US TOO® PROSTATE CANCER EDUCATION & SUPPORT

HOTSHEET

JUNE 2010

FDA APPROVES PROSTATE CANCER VACCINE

The FDA recently approved the immunotherapeutic agent sipuleucel-T (Provenge®) for the treatment of advanced prostate cancer, almost 3 years after the agency rejected an advisory group's recommendation in favor of the drug. The approval makes the agent available for treatment of men with asymptomatic or minimally symptomatic metastatic prostate cancer.

"The availability of Provenge provides a new treatment option for men with advanced prostate cancer, who currently have limited effective therapies available," Karen Midthun, MD, acting director of the FDA Center for Biologics Evaluation and Research (CBER), said in a statement. Often described as a vaccine, sipuleucel-T is an autologous cellular immunotherapy designed to stimulate a patient's immune system to mount a response against prostate cancer. The agent consists of a patient's own peripheral mononuclear cells, activated in vitro with a recombinant fusion protein consisting of prostatic acid phosphatase (PAP) and granulocyte macrophage-colony stimulating factor. A complex of the activated cells and antigen presenting cells is infused back into the patient.

The pivotal sipuleucel-T clinical trial involved 512 men with metastatic, castration-resistant prostate cancer, ran-

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ACTIVE SURVEILLANCE IN PROSTATE CANCER PATIENTS MAY NOT BE BEST OPTION

Men with seemingly low-risk prostate cancer who are considered candidates for an active surveillance (AS) strategy might want to consider robotic-assisted laparoscopic prostatectomy (RALP) instead, a team from Mount Sinai Medical Center in New York City reported at the European Association of Urology (EAU) 25th Annual Congress (abstract 578, presented on 18 April 2010).

AS, otherwise known as watchful waiting, has been enjoying a surge in popularity as a management option for men with low-risk localized prostate cancer.

The new results are drawn from a trial that evaluated the final histopathologic and functional outcomes of a large cohort of men who qualified for AS under conventional AS criteria, but who opted instead for RALP. Researchers found a 44% rate of upgrading of cancers. However, there was a low rate of upstaging, and a nerve-sparing procedure was performed in most patients with excellent potency and continence outcomes.

"The findings are extremely important," David Samadi, MD, chief of the Division of Robotics and Minimally Invasive Surgery, told Medscape Urology.

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MDV3100 SHOWS "SUBSTANTIAL ACTIVITY" IN ADVANCED PROSTATE CANCER

Encouraging results with the investigational drug MDV3100 (Medivation) in patients with metastatic castration-resistant prostate cancer were published online 15 April 2010 in *The Lancet*. These results show that the drug has "substantial antitumor activity" in men who have and who have not had previous exposure to chemotherapy, say the authors, headed by Howard Scher, MD, chief of genitourinary oncology at the Memorial Sloan-Kettering Cancer Center in New York. "MDV3100 could have the potential to significantly change the treatment options in metastatic disease," they conclude.

Results come from a phase 1/2 trial of 140 men, 65 of whom were chemotherapy-naïve. The drug was associated with tumor regression and stable disease in soft tissue, and stable disease in bone. Preliminary trial data were released last year. These results with MDV3100 are similar to those seen with another investigational agent, abiraterone. Although the 2 drugs have different mechanisms of action – MDV3100 is an androgen-receptor antagonist and abiraterone is an androgen-synthesis inhibitor – both offer new options for hormonal manipulation.

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RADIATION FOR PROSTATE CANCER LACKS DATA

There is not enough evidence to sort out the effect of various radiation treatments (RT) for prostate cancer patients, especially newer, so-called focused RT, an advisory panel told the US Medicare agency in April.

The Center for Medicare and Medicaid Services (CMS) panel of outside experts said large gaps in available data make it hard to weigh the impact particular RT options may have on patients, including possible death or side effects. But it was divided over how to collect much-needed information. There is "insufficient evidence across the board," said panel chairman Clifford Goodman, a senior vice president at the Lewin Group.

CMS, which oversees the Medicare insurance program for 45 million elderly and disabled Americas, is taking a closer look at such treatments at a time of great debate over how to treat the cancer that affects roughly more than 2 million men in the US. About 40 percent of Medicare patients are men. While the agency has no immediate plans to change its reimbursement rates for RT, it will weigh the advice and could use it to later revisit its payment policies. Any changes could impact device makers such as Accuray Inc, Siemens AG, TomoTherapy, and Varian Medical Systems.

Surgery, RT and simply "watchful waiting" are all possible courses of action. But researchers are increasingly concerned that excessive screening may be leading to over-aggressive treatment when studies show many prostate cancers grow so slowly that most men will die from other causes first.

CMS said reviewing all of the possible therapies would be too big a task for its advisers at one meeting. In looking just at RT, the advisers lamented the fact that just a handful of studies have been done and that most don't follow patients long-term for at least five years. Radiologists that use the treatments told the panel more data is being done. Panelists were split over whether strict, randomized controlled trials, patient registries and other types of informational gathering were most needed. Many urged various medical groups to band together to

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PROSTATE CANCER PROGRESSES MORE QUICKLY IN AFRICAN-AMERICAN MEN

Prostate cancer appears to transition from latent to aggressive disease sooner, and to grow more rapidly, in African-American (AA) men than in men of European-American ancestry, US researchers report in the May 2010 issue of the *Journal of Urology* (Vol. 183, pp. 1792-7, 2010). The study drew data from three sources: a collection of prostate specimens following autopsies, a radical prostatectomy (RP) database and a Detroit public health database.

Using these sources, Dr. Isaac J. Powell of Wayne State University School of Medicine in Detroit and colleagues found that although the average age at diagnosis did not differ between the two races, RP specimens from black men had greater cancer volume and higher Gleason grade. Prostate cancer was four times as likely to be advanced or metastatic in black as in white men.

Even after adjusting for socioeconomic disparity, treatment differences and less-aggressive screening, the incidence of prostate cancer was 60% greater among AA than European-American men, Dr. Powell stated. This difference is "based on genetic and biologic factors which may include lifestyle variations," Dr. Powell said, but he couldn't assign a percentage to any of the contributions to the increased incidence. Lifestyle factors that might contribute to the higher rate of prostate cancer among black men include obesity and diets high in fat.

Two commentaries, one by Dr. Stephen Freedland of Duke University Medical Center and another by Dr. James Mohler of the Roswell Park Cancer Institute, both emphasize the complexity of the factors underlying the racial disparity in prostate cancer incidence and mortality.

Dr. Freedland writes, "Although (the authors') contention that prostate cancer grows more rapidly and transforms earlier from latent to aggressive disease in AA men requires validation, it is undisputed that AA men bear a greater prostate cancer burden....Continued efforts to vigorously screen for prostate cancer and understand underlying reasons for more aggressive disease in AA men are desperately needed."

Reuters Health, 20 April 2010

MDV3100

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"Both of these drugs look promising," said William Dahut, MD, clinical director of the National Cancer Institute in Bethesda, MD, who co-wrote an accompanying editorial. In an interview with Medscape Oncology, he predicted that – if and when they reach the market – these drugs will be used in men who have progressed on hormonal therapy before they consider chemotherapy, pointing out that these new drugs are oral and are better tolerated.

Until recently, prostate cancer that progressed despite hormonal treatment was considered to be "hormone refractory," Dr. Dahut explained. However, this term has been changed to "hormone resistant," or castration-resistant, because there are men who respond to further hormone manipulation. But for those who are not responding, often the only remaining option has been chemotherapy with docetaxel, which has been shown to improve survival.

So far, there are no survival data for the new drugs, but results seen so far related to PSA levels and time to progression closely compare with those seen in older trials with docetaxel, Dr. Dahut said.

Both new drugs are now in phase 3 trials with a survival end point, and the hope is that they will show an increase in survival. These trials are being conducted in men who have progressed on chemotherapy – the patient population with the greatest medical need, Dr. Dahut explained. This is also the population in which an impact on survival (needed for regulatory approval) can be shown most quickly.

However, these are not the patients in whom these drugs are likely to be used in clinical practice, or in whom "they will work the best," Dr. Dahut said. The new agents are more likely to be used as an option in men who have progressed on hormonal therapy, before chemotherapy, he said.

Dr. Scher agreed, and pointed out that a trial in this chemotherapy-naïve population is already underway with abiraterone, and one with MDV3100 is planned to start soon. Dr. Dahut added that in the MDV3100 trial, where the PSA decline

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ASK DR. SNUFFY MYERS

Editors' note: In the spirit of information sharing, we have invited certain physicians and others to provide comments and opinions for Us TOO's *HotSheet.* It is our desire to enrich the content of the *HotSheet* to empower the reader. This piece contains the opinions and thoughts of its author and is not necessarily those of Us TOO International.

On what basis do you decide that a man is a good candidate for active surveillance for his prostate cancer? If so, what follow-up should the patient do?

I have delved into this question in great detail in two recent issues of my newsletter – Prostate Forum, Vol. 11, #9 and Vol. 11, #10. First, it is important to make sure your cancer is not too aggressive for active surveillance. At present, I think the best candidates have a Gleason 6 (3+3) that is less than one cm in diameter. I also want to make sure that the cancer does not approach or invade the prostate capsule. I also think the cancer should not be highly vascular.

Our typical work up at AIDP would include an endorectal MRI to make sure the cancer does not involve the capsule. We also like to have a color Doppler ultrasound done. This technique can tell us if the lesion is vascular. It also excels at finding lesions missed by endorectal MRI and routine transrectal ultrasound. About a quarter to a third of the patients we send for color Doppler ultrasound are found to have a higher grade or larger lesion missed by the other methods. The saturation biopsy has been advocated because it is also not likely to miss any high-grade cancer. While this certainly seems to be the case, it also causes significant side effects and I rarely recommend this at present.

There are several blood tests I think are important. At AIDP, we use the total and percent free PSA to both identify high-risk patients and to follow the impact of active surveillance. If the percent free PSA starts to increase toward normal (approaching 25%), repeat imaging studies will commonly show disappearance of the cancer. I like to include the serum prostatic acid phosphatase (PAP) as it tends to go up if the cancer has spread beyond the gland. Recently, a test has become available that can detect circulating prostate cancer cells. This is of considerable use in advanced disease. I am looking at it as a means of identifying high-risk prostate cancer.

Active surveillance should also include optimal health. I measure serum 25-hydroxyvitamin D levels and treat any vitamin D deficiency. I measure the dihydrotestosterone and discuss with the patient the value of suppressing this. I also recommend a Mediterranean heart-healthy diet. And I aim for an LDL cholesterol level below 100 and a systolic blood pressure less than 130.

DOC MOYAD'S WHAT WORKS & WHAT IS WORTHLESS COLUMN, ALSO KNOWN AS "NO BOGUS SCIENCE" COLUMN

"Provenge® gets FDA approved! My strike/boycott of my own column is officially over!"

Mark A. Moyad, MD, MPH,
University of Michigan Medical Center, Department of Urology

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Bottom Line: The FDA approved Provenge, and now it is time to pass some of the most important information on to you about this therapy. The company (Dendreon Incorporated) phone number that can help answer most of your immediate questions is 1-877-336-3736 (open Monday through Friday 8 AM to 11 PM Eastern Standard Time). Once you call the number there will be an initial recording that will tell you if you are a "health care provider… press 1" and if you are a "patient or caregiver… press 2". And, after this you get to talk to a real person that can answer many of your questions! The other choice is to go to <www.provenge.com> for more information.

I have very little to say here because I am almost speechless (okay, not really – I always have plenty to say). It was one of the best days of my life! I got a call from a patient advocate who said Provenge was approved! Wow! Wow spelled backwards.

I just want to first and foremost thank Tom Kirk, Jim Kiefert, Tom Farrington, Jan Manarite and her son Mico, Dr. Paul Schellhammer, my son Nicholas, my wife Mia, and all the other peaceful and wonderful rally members that were there on June 7, 2007 in Washington, DC. It took almost 3 years and another clinical trial, but the results came in and the FDA approved the product, and this is simply wonderful.

Am I bitter and upset that it took so long? No way! It was worth the fight, and I do believe that it changed the way cancer medications and human beings will be treated in the future. The one lesson on life is that when there is clear positive vote in 2007 that the drug is safe and efficacious, and it does NOT get approved in a clinical situation where patients and their families are desperate for anything, well of course there is going to be a potential controversy. There should have been an official statement, press conference, or logical and simple explanation for the non-approval that could have been transmitted to all advocacy groups, and to the patients. Us TOO and other groups would have welcomed and helped with this educational opportunity! This was one of the primary requests that we asked for in our private meeting in Washington DC in 2007. So, when this basic explanation that the patients deserved on some level did NOT occur there was a lot of confusion, sadness, and eventual anger that followed.

I hope that this is one of the biggest lessons that get passed on to the next generation. When a decision is being made by human beings, that seem so critical to the future of many other human lives, doesn't it seem to be just as critical for all of us to behave in a humane way, for the sake of humanity. Would this have been an acceptable way of handling things if this was a breast cancer, or AIDS drug for example, and the vote was overwhelmingly positive yet the medication was still delayed or rejected?

We were not really asking for immediate approval in 2007, just primarily an explanation of why the perception and reality of the Provenge decision by the FDA was so oppositely juxtaposed. Finally, I am just happy for the patients and their families, and I am appreciative for all those men and their families that volunteered for the Provenge clinical trials so that this day could be reached.

Thank you! Thank you! Thank you!

Reference:

Patient advocates and Us TOO

FDA SCRUTINY OF GNRH AGONISTS CONTINUES

Although an FDA safety review of the gonadotropin-releasing hormone (GnRH) agonist class of prostate cancer drugs has not yet been concluded, the agency is advising that the risks of these drugs be considered carefully before beginning treatment.

Risks include diabetes, myocardial infarction, stroke, and sudden death and were detailed this year in a joint advisory issued by the American Heart Association, the American Urological Association, and the American Cancer Society.

In a statement announcing its ongoing review, the agency recommended that physicians monitor patients on GnRH therapy for diabetes and cardiovascular disease and that they manage cardiovascular risk factors, including increases in blood pressure, cholesterol, blood sugar, weight, and smoking "according to current clinical practice."

GnRH agonist therapy is also used for some conditions in female and pediatric patients, but a comparative risk of side effects has not been studied or evaluated, the agency release noted.

In describing its review to date, the FDA noted that most of the observational studies done to date found small increased risks for diabetes and cardiovascular disease with GnRH agonists, the studies had limitations, including variable definitions of androgen deprivation therapy and cardiovascular disease, detection bias, missing data on risk factors, and limited information on drugs, doses, and dosing schedule.

GnRH agonists currently on the market include leuprolide acetate (Lupron®, Viadur®, Eligard®, and various generics), goserelin acetate (Zoladex®), triptorelin pamoate (Trelstar®), histrelin acetate (Vantas®), and nafarelin acetate (Synarel®).

MedPage Today, 3 May 2010

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DEGARELIX SHOWS PROMISE AS SECOND-LINE HORMONAL THERAPY FOR PATIENTS WITH PROSTATE CANCER

Degarelix, a new gonadotrophin-releasing hormone (GnRH) receptor blocker, could stabilize or reverse disease progression in men with prostate cancer after failure of GnRH agonist treatment, researchers reported at the 25th Annual European Association of Urology (EAU) Congress. Results showed that degarelix maintained PSA suppression and lowered levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), and testosterone. Kurt Miller MD, Department of Urology, Charité Universitätsmedizin Berlin, Berlin, Germany, discussed the 3-month results of an open-label, multicenter study exploring the utility of degarelix as second-line therapy for prostate cancer with signs of hormone resistance.

This study included 25 men with histologically-confirmed prostate cancer who had experienced PSA progression despite at least 1 year of GnRH agonist treatment. PSA progression was defined as 2 consecutive 50% rises in PSA above nadir at least 2 weeks apart and at least 1 PSA value of $\geq$2.5 ng/mL in the last 6 months of treatment. Most men had locally advanced (44%) or metastatic (28%) disease and a Gleason score of 7 to 10 (76%). Men received an initial dose of degarelix 240 mg followed by monthly maintenance doses of 80 mg, all given by subcutaneous injection.

Stabilization of PSA was defined no

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PCRI Announces the Search for the 2010 HARRY PINCHOT AWARDEE for Personal Dedication and Support to the Prostate Cancer Community

Harry lost his 13-year battle against prostate cancer in January 2008. In his honor, PCRI would like to recognize unsung heroes like Harry that are out there making a difference in other people's lives. Harry served on the staff at PCRI, and was an active and essential member of the Us TOO International Board of Directors.

Please visit <www.prostate-cancer.org/pcricms/node/384> for more info, or request a nomination form from PCRI at 1-800-641-PCRI.

BIOMARKERS PREDICT PROSTATE CANCER PROGRESSION

Researchers at Johns Hopkins have evaluated a simple, more specific blood test that identifies men undergoing proactive surveillance for low-grade, low-stage, non-palpable prostate cancer who would eventually require treatment. These results, presented at the American Association for Cancer Research 2010 Annual Meeting, may be a major advance in prostate cancer risk assessment.

"Finding biomarkers that can predict future unfavorable biopsy conversion will help us to identify men with prostate cancer who may or may not need treatment," said Robert W. Veltri, PhD, associate professor of urology and oncology and director of the Fisher Biorepository & Biomarker Laboratory at The Brady Urological Research Institute, Johns Hopkins Hospital, in Baltimore, MD.

Using the novel application of the Prostate Health Index immunoassay and DNA content measurements performed by image analysis, Veltri and colleagues tested 71 men enrolled in the Johns Hopkins Hospital Proactive Surveillance Program. They measured serum total PSA, free PSA and pro-PSA, performed a digital rectal examination semiannually and conducted a surveillance biopsy examination each year. The Prostate Health Index, developed by Beckman-Coulter, Inc., is a calculation involving at least three forms of PSA, one of which is pro-PSA.

Thirty-nine men developed an unfavorable biopsy, which is cancer progression defined as an increase in grade or tumor volume. The remaining men maintained favorable biopsies. Results showed that the level of Prostate Health Index was higher in men who were determined to have unfavorable biopsies, according to Veltri. Additionally, the researchers found that DNA content in biopsy tissue from the prostate gland next to the cancer area and area itself were significant predictors of a change from a favorable to an unfavorable biopsy in the men in the Proactive Surveillance Program.

"Our findings were slightly surprising; serum pro-PSA level by itself was not able to predict unfavorable biopsy conversion in our Proactive Surveillance Program," Veltri said. "However, Prostate Health Index, which incorporates pro-PSA, free PSA and total PSA in the index, was significant for predicting unfavorable biopsy conversion."

While PSA testing may be responsible for the decreasing US prostate cancer death rates, Veltri said the question is raised "are we over-diagnosing and over-treating prostate cancer?"

Several studies have indicated that between 35 and 50 percent of men diagnosed with prostate cancer using a PSA test have cancers that would not have been detected if a PSA test had not been performed. This is the case especially with low-grade, low-stage and non-palpable, small-volume prostate cancers.

Medical News Today, 20 April 2010

RT LACKS DATA

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compare all types of treatments, not just RT, to each other – also known as comparative effectiveness research.

"Given the paucity of evidence ... any evidence that can be gathered will be useful," said panel member Jeffrey Jarvik, a radiologist at the University of Washington. How that evidence impacts the potential for future payments is a particular concern for newer types of RT, such as Accuray's CyberKnife, that are not paid for by Medicare in some US states. Several prostate cancer patients from Oklahoma and Texas, two states that don't cover it, called on the panel to back such treatments.

Marcel Salive, head of the CMS's division that oversees prostate cancer coverage, said the agency would weigh the panel's advice as it decides whether further action is needed. But he added that the overall lack of data on RT would likely cause "a real difficulty in drawing conclusions" and make it tough to make any nation-wide coverage decisions.

Officials from Accuray did not speak at the meeting but have stated that they are concerned that CMS could reject payment for use of the Company's device in prostate cancer patients in the future.

Reuters, 21 April 2010

DISCUSSING PROVENGE WITH PROSTATE CANCER PATIENTS

Clinicians are likely to be hearing from patients about sipuleucel-T (Provenge, Dendreon), the immunotherapy that has just been approved by the US FDA for the treatment of metastatic castration-resistant prostate cancer (mCRPC). Media coverage has been widespread about both the approval and anticipation of the approval, with stories by many outlets.

Because of the news coverage and for other reasons, patient expectations might need to be dampened and some education provided, suggested Richard Greenberg, MD, chief of urologic oncology at Fox Chase Cancer Center in Philadelphia, PA. "It's not a home run," Dr. Greenberg told Medscape Oncology.

"The median improvement in survival was about 4 months, compared with placebo. That's not insignificant, but it's not a big change in the treatment of metastatic prostate cancer." The survival benefit with Provenge is not that much greater than the 2.4 month advantage with docetaxel (Taxotere®), he added. However, the survival benefit with Provenge comes with another advantage – less toxicity, Dr. Greenberg noted. "It's well tolerated."

"Patients may think that Provenge is like a vaccine for polio," said Dr. Greenberg. "It's not preventative or a cure – that must be communicated to patients," he said. "It's really not a vaccine. It's an immunotherapy," he added.

Another important point is that Provenge is only for men with metastatic disease who have progressed on hormonal therapy and, among those men, only those with asymptomatic or minimally symptomatic disease, said Dr. Greenberg. The best candidates for treatment are "appropriately selected" men – those with "good performance status" and a "low volume of bone involvement," he explained. "Those are the patients who do best with this treatment."

Dr. Greenberg believes that combination therapy with Provenge is likely. "I would imagine that Provenge will be used with chemotherapy agents in a multimodal approach in the future," he said. "If we are to get a major improvement in overall survival, it will be with a multimodal approach," he said, not referring to Provenge specifically.

Investment firm J.P. Morgan estimates that a full course of Provenge will cost $65,000; estimates by other analysts range from $50,000 to $100,000. It's a lot of money, said Dr. Greenberg, but comparable to the cost of using bevacizumab (Avastin®) and other targeted therapies used in other advanced cancers.

Money issues aside, Provenge will not be available to many men in the next year, according to the company Web site. The manufacturer, Dendreon, reports that the therapy will be available through approximately 50 centers, all of which were approved clinical trial sites. However, due to the manufacturing requirements for the autologous cellular immunotherapy, only 2000 men will be able to be treated in the first year. However, the company expects to increase capacity once licensure of facilities in New Jersey, Georgia, and California occur in mid-2011.

Medscape Medical News, 3 May 2010

PROVENGE FDA APPROVED

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domized to the immunotherapy or placebo. Treatment with sipuleucel-T improved median overall survival by 4.1 months compared with placebo (25.8 versus 21.7 months).

At a 2007 meeting, an FDA advisory committee recommended approval of sipuleucel-T, deciding in a 13-4 vote that sipuleucel-T is efficacious and agreeing unanimously on the agent's safety. However, the FDA is not bound by an advisory group's recommendations and decided instead to request more data from the manufacturer, Dendreon, of Seattle, WA.

In an interview with ABC News, David Penson, MD, from Vanderbilt University in Nashville, TN and an investigator in the sipuleucel-T pivotal trial, said the FDA had unresolved issues with earlier trial results because the biologic did not meet the primary endpoint of progression-free survival in some earlier trials.

Nonetheless, some patients treated with sipuleucel-T clearly lived longer than those treated with placebo. Results of the pivotal trial resolved the analysis issues seen in the earlier studies, he said.

MedPage Today, 29 April 2010

AS MAY NOT BE BEST

(Continued from page 1)

"First, the 44% upgrading rate in men whom we thought had slow growing disease represents men who never should have been placed on AS in the first place," he said. "Second, we demonstrated that we can eliminate the risk of missing an aggressive cancer by successfully treating these men with minimal compromise to their quality of life."

Recent studies have questioned the use of radical prostatectomy (RP) for all patients with prostate cancer, especially those with low-risk disease, in favor of AS, Dr. Samadi observed. At the same time, improvements in RP and radiotherapy techniques and perioperative management have decreased the morbidity of prostate cancer treatments.

Although AS has been shown to be a valid treatment option for patients with low-risk disease, clinically low-risk prostate cancer does not necessarily translate into indolent or insignificant disease on final pathology, he added. Given the difficulties of accurate preoperative staging and grading of prostate cancer, upgrading and upstaging are extremely common at the time of RP.

When discussing treatment options for men who are candidates for AS, it is important to be able to provide solid data on outcomes, both histopathologic and functional, following RP. This study was designed to provide such data to men deciding between RALP and AS.

Dr. Samadi presented data on 368 men deemed candidates for AS who were drawn from a "prospectively maintained" database of 1,249 RALPs. Men who were categorized as eligible for AS had a PSA below 10 ng/mL, a clinical

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DOCTOR CHODAK'S BOTTOM LINE

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After what seemed an endless delay, the FDA has approved Provenge for the treatment of men with hormone refractory prostate cancer. This is an exciting addition to the treatments for this disease and now gives men with prostate cancer a second option when hormone therapy is no longer effective.

Several key points are worth noting. First, it will only be suitable for men having progressive metastatic disease with no or minimal symptoms. The treatment can only be given by one of the 300 centers that enrolled men in the study, so men may have to travel to receive this therapy. The number of men who can be treated in the first year will be limited until new production facilities are available. A full course of therapy will cost about $90,000, which means that Medicare patients without secondary insurance may have trouble paying for it.

Lastly, although it definitely improves survival more than chemotherapy, it is not a home run; the average improvement in survival is about 4 months. The good news is that the treatment has far fewer side effects than chemotherapy and may become the first line of treatment for men failing hormone therapy.

The Bottom Line: Provenge offers men a novel way to treat progressive metastatic disease that is well tolerated.

The FDA has decided to review the side effects of GnRH (LHRH) therapy, specifically addressing the potential risk of cardiovascular disease and diabetes. A recent guideline from the American Heart association and the American Urological Association recommended that men be carefully monitored and risk factors for these diseases be addressed. The problem is that randomized studies of these medications have not shown an increased risk but uncontrolled, retrospective analyses suggest a cause and effect.

The Bottom Line: Hormone therapy like all treatments has pros and cons. This advisory does not mean men should stop their treatment, but more careful monitoring and checking for underlying heart disease is worth doing.

An interesting study was presented in Europe in which a small group of men were given the LHRH Antagonist, Degarelix after developing a rising PSA while receiving an LHRH agonist. The study found a drop in the PSA in some of these men. Until this study is published, it must be interpreted with caution.

The main issue has to do with what testosterone (T) level is needed for an LHRH agonist. There are some studies that suggest better results on hormone therapy when the T level is much lower than 50 ng/dL. Surgical castration drops the testosterone level to less than 20 ng/dL. If the T level is above 20 but less than 50, even surgical castration can lower the PSA level after an LHRH has been used. Studies also have shown that the PSA can drop by switching to a different LHRH agonist when the PSA is rising and the T level is not below 20 ng/dL.

The Bottom Line: Monitoring T is an important part of treating men with either an LHRH agonist or antagonist. If the PSA is rising and the T level is not below 20 ng/dL, trying another one of these drugs should be considered before moving on to some other therapy.

The full benefit of hormone therapy may not have been achieved yet. New drugs that block or lower male hormones appear to help men who have already been treated with an LHRH agonist or antagonist. One is MDV3100, which is discussed in this *HotSheet*. The latter drug has different results at different doses and now is ready to move on to further testing. The good news is that new therapies for advanced disease may become available in the next few years.

The Bottom Line: Men who progress while on LHRH therapy still can benefit from medications that also block male hormones. Randomized studies are now needed to find out the overall effect.

In previous columns, I have raised concerns about articles promoting different types of radiation for prostate cancer including Cyber knife and Proton Beam. The problem has been a lack of proof that these are better than less expensive alternatives. Now the Center for Medicare Services or CMS, which is responsible for deciding what therapies should be covered under Medicare, is conducting a review of the different radiation therapies it covers. This is an important project because the publicity surrounding these newer treatments has not been supported by a single study proving it is better.

The Bottom Line: Men considering newer forms of radiation therapy such as Cyber knife or Proton Beam should realize that long-term survival is not known. What happens to the PSA in 5-7 years is not a valid way to compare different forms of radiation.

The article by Powell and co-workers revisits a long-standing question; Does prostate cancer progress more rapidly in African-American (AA) men compared to Caucasians or do they just get diagnosed at a later time. Studies support both concepts. In this study, the authors found similar disease beginning at age 20 in autopsies of men without a diagnosis of prostate cancer but they found more advanced disease in men having radical prostatectomy in the Detroit area. There is no question that the death rate for AA men has been higher during the last 20 years but this study still does not clear up the exact cause. Nevertheless, the results do have important implications for Active Surveillance (AS).

The Bottom Line: There is a growing recognition that many men with prostate cancer are getting treated unnecessarily. A number of AS studies are in progress but the proportion of AA men in those studies is very low. Therefore, AA men should be very cautious about undergoing AS until more data is available.

As the popularity of AS increases, there is a great need to tell which cancers need to be treated. The study reported on men using several biomarkers may be one way to make this decision. The preliminary results are encouraging but much further research is needed.

The Bottom Line: New ways are needed to decide who is a good candidate to go on and stay on AS.

MDV3100

(Continued from page 3)

was similar in chemotherapy-naïve and chemotherapy-treated men, but the time to progression was greater in the chemotherapy-naïve group (41 vs. 21 weeks).

The editorial makes the point, however, that even this 21-week time to progression after chemotherapy is "clinically meaningful, particularly for a class of agents believed, until recently, to have no rationale whatsoever in this patient population."

MDV3100 is a very potent androgen receptor antagonist, lead author Dr. Scher told Medscape Oncology. It is also more specific than the older antiandrogens, such as flutamide (Eulexin®, Drogenil®) and bicalutamide (Casodex®), which have been and still are used in prostate cancer, usually with gonadotropin-releasing hormone agonists/antagonists, such as leuprolide (Lupron®) and goserelin (Zoladex®). However, these older antiandrogen compounds also have some agonist activity and have been found to stimulate prostate cancer growth in some men, Dr. Scher explained. This has not been seen with MDV3100, he noted.

Adapted from Medscape Medical News 15 April 2010

AS MAY NOT BE BEST

(Continued from page 6)

stage of T2A or below, and a biopsy Gleason score of 6 or less in 1 or 2 cores, with less than 50% tumor volume in a single core.

The study found that, on final histopathology, 147 AS candidates (40%) were upgraded from a Gleason 6 biopsy score to 3+4=7. Fifteen (4.1%) men were upgraded to 4+3=7, and 1 was upgraded to Gleason 8 or higher. Seventeen men (4.6%) were upstaged to pT3 or pT4 disease, and 12 of them were also upgraded.

Bilateral nerve-sparing was performed in 97% of patients. Follow-up of 221 patients at 12 months showed that 88% of men had recovered potency (potent preoperatively and having a Sexual Health Inventory for Men score of 16), and 95% were continent (meaning they needed 0 or 1 security pad per day).

Biochemical recurrence, defined as a PSA of 0.2 ng/mL at least 6 weeks after RALP, occurred in 1.6% of patients at a median follow-up of 13.9 months.

As for which men with prostate cancer should choose AS over RALP, Dr. Samadi said, "I think that AS is ideal for older men and those whose PSA doubling time and velocity are slow."

Medscape Medical News, 28 April 2010

DEGARELIX

(Continued from page 5)

more than a 10% relative change from baseline after 3 months of treatment. At month 1, there appeared to be 8 responders; however, 4 men (16%) achieved the primary endpoint. One man had castrate testosterone at screening but a borderline testosterone value and high LH at entry. A second responder had castrate testosterone but measurable LH at entry, while the remaining 2 responders had castrate testosterone and undetectable LH.

PSA doubling time was prolonged in 64% of men (n=14). LH levels became undetectable in 88% of men after the switch to degarelix. Levels of FSH and testosterone fell in 84% and 40% of men. Some men appeared to have responded after 3 months. A total of 60 adverse events were reported by 18 men (72%); most were mild (56%) or moderate (32%), and 1 man discontinued due to adverse events.

Funding for this study was provided by Ferring Pharmaceuticals.

"Open-Label, Exploratory Study of Degarelix as Second-Line Hormonal Therapy in Patients with Prostate Cancer," abstract 144, presented at the 2010 EAU Congress.

Doctor's Guide News, 20 April 2010

US TOO INTERNATIONAL: OUR MISSION

Be the leading prostate cancer organization helping men and their families make informed decisions about prostate cancer detection and treatment through support, education and advocacy.

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From Passion To Action : Us TOO at 20

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for Men and their Families Battling Prostate Cancer

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August 20 - 21, 2010
Chicago, Illinois

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From Passion To Action : Us TOO at 20

The UsTOO International Summit, Symposium & Celebration

for Men and their Families Battling Prostate Cancer

August 20 - 21, 2010 • Chicago, Illinois

This year, Us TOO International turns 20 years old, and the Us TOO Board of Directors has a vision to build on our anniversary with a celebratory symposium to bring prostate cancer awareness and action to the forefront in 2010.

We are all aware of the recent increased controversy in PSA screening, when to initiate prostate cancer treatment and research funding needs. Also very importantly, we can't forget that men in the baby boom generation are now reaching the "age of increased risk" for prostate cancer, with 70 million boomers now aged 46 to 65. More men than ever are being diagnosed with prostate cancer now, and will continue to be at an increasing rate over these next 20 years. What can we do to help guide and support them?

Here is our chance for the Us TOO network and brotherhood of survivors to take action and get involved! We invite you to our upcoming two-day, patient educational symposium, national advocacy summit, and anniversary celebration event:

"From Passion To Action: Us TOO at 20"

The Us TOO International Summit, Symposium & Celebration for Men and their Families Battling Prostate Cancer

to be held August 20-21, 2010 at the Hyatt Regency O'Hare (Rosemont, IL) in the Chicagoland area.

Learn and share information for yourself, your family, your community. Reconnect with old friends and meet new ones. Come to honor the men and women who have carried the Us TOO banner forward over the last 20 years, and join with them. Get involved with your brothers and families in the fight against prostate cancer.

Speakers

The educational symposium includes nine sessions over two days, with presentations by Damon Arnold, MD, Director, Illinois Department of Public Health; Michael J. Dattoli, MD; Mark Moyad, MD; John Mulhall, MD; Charles "Snuffy" Myers, MD; Paul Schellhammer, MD; Captain E. Millissa Kaime, MD, Director of the Congressionally Directed Medical Research Programs; Jonathan McDermed, PharmD, Us TOO HotSheet newsletter co-editor and Director, Scientific & Clinical Affairs at IRIS Diagnostics; and a survivor and his wife, David and Kathie Houchens.

Us TOO University
Learn. Laugh. Lead.

Exhibits

The Friday Exhibits will feature informational displays from vendors, non-profit organizations and a "Meet the Authors" area where attendees can speak with and purchase prostate cancer and prostate health-related publications.

Attendees

Event attendees will include men and their families responding to a prostate cancer diagnosis or recurrence, local Us TOO affiliated chapter support group leaders and other volunteers from around the country, Us TOO International Board members and other leadership, interested medical professionals, supporters and collaborators from the non-profit and for-profit prostate cancer communities, and anyone who has had a special connection to Us TOO International over our last 20 years.

...continued

Summit

A highlight of the event will be the **ADVOCACY SUMMIT: *Moving Beyond the Confusion About Prostate Cancer Screening and Treatment*, to be held on Friday, August 20, 2010 from 10:00 am to 1:30 pm**. The summit provides the opportunity for survivors and family members, Us TOO leaders and volunteers, and representatives from the prostate cancer non-profit community to discuss common ground and next steps in the national debate surrounding prostate cancer screening and treatment.

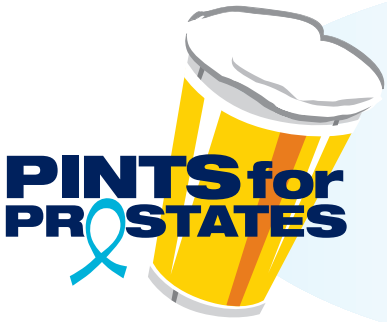
The summit will be facilitated to assure open discussion from panelists and the audience. One expected outcome will be the creation of an Us TOO International position statement on early detection, screening and treatment for prostate cancer – from the patients' perspective.

The agenda will include a presentation on plans for imaging advancements to improve prostate cancer diagnostic and treatment tools by Faina Shtern, MD, President and CEO, AdMeTech Foundation, an update of NCCN Clinical Practice Guidelines in Oncology for Prostate Cancer by James L. Mohler, MD, of Roswell Park Cancer Institute and chair of the NCCN Guidelines Panel for Prostate Cancer, and othe invited presenters from the American Cancer Society and the American Urological Association. Representatives from other prostate cancer non-profits making up America's Prostate Cancer Organizations will also be invited to participate.

20th Anniversary Celebration & Awards Dinner!

The Friday night **20th Anniversary Celebration & Awards Dinner** will provide a platform to recognize the progress Us TOO has seen in the last 20 years, celebrate the contributions of our volunteers, and promote the opportunities Us TOO has in store for the future. A panel discussion of past and present Us TOO International leaders will be featured, including moderator Fred Mills, current Us TOO International Chairman of the Board, past chairmen Edward C. Kaps, Lew Musgrove, Jim Kiefert, and founding physician Gerald Chodak MD. All event attendees and dinner guests are asked to bring a blue item for the **Us TOO *True Blue* Fundraiser Raffle**.

US TOO® 1990-2010
20 Years of Peer Support & Education
Moving Forward the SEA Blue Campaign



The Symposium ends with an exciting and casual

Pints for Prostates

Beer Tasting Fundraising Event on Saturday Evening from 5:30 – 8:00 pm.

All proceeds benefit Us TOO International.

Register Now!

Us TOO Summit, Symposium & Celebration for Men and their Families Battling Prostate Cancer

August 20-21, 2010 • Hyatt Regency O'Hare, Rosemont, IL

See **www.ustoo.org/2010symposium** for details

Register by August 6, 2010 and SAVE!

Questions? Call **1-800-80-UsTOO (1-800-808-7866)**

We hope to see you in Chicago this summer!

...And DON'T FORGET!

All event attendees and dinner guests are asked to ***bring a blue item*** *for our fun*

Us TOO *True Blue* Fundraiser Raffle

Friday night!

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AUGUST 20 - 21, 2010 • CHICAGO, ILLINOIS

Registration Form

Name_____

Phone Number (_____)_____ Email _____

If you are purchasing more than one ticket, please write the name(s) of the person(s), other than yourself, that will be attending:

_____

_____

Event	Before Aug. 6th	Qty.	After Aug. 6th	Qty.	Sub Total
Advocacy Summit.....	$10		$15		
Us TOO University Education Symposium - Friday Only.....	$30		$35		
Us TOO University Education Symposium - Saturday Only.....	$40		$45		
Us TOO University Education Symposium - Friday & Saturday....	$50		$75		
Us TOO's 20th Anniversary Celebration & Dinner - Friday.....	$50		$50		
Pints for Prostates Beer Tasting Event - Saturday.....	$50		$50		
If you cannot attend the Symposium, but would like to make a donation to Us TOO in honor of our 20th Anniversary please indicate Your Additional Tax Deductible Donation to Us TOO: $_____ **Total Paid**:_____					

❑ Check enclosed, made payable to: **Us TOO International**

❑ CREDIT CARD *(please circle one)* Visa Diners Club Discover American Express Mastercard

Name *(as it appears on the card)*_____

Organization_____

Billing Address _____

City_____ State_____ ZIP _____

Credit Card Number _____

Verification Code *(3 or 4 digit number)*_____ Expiration Date _____

Signature_____Date _____

Please select any/all that apply:

❑ I am a Patient/Survivor

❑ I am a Family Member of a Patient/Survivor

❑ I am a Friend of a Patient/Survivor

❑ I am representing my Chapter Support Group at this event:_____

❑ I want to help men and their families diagnosed with prostate cancer in my community

❑ I want to conduct an awareness/fundraiser project for Us TOO International in my community

❑ I will bring a blue item for the Friday raffle:_____

To register by mail send this form and your payment to: Us TOO International, 5003 Fairview Ave., Downers Grove, IL 60515-5286

You can also fax in this form: Fax **1-630-795-1602** • **Register online at: www.ustoo.org/2010symposium**

Questions? Call **1-800-808-7866** • **Advance discounted registration ends: August 6, 2010**