have metastatic disease and you delay starting hormonal therapy, you are more likely to get complications that are likely to lead to your death. There is broad scientific agreement that once you are metastatic you should start hormonal therapy.

Question: How do you pick the hormonal treatment that is most appropriate for each patient?

Answer: Let's say you are newly diagnosed with metastatic disease and I've got six different LHRH drugs that I could select, how do I pick? I guess whichever one I have in stock! Seriously, there are practical factors such as cost because Medicare will only reimburse for a certain amount. All the principal LHRH drugs like Lupron, Zoladex, and Eligard are considered to be equal. Your doctor likely has a preference based on clinical experience. If it is important to get your PSA down as fast as possible, there is a trend to use the LHRH Degarelix, at least for the first couple of months.

If and when a patient gets to the castrate-resistant stage and must decide among those therapies that I mentioned earlier, that's when physicians like me get involved. My task is to evaluate the patient's condition so that hopefully the most appropriate course of action is established. I actually develop a table that considers survival, the location of the metastasis, pain levels, available treatment options, and like considerations. For example, if you have the disease in your liver, then Radium-223 is not an appropriate therapy for you. Again, if you had Hepatitis C and impaired liver function, then abiraterone wouldn't work for you because you wouldn't be able to tolerate it. So treatment for metastatic prostate cancer depends on the cancer's location, any comorbidities, available options, the order of their employment, and your doctor's knowledge of the pros and cons of the different therapies. The treatment process is getting complicated with the advent of new drugs and therapies.

Question: What about insurance coverage for some of these new therapies?

Answer: Abiraterone is approved for post-chemotherapy situations. When it first became available, very few doctors were using it for pre-chemotherapy situations because insurance companies would not approve payment. Over time they have relaxed their policy, so right now almost half of the patients going on Abiraterone have not had chemotherapy. I am discovering that the majority of patients can get Abiraterone for pre-chemotherapy situations. It's not that the drug doesn't work in pre-chemotherapy situations. It costs $8,000 per month and insurance companies often are hesitant to pay for what is an off-label use of the drug.

Question: It seems that oncologists rely on the PSA as a marker, yet I read that reliance on the PSA is being challenged.

Answer: What you are reading about is the controversial use of the PSA as a routine screening technique for detection of prostate cancer in asymptomatic men. The issue is whether routine PSA screening overall does more harm than good. Routine screening could lead to the unnecessary treatment of men whose detected prostate cancer is not life-threatening, yet they undergo primary therapy with all the well-known potential side effects such as impotence and incontinence. The PSA is an imperfect test in diagnosing men for prostate cancer, and for identifying men whose detected disease requires prompt therapy, or any therapy, for that matter.

Once you have prostate cancer and are undergoing treatment, that is a different story as far as the role of the PSA is concerned. My discussion of PSA is related to monitoring the progress of the disease and whether a particular therapy, e.g., hormonal therapy, is effective. Said another way, medical oncologists use the PSA as one indicator of how the patient is responding, or not responding, to a treatment.

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♦ WRAMC US TOO COUNSELORS ♦ (As of October 31, 2012)

(THESE PERSONS ARE WILLING TO SHARE THEIR EXPERIENCES WITH YOU. FEEL FREE TO CALL THEM.)

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♦ MEETING ANNOUNCEMENT ♦

THURSDAY, NOVEMBER 1, 2012
7 PM

RIVER CONFERENCE ROOM
AMERICA BUILDING (3D FLOOR)
WALTER REED NATIONAL MILITARY MEDICAL CENTER

♦ SPEAKER ♦

CLESSON E. TURNER MD

DIPLOMATE, AMERICAN BOARD OF MEDICAL GENETICS
FELLOW, AMERICAN COLLEGE OF MEDICAL GENETICS
ASSISTANT CHIEF OF GENETICS, DEPARTMENT OF PEDIATRICS
WALTER REED NATIONAL MILITARY MEDICAL CENTER, BETHESDA

♦ TOPIC ♦

"FAMILIAL PROSTATE CANCER - GENETIC ISSUES"

We meet at the River Conference Room (3d floor) at the Walter Reed National Military Medical Center located at 8901 Wisconsin Avenue, Bethesda, MD 20889. This is the same location as our monthly meetings.

Gate/Parking: If you enter the base through South Gate (Gate 2) off Rockville Pike/Wisconsin Ave, take the first right (Palmer Road South). On your left you will see the Emergency Room. Continue to follow signs to the America Building and the America parking garage.

Security: A military ID is required to get on base. Persons without a military-related ID card who are attending the meeting are required to register in advance in order to gain entry. To register, contact the CPDR front desk at 301-319-2900 **no later than noon on Wednesday, October to arrange for entry**. Have a photo ID card ready when arriving at the gate.