Us TOO® PROSTATE CANCER EDUCATION & SUPPORT

HOTSHEET

JANUARY 2011

US TOO BOARD WELCOMES NEW MEMBER

The Us TOO International Board of Directors welcomed another new member at their most recent meeting, held December 3-4, 2010 in Chicago IL – John D. Shaff, Jr.

Mr. Shaff is a prostate cancer survivor having radical prostatectomy in 2005. Since then, he has been involved in the OHSU Prostate Cancer Support and Advocacy Groups and is now a Consumer Reviewer for the Department of Defense Prostate Cancer Research Program.

He served for 30 years in the US Public Health Service where he worked in a number of states, first with the Indian Health Service as a Hospital Adminis-

(Continued on page 6)

John D. Shaff, Jr., New Director

FDA APPROVES XGEVA® TO HELP PREVENT CANCER-RELATED BONE INJURY

The US Food and Drug Administration approved Xgeva (denosumab) in later November to help prevent skeletal-related events (SREs) in patients with cancer that has spread (metastasized) and damaged the bone. SREs include bone fractures from cancer and bone pain requiring radiation.

Xgeva is a monoclonal antibody that targets a protein involved in cancer-related bone destruction called human RANKL. Other FDA-approved drugs for similar conditions include Zometa® (zoledronic acid) and Aredia® (pamidronate disodium). Xgeva is not approved for patients with multiple myeloma or other cancers of the blood.

"Bone metastases represent a major cause of pain and suffering in patients with cancer and can affect a patient's quality of life," said Richard Pazdur, MD, director of the Office of Oncology Drug Products in the FDA's Center for Drug Evaluation and Research. "Xgeva has a different mechanism of action than currently approved drugs aimed at reducing bone complications from cancer."

Xgeva's safety and effectiveness were confirmed in three randomized, double-blind clinical studies in 5,723 patients comparing Xgeva with Zometa. One study involved patients with breast can-

(Continued on page 5)

US PANEL BACKS DENDREON'S PROVENGE® FOR MEDICARE

A US advisory panel backed Dendreon Corp's Provenge prostate cancer therapy on Wednesday, telling the Medicare insurance program for the elderly that available data showed it could help patients. A majority of the outside advisers said there was enough evidence to show that Dendreon's therapeutic vaccine helped patients live longer. The agency is weighing whether to pay for the product nationwide.

"We have some pretty good evidence here," said the panel's chairman, Lewin Group Senior Vice President Clifford Goodman. But he said the evidence is "not really wide, it's not really deep, so much work is needed to collect" more data. Centers for Medicare and Medicaid Services (CMS) officials will take the panel's advice into account in making a final ruling, expected next year. Their decision is not only critical for patients but also for Provenge sales, which could reach $1.9 billion by 2014, according to Thomson Reuters.

JP Morgan analyst Cory Kasimov said the panel's assessment "was a clear positive" for Dendreon. "It's increasingly clear that CMS will cover Provenge" for approved uses, Kasimov wrote in a research note. "Investors should take a significant amount of comfort."

(Continued on page 4)

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FDA PANEL REJECTS PROSTATE DRUGS FOR CA PREVENTION

An FDA advisory panel has voted overwhelmingly that GlaxoSmithKline's dutasteride (Avodart®) and Merck's finasteride (Proscar®) should not be used to prevent prostate cancer because the drugs are linked to a higher incidence of high-grade tumors. The FDA's Oncologic Drugs Advisory Committee voted 17-0, with one member abstaining, that the risks outweigh the benefits of finasteride; and 14-2, with two members abstaining, that the risks of dutasteride outweigh the benefits.

FDA is not required to follow the advice of its advisory committees, but it often does. If approved to prevent cancer, the drugs could potentially be given to hundreds of thousands of otherwise healthy men with elevated PSAs who are concerned about dying from prostate cancer.

That means "we [would] use this to treat men – not patients – men who don't have a disease," said Richard Padzur, MD, director of oncology drugs at FDA.

Dutasteride and finasteride are currently approved to treat benign prostatic hypertrophy, or an enlarged prostate. GlaxoSmithKline is seeking to expand dutasteride's indication to include reducing the risk of prostate cancer in men who have had a prior negative biopsy, and who have an elevated PSA. Merck isn't seeking an expanded indication, but the company would like the label of finasteride to detail positive results of the Prostate Cancer Prevention Trial (PCPT), which demonstrated the drug's chemopreventive potential.

How to handle low-grade prostate cancer is controversial in the urology community, in part because it is unknown if the low-grade tumors would ever develop into high-grade tumors, and also because the method used to originally detect prostate cancer – the PSA test – is inexact.

The panel agreed that a reduction in the less-risky tumors – which may never even turn into serious cancers – is not a big enough benefit if the drugs may actually lead to life-threatening cancers. In addition, the standards need to be much higher for a chemopreventive agent. Both GlaxoSmithKline and Merck argued at the meeting that their trials didn't show the drugs lead to serious prostate cancers and offered other explanations for the higher number of high-grade cancers in the treatment arms.

If the drugs were intended to treat terminal cancer patients, some risks might be tolerated, said Patrick Walsh, MD, a urologist who has studied 5-alpha reductase inhibitors for 40 years. "If you're going to give normally healthy people a drug, there need to be no side effects," said Walsh, who was brought in by the FDA as a guest speaker.

The panel spent much of Wednesday discussing the Reduction by Dutasteride of Prostate Cancer Events (REDUCE) trial, which randomized 8,200 high-risk men ages 50 to 75 from 250 sites in 42 countries to receive either dutasteride or placebo. The men took dutasteride daily for four years and had prostate biopsies at two years and at the end of the study. REDUCE found that men assigned to dutasteride had a 23% lower risk of being diagnosed with biopsy-detectable prostate cancer when compared with men on placebo ($P<0.0001$).

The panel agreed with an earlier FDA assessment that the reduction in cancer risk was driven by a reduction in low-risk cancers. "This study met an unneed," said panelist Patrick Loehrer, MD, an oncologist who is the director of the Melvin and Bren Simon Cancer Center at Indiana University. "It decreased the risk of low-grade cancers."

The panel also examined data from Merck's Prostate Cancer Prevention Trial (PCPT) which randomized nearly 19,000 healthy men over 55 to receive finasteride or placebo. At the end of the PCPT, 9,060 men had prostate needle biopsy data available for analysis, and prostate cancer was detected in 803 (18.4%) men receiving finasteride and 1,147 (24.4%) men receiving placebo.

Taken together, data from both trials showed the 5 alpha-reductase inhibitors both provided a statistically significant reduction in the cumulative incidence of prostate cancer after four years (REDUCE) and seven years (PCPT) of treatment with dutasteride and finasteride, respectively.

(Continued on page 5)

COULD A PROSTATE CANCER TREATMENT RAISE COLON CANCER RISK?

Study finds link between hormone therapy, colorectal tumors, but absolute risk is small, experts say

Men taking androgen deprivation therapy (ADT) for prostate cancer may have a slightly increased risk of developing colorectal cancer, a new study published online 10 November 2010 ahead of print in the *Journal of the National Cancer Institute* suggests. The researchers say ADT is often prescribed to treat prostate cancer, but its use in treating low-risk cancer is controversial, because diabetes and obesity, two potential side effects, are risk factors for colorectal cancer.

"We found that the use of ADT, either through injections or through surgical castration, for prostate cancer was associated with a 30 to 40 percent increase in risk for colorectal cancer," said lead researcher Dr. Vahakn B. Shahinian, an assistant professor of internal medicine at the University of Michigan. Shahinian noted that the absolute risk of developing colorectal cancer because of ADT is very small. "Over a five-year period, I would say there would be no more than a 2.5 percent absolute risk of developing colorectal cancer," he said.

ADT's value in treating late-stage prostate cancer that has metastasized is well-grounded, Shahinian said. And when combined with radiation, it is considered beneficial for treating locally advanced prostate cancer, he added. But as primary therapy in lower-risk or localized tumors, he disagrees. "A lot of men are getting it in settings where they just have a biochemical recurrence of their tumor, so they just have an elevated PSA, but are otherwise doing fine – that's a scenario where there isn't a proven benefit," he said.

Shahinian and colleagues used data from the Surveillance, Epidemiology, and End Results database of the US National Cancer Institute. They identified 107,859 men aged 67 years or older diagnosed with prostate cancer between 1993 and 2002, and followed-up through 2004. Investigators found a 30

(Continued on page 5)

PROSTATE CANCER STAGING CAN'T PREDICT RECURRENCE

One of the first things that a man wants to know after he has been diagnosed with prostate cancer is the cancer's stage, which is supposed to indicate the extent of the disease and help predict the likelihood of recurrence after treatment. But when it comes to localized or non-spreading prostate cancer, staging may not be an important predictor of recurrence after the prostate gland is removed, a study published online in the journal *Cancer* shows.

Localized prostate cancer is staged as T1-T2, but there are several problems with the system. The stage is based on your doctor's estimate of the extent of the prostate cancer. This assessment is based on the results of a physical exam, lab tests, biopsy, and imaging tests.

In the new study, researchers analyzed data on 3,875 men who were diagnosed with localized prostate cancer at 40 urology practices between 1995 and 2008. They found that doctors improperly staged the cancer 35.4% of the time. Even after researchers corrected for these inaccuracies, the stage still did not correlate with risk of recurrence after removal of the gland, a procedure called radical prostatectomy (RP).

"There appear to be several problems with our current clinical staging criteria for prostate cancer," explains study researcher Adam Reese, MD, chief urology resident at the University of California, San Francisco. But "there are several other variables available to the practitioner at the time of diagnosis which are strongly associated with prostate cancer recurrence after RP," he says.

These variables include PSA levels, the tumor's Gleason score or grade and the percent of positive biopsy cores or the number of cancerous cells taken during the prostate biopsy. "These variables seem to be more powerful predictors of recurrence than clinical stage," Reese says. "These data should be emphasized in preoperative counseling and less weight should be placed on clinical stage data," he says.

"We don't have a good way of staging localized prostate cancer," says Reza Ghavamian, MD, director of the prostate cancer program at the Montefiore-Einstein Center for Cancer Care and director of urologic oncology and robotic urology at Montefiore Medical Center in New York. "There are more important predictors of prostate cancer outcome including PSA level, Gleason score, and positive biopsy samples," he says.

Clinical stage is still important for prostate cancers that have spread outside of the prostate gland, he tells WebMD.

"Some patients say, 'What stage am I?' and we usually tell them that they have local disease or that their chances of a spreading cancer are such and such," he says.

One of the issues with staging is the lack of a good way to capture images of the prostate, he says. "Ultrasounds are not a very accurate way of visualizing the prostate," he says. "You can't do an ultrasound and say 'you have prostate cancer,'" he says. Most urologists use transrectal ultrasound to direct the needle during biopsy, he says.

Digital rectal exams (DRE) are also very subjective, he says. During a DRE, your doctor uses a finger to feel for lumps or enlarged areas that could suggest prostate cancer. "Some doctors may feel something subtle and some may not," he says. "These tests are subject to tremendous intraobserver variability and the assignment of clinical stage is fraught with difficulty."

American Cancer Society Chief Medical Officer Otis W. Brawley, MD, says it can be hard to determine which localized prostate cancers will recur. "There are some small localized prostate cancers where some of the disease has already broken off and moved outside the body to the bones, and there are some large localized prostate cancers where some of the disease has not moved off to bone and will never move off to bone and cause harm," he says.

The issue is that doctors don't know how to predict which way the tumors will go, he says. What is really needed is a genetic screening test that can tell whether or not this tumor is likely to spread or stay put, he says.

WebMD Health News, 22 November 2010

LONG TERM EFFECT OF EARLY POSTOPERATIVE PELVIC FLOOR BIOFEEDBACK ON CONTINENCE IN MEN UNDERGOING RADICAL PROSTATECTOMY (RP)

One of the primary treatment options for men with prostate cancer is RP, either done via an abdominal incision or a minimally-invasive approach. Before deciding to undergo any type of surgical approach, patients often are concerned about the risks for postoperative urinary incontinence and erectile dysfunction. Dr. Ribeiro and colleagues evaluated the impact of early postoperative pelvic floor biofeedback to minimize incontinence in patients undergoing RP.[1]

Of 122 patients screened, a total of 73 patients were randomly assigned to 2 groups after RP. The 2 groups included a control group of 37 patients and a treatment group of 36 patients who received biofeedback-pelvic floor muscle training (BFB-PFMT). The intervention was initiated after catheter removal 15 days post-RP and continued weekly for as long as patients were incontinent up to 12 weeks. Sessions lasted 30 minutes and included verbal and written instruction, as well as electromyography to aid the patient in identifying the proper muscle bodies. During these sessions, patients practiced 3 series of 10 rapid pelvic floor contractions, sustained up to 10 seconds and performed during prolonged expiration, avoiding a Valsalva maneuver. Patients in the control group received only a brief instruction from their urologists on how to contract the pelvic floor and nothing else. The average number of sessions in the treatment group was 8.8.

Fifty-four patients (28 controls, 26 treated) completed study. All 19 patients who dropped out did so in the first month because they could not attend follow-up visits. Patients were evaluated at baseline and at 1, 3, 6, and 12 months after urinary catheter removal. The primary outcome was continence, defined as using no more than 1 pad per day. Continence severity was defined using a 24-hour pad test: mild (less than 20 g leakage), moderate (between 21 and 74 g leakage), and severe (greater than 75 g leakage).

The results clearly showed an advantage in the treatment arm. At 12 months, continence rates were 96% for the treatment group and 75% for the control group (P=0.028). This resulted in an absolute risk reduction of 21.2%. In addition, the intervention was associated with a shorter duration of incontinence, with a median duration of 1 month in the treatment group compared with 6 months in the control group. Median pad weights and percentage of patients with severe incontinence improved with time in both groups and were significantly higher in the control group (P=0.017 for severe incontinence, P <0.001 for pad weight). Looking specifically at the number of patients who were classified as being severely incontinent, the treatment group was superior to the control arm with rates of 27% vs. 69% at 1 month, 15% vs. 43% at 3 months, 4% vs. 32% at 6 months, and 0% vs. 18% at 12 months.

Viewpoint by David Ginsberg, MD

This article nicely reviews the authors' experience and provides a good review of the literature on this subject. Previous research has provided mixed results. Questions in the past have included: does this therapy actually help improve continence? Does it only achieve continence sooner but the end result is the same? Can BFB-PFMT minimize the severity of incontinence if the continent state cannot be achieved?

This was a well-done trial in that the control patients were true controls; older studies provided significant interaction with a nurse or physiotherapist, which can influenced the quality of the data. The investigators state that the treatment schedule was simple and it is possible that a more intense or longer regimen could lead to even better results. An important point to take home is that BFB-PFMT is minimally invasive. This is not a surgical intervention, and it has no side effects like those that can be seen with medications. With this risk-benefit ratio, this is clearly a nice option to attempt to maximize post-RP continence.

Reference:

1. Ribeiro LH, Prota C, Gomes CM, et al, *J Urol* 184:1034-9, 2010

Medscape, 11 November 2010

US PANEL BACKS DENDREON'S PROVENGE FOR MEDICARE *(Continued from page 1)*

Medicare coverage could also encourage more private insurers to follow suit. Aetna Inc, Humana Inc and several other health insurers have already agreed to pay for the vaccine, which does not prevent cancer but fights the tumors. Patients, doctors and the company urged Medicare's advisers to support their pleas to have the federal government pay for the treatment regardless of its hefty price tag.

"This is a new agent that is clearly beneficial for patients," said Dr. Mark Scholz, a California-based prostate oncologist and one of nearly two dozen public speakers urging the Medicare panel's support.

Provenge was approved for the US market in April to treat men with advanced prostate cancer after company data showed it helped men live another 4.1 months on average. It costs $93,000 for three infusions given over the course of about one month. While many cancer therapies are also expensive, their costs are spread out over more time or are stopped when they do not seem to be helping. While the FDA approved Provenge as safe and effective, CMS is deciding whether its use is "reasonable and appropriate." By law, it cannot consider cost in that decision.

Dendreon says the high price reflects a unique manufacturing process that takes cells from a patient's tumor, mixes them with some of the patient's own immune cells and then infuses the cells back into the patient to attack malignant cells.

At the meeting, Medicare's advisers said they were fairly confident in Provenge's effect on survival, but were less sure over whether it helped patients avoid side effects and other treatment issues. They told CMS they had less confidence in wider uses not approved by the Food and Drug Administration. They also urged Medicare to collect more data as part of its payment decision to learn more about the therapy's use.

In a statement after the meeting, Dendreon said patients can still get Provenge from regional Medicare contractors until CMS makes its national decision. It was not immediately clear how much of a co-pay Medicare patients would face even if CMS covers Provenge.

Reuters, 17 November 2010

ADT & COLON CANCER

(Continued from page 3)

to 40 percent relative increase in the rate of colorectal cancer among the men who received ADT compared with those who did not. The longer the men received ADT, the greater was their risk of developing colorectal cancer. The highest risk was seen in men who had their testicles removed.

Jennifer H. Lin, an instructor in preventive medicine at Brigham and Women's Hospital in Boston and co-author of a journal editorial, said this is the first large observational study showing that androgens may prevent colorectal cancer development in men. Earlier research has shown that hormone replacement therapy lowers the risk for colorectal cancer in postmenopausal women, she added. "Obesity is an important risk factor, especially in men, for colorectal cancer development," she added. "Obese men also tend to have lower androgen levels, suggesting a potential role of androgens in colorectal cancer development."

The findings support the need for routine screening for colorectal cancer and the adoption of lifestyle practices, such as physical activity, to help prevent colorectal cancer, she said. "This is especially important among prostate cancer patients who undergo anti-androgen therapies," Lin stressed.

Dr. Anthony D'Amico, a prostate cancer expert at Brigham and Women's Hospital, sees the study results differently. "This is a classic example of true, true and unrelated," he said. Many men diagnosed with prostate cancer get screened for colorectal cancer for the first time, so cancers are picked up because of screening that has nothing to do with treatment, he said.

"To discern if this is a real effect or not, the researchers would have to assess the intervals of colorectal screening in the men who got long-term hormones or prostatectomy or none. I'll bet you'll find that the incidences of this are affected by the fact that most of them are having their screening for the first time," D'Amico said.

"So I am not convinced," he added.

HealthDay News, 10 November 2010

XYGEVA FDA APPROVED *(Continued from page 1)*

cer, another in patients with prostate cancer, and a third included patients with a variety of other cancers. The studies were designed to measure the time until occurrence of a fracture or spinal cord compression due to cancer or until radiation or surgery for control of bone pain was needed.

In patients with breast or prostate cancers, Xgeva was superior to Zometa in delaying SREs. In men with prostate cancer, the median time to an SRE was 21 months with Xgeva compared to 17 months with Zometa. In patients with breast cancer, the median time to an SRE was 26 months with Zometa and has not yet been reached with Xgeva. In patients with other solid tumors, time to development of an SRE was similar for both Xgeva and Zometa. The most common solid tumors were non-small cell lung cancer, multiple myeloma, kidney (renal) cancer, and small cell lung cancer.

The most serious side effects experienced with Xgeva were low calcium levels in the blood (hypocalcemia), and osteonecrosis of the jaw, a severe disease resulting from reduced blood flow to areas of the jaw and exposed jaw bone, causing pain, swelling, numbness, or infection.

Denosumab was originally approved under another trade name, Prolia®, in June 2010. Prolia is indicated to treat postmenopausal women with osteoporosis who are at high risk for bone fractures. Xgeva is administered using a higher dose and with more frequent dosing than Prolia. Denosumab has a different safety profile in patients with osteoporosis than in patients with cancer and bone metastases.

Xgeva is marketed by Thousand Oaks, Calif.-based Amgen.

FDA news release, 19 November 2010

PANEL REJECTS DRUGS FOR PROSTATE CA PREVENTION

(Continued from page 2)

Both trials also found an unexpected increase in the incidence of high-risk prostate cancers among men receiving the 5-alpha reductase inhibitors. In the REDUCE trial, 29 high-grade tumors were found among patients being treated with dutasteride compared with 19 in the placebo group. In the PCPT, there was a 26% decrease in all prostate cancers but an absolute increase of 1.3% in the incidence of high-grade tumors.

According to an FDA statistician, if 200 men are treated with the drugs, it is expected that there will be one additional tumor with a Gleason score of eight to 10. And the benefit didn't appear great when boiled down to a statistical snippet: 60 men would need to be treated with one of the 5 alpha-reductase inhibitors in order for one man to avoid developing a clinically relevant prostate cancer, the statistician said.

In a prepared statement, GlaxoSmith-Kline expressed disappointment with the panel's decision on dutasteride and said it would work with the FDA to answer any questions as the FDA completes its review of the drug.

MedPage Today, 1 December 2010

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. The columns by Drs. Chodak, Moyad and Myers contain the opinions and thoughts of its author and is not necessarily those of Us TOO International.

ASK DOCTOR SNUFFY MYERS

I was diagnosed with a Gleason 8 prostate cancer that was still contained within the prostate gland. I have been treated with radiation therapy and two years of Lupron. It has been a year since Lupron stopped and my testosterone is only up to 250 ng/dL. While I get erections, they are not firm enough for intercourse. Also, my sex drive is not as good as it once was. My wife and I miss the good times we used to have. Is there anything that we can do to improve things?

This is a very common problem. There are a number of things to consider. Cialis, Levitra, and Viagra work quite well after radiation therapy. In this setting, the best results come from a Monday, Wednesday, Friday schedule. We have found that many insurance companies respond favorably when we appeal based on penile rehabilitation. After one year of this, many men can then sustain themselves with less frequent medication.

Nitric oxide release is the trigger for erections — this drug works by increasing the sensitivity of the penis to nitric oxide. Nitric oxide is produced from arginine and taking 2,000 to 3,000 mg of arginine twice a day will often make the Viagra-class drugs more active.

Low testosterone is one of the major causes of failure for Viagra-class drugs. The reason for this is that the production of nitric oxide lessens as the testosterone levels fall. So, it is important to know why your testosterone has not recovered. In your case, several different things could be going on. Luteinizing hormone (LH) is released from the brain and instructs the testes to produce testosterone. Lupron works by suppressing LH release. Recovery of LH production is often incomplete after hormonal therapy ends. The testes use DHEA to synthesize testosterone and adrenal production of this hormone falls dramatically during hormonal therapy. After hormonal therapy is over, its recovery may be incomplete. If this is the case, oral DHEA can improve testosterone production. Finally, the testes may receive scattered radiation from prostate cancer treatment. The testes are very sensitive to radiation and this can cause a decrease in testosterone production.

I treat aggressive prostate cancer and use intermittent hormonal therapy. We routinely monitor serum testosterone and I find that prostate cancer growth rates are generally maximal by the time testosterone levels hit the 250 ng/dL level. Increasing testosterone from 250 to 800 ng/dL will not usually cause a further increase in PSA doubling times. However, your quality of life and sexual function will be much better at a higher testosterone level. Additionally, you will be better able to benefit from Viagra-class drugs. At my clinic, AIDP, we would likely be talking to you about the benefits of testosterone supplementation.

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

"Can dogs smell more than the mid-lower front, or backside of a human body?"

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

Bottom Line:

Recent research has shown that some trained dogs can detect bladder cancer, and now a new study shows that they may be able to detect prostate cancer.

We lost to Ohio State again! The world is going to the dogs! And, speaking of dogs (how did you like that smooth transition into my column???)…well you probably heard a story last year of how some trained dogs were able to detect bladder cancer from urine samples, and this was an interesting medical study.

Now comes a research study out of France that took a dog and trained it for 2.5 years to detect prostate cancer from the smell of urine. Out of 33 samples with cancer, it could detect 30 of them, for a detection rate better than conventional medicine! In addition, in the 3 patients that the doggie was wrong the patients were rebiopsied and one was found to actually have prostate cancer. Wow! This dog appears more impressive than Old Yeller, Lassie, and Benji combined! And, the dog only had 30 seconds to find the cancer because it was given 6 urine samples to smell and only 1 would have cancer during each test.

So, if dogs can perhaps smell bladder cancer, explosives and find drugs at airports and can locate squirrels in the backyard, is it such a stretch to believe that they can also find some compounds in prostate cancer that can be found in the urine? Probably not, because there may be a host of volatile organic compounds in the urine that are released as a prostate tumor grows. So, this is the interesting part, which is dogs may help humans find compounds unique to cancer that can be used along with the PSA test one day.

So, the next time your dog licks itself for a long time in front of your dinner party guests, or jams his/her nose into your friends' crotch or buttocks for a long period of time, please please please remind those embarrassed folks that your dog is only trying to determine if someone in the house has cancer. Now you know why they really call the dog "Man's best friend!" And, now you know the rest of the story… "This is Paul Harvey…Good Day…"

Reference:

Cornu J-N, Sèbe P, Ciofu C, et al. *Eur Urol* 15 October 2010; Epub ahead of print

NEW BOD MEMBER

(Continued from page 1)

trator (MHA University of Minnesota) and then with the Facilities Construction Program (Hill-Burton Program) as a Public Heath Advisor. He has extensive experience in both acute hospitals and in primary care settings, especially those found in community health centers in both rural and culturally diverse areas of the country.

Before his retirement in 1996, he graduated with an Associate of Science in Occupational Therapy from Sacramento City College. During the last 14 years, he worked as a occupational therapist in various rehabilitation departments in long term care facilities, including one in Hilo, HI specializing in Alzheimer's disease. He also worked in school health programs in Davis, CA, where he lived for 25 years and raised three daughters.

DOCTOR CHODAK'S BOTTOM LINE

This month's *HotSheet* gives us some interesting questions to address. First, two articles about Provenge force us all to face difficult questions about the benefit and costs of our health care. Fair evidence indicates that Provenge increases survival by about 4 months. At a cost of $93000, that translates into about $360,000 for one year of life. Is that too much? Is any price worth paying to help someone or is there some dollar amount that does not justify the cost of treatment? If our health care dollars are indeed limited, could that amount help many more individuals if used for a different purpose? These questions are not easily answered but they do need to be addressed unless we either raise taxes or find a different way to pay for our exploding health care costs.

The Bottom Line: Cost cannot be taken out of the equation when deciding if medical treatments are worth the cost. At some point, we must face the fact that certain treatments are just too expensive. Fortunately for men with prostate cancer, for now Provenge is likely to be paid by Medicare.

An important article addresses post prostatectomy urinary control using biofeedback and pelvic floor stimulation. The study is well designed and although the number of men completing the study was not very high, the results show a significant difference in recovery time and urinary control. One weakness is that the definition of continence was the use of one pad per day. This may overestimate the program's success. Continent really means NO leakage and no pads but many investigators choose a less strict definition, which can underestimate the problem.

The Bottom Line: This randomized study showed biofeedback and pelvic floor stimulation clinically beneficial after radical prostatectomy but more work is needed to establish the optimal frequency and intensity of the program.

Good news for patients with advanced disease. Xgeva is a new drug approved by the FDA for the treatment of men with prostate cancer in the bones. It provides even better results than a previously approved drug called Zometa. It also works differently than Zometa and does not require an intravenous infusion. This should make it easier for men to get this treatment with well-tolerated side effects.

The Bottom Line: Patients now have a new, more effective treatment to reduce the bone complications of metastatic prostate cancer compared to previously available options. All men with metastatic disease should make sure to discuss this drug with their doctor.

The article about incorrect staging may be a case of "much ado about nothing." Clinical staging is not completely accurate but it in most cases it may matter very little. The man who is told he has local disease but does not, might get the wrong treatment. The same is true for the man who is told his cancer is outside the prostate when it is not. The authors did not find that correcting the staging resulted in a different PSA failure rate.

The Bottom Line: Patients may not need to worry too much about their stage assignment, even though errors occur, because it has little impact.

As men age, the testosterone level often declines, leading to many changes in men's health. Is androgen supplementation dangerous for these individuals? That question was addressed in a randomized study of healthy men. They received either a placebo or DHT gel for two years. Importantly, neither the prostate size nor the PSA was affected when compared to placebo. More information would be needed to know if the drug has any affect on prostate cancer. The authors could have performed routine biopsies before and at the end of the study to gather some of this information. They did find the DHT reduced lumbar spine bone mineral density.

The Bottom Line: The study does not reveal whether testosterone or DHT is safe in men with prostate cancer.

Does hormone deprivation increase the risk of developing colon cancer? This uncontrolled study makes that suggestion with an absolute risk increase of perhaps 2.5%. Is that real or not? Can this study design make that determination? The answers are "who knows" and "no".

The Bottom Line: Yet another example of an uncontrolled study getting headlines in the media and raising concerns prematurely. This study design does not allow any conclusions about the relationship between hormone therapy and colon cancer.

PROSTATE BIOPSIES ARE NOT ASSOCIATED WITH INCREASED MORTALITY

The largest prostate cancer screening study found no evidence of increased mortality associated with the procedure.

"This is very reassuring and adds an important piece of knowledge to the risk-versus-benefit discussion in prostate cancer screening," Dr. Sigrid Carlsson at the University of Gothenburg in Sweden told Reuters Health in an email.

As an invasive procedure, biopsies can produce severe, but rare, complications including rectal hemorrhage and sepsis in some cases reportedly leading to death. The new findings, however, indicate that the risk of death is not a valid reason to dismiss population-based prostate screening programs, Dr. Carlsson's team concludes in a paper published online 15 October 2010 in the *British Journal of Urology International*.

The researchers examined records from 50,194 men, ages 50-78, in the European Randomized Study of Screening for Prostate Cancer (ERSPC), a three-center study in Finland, the Netherlands and Sweden. Laterally directed sextant transrectal prostate biopsies were done in the 12,959 men who screened positive for elevated prostate-specific antigen (PSA) levels. Of those, 11,721 (90.4%) actually underwent a biopsy.

At both 120 days and one year after the procedure, there was no significant difference in mortality between those who screened positive and underwent biopsies compared to those who screened negative. Regression model analysis showed that neither PSA level nor screening center affected the risk of mortality after one year of follow up.

When they compared the two groups of patients who screened positive, the researchers found that the 1238 that didn't undergo a biopsy had a fourfold risk of death (by all causes other than prostate cancer) during the first 120 days.

While biopsies may not increase mortality risk, the procedure is uncomfortable for the patient and costly for the health-care system. Research is now underway to find new markers and algorithms for screening programs to avoid unnecessary biopsies.

Reuters Health, 4 November 2010

DHT MAY NOT AFFECT PROSTATE SIZE BUT MAY REDUCE BMD

DHT (dihydrotestosterone) treatment for 24 months does not affect prostate growth but decreases bone mineral density (BMD), according to a randomized, placebo-controlled, parallel-group trial reported in the *Annals of Internal Medicine* (Vol. 153, pp 621-32, 2010).

"Benign prostatic hypertrophy (BPH) increases with age and can result in substantially decreased quality of life for older men," writes Amanda Idan, BSc, MHSc and colleagues from Concord Hospital, ANZAC Research Institute, University of Sydney in Australia. "It has been hypothesized that long-term administration of a non-amplifiable pure androgen might decrease prostate growth, thereby decreasing or delaying the need for surgical intervention."

At an ambulatory care research center, 114 healthy men older than 50 years without known prostate disease were randomly assigned to receive transdermal DHT (70 mg) or placebo gel daily for 2 years. Every 6 months, blood samples and questionnaires were collected, prostate volume was measured with ultrasonography, and BMD and body composition were measured. Data were analyzed by mixed-model analysis for repeated measures.

With time on study, increases in total prostate volume (29%), central prostate volume (75%, $p < 0.01$) and serum PSA level (15%) occurred, but DHT did not effect these changes ($p > 0.2$). Compared with placebo, DHT reduced lumbar spine BMD (1.4%, $p < 0.001$) at 24 months but not hip BMD ($p > 0.2$) and increased urine levels of a bone turnover marker in the 2nd year of the study. In the DHT group, serum DHT levels and its metabolites were increased, whereas serum testosterone, estradiol, luteinizing hormone, and follicle-stimulating hormone levels were suppressed. DHT significantly increased hemoglobin (7%), serum creatinine (9%) and lean mass (2.4%) but reduced fat mass (5.2%).

"Negative findings on prostate growth cannot exclude adverse effects on the natural history of prostate cancer," the study authors write. "DHT treatment for 24 months has no beneficial or adverse effect on prostate growth but causes a decrease in spinal but not hip BMD. These findings have important implications for the wider use of nonsteroidal pure androgens in older men."

In an accompanying editorial, Ronald S. Swerdloff, MD, from Harbor–University of California, Los Angeles, and Christina Wang, MD, from David Geffen School of Medicine at the University of California, Los Angeles, note that this study was not adequately powered to definitively answer the question of long-term safety of testosterone use.

"Idan and colleagues argue that their findings provide insight about the potential efficacy of future synthetic androgen receptor modulators that will likely share (with DHT) the anabolic effects on muscle and fat, as well as the sparing effects on the prostate. However, we caution that each synthetic androgen-receptor modulator could have a different target organ profile.

We conclude that DHT acts as a hormone in tissues without high concentrations of 5α-reductase enzymes but mainly in an autocrine–paracrine manner in tissues like the prostate, in which 5α-reductase is abundant."

Medscape Medical News, 16 November 2010

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INDEX OF MEDICAL ARTICLES PUBLISHED IN US TOO'S *HOTSHEET* DURING 2010

Name of Article	Month
2009 Us TOO Annual Meeting Highlights	January
A Treatment for Prostate Cancer "Inadequate" Half the Time	May
Abiraterone Study Meets Pre-Determined Criteria	October
ACS – Ignorance is Bliss When it Comes to Prostate Cancer	April
Active Surveillance May Not Be Best Option	June
Alternative Prostate Cancer Vaccine Shows Promise	March
American Cancer Society Updates Guidelines	April
An Update of the Gleason Grading System	February
ASCO on Patient Protection & Affordable Health Care Act	May
Ask Dr. Myers – 2nd line hormone treatment	February
Ask Dr. Myers – Thoughts about European Screening Study	March
Ask Dr. Myers – Supplements Interact with Prostate Drugs	April
Ask Dr. Myers – Are Men Ever Cured of Prostate Cancer?	May
Ask Dr. Myers – Who Benefits from Active Surveillance?	June
Ask Dr. Myers – Thoughts About the Combidex Scan	July
Ask Dr. Myers – The Most Critically Important Supplement	August
Ask Dr. Myers – Treating Taxotere Resistant CRPC	September
Ask Dr. Myers – Thoughts About Entering Clinical Trials	October
Ask Dr. Myers – Coffee/Caffeine & Prostate Cancer	November
Ask Dr. Myers – Farm-Raised versus Wild Salmon	December
Aspirin & Reduced Risk of Prostate Cancer Death	December
AstraZeneca Drug Fails vs. Prostate Cancer	November
Atypical Prostate Biopsy Should Be Repeated	December
AUA Responds to Updated ACS Guidelines	April
Avastin® Fails to Prolong Survival in CRPC	July
Barbers Against Prostate Cancer Program Succeeds	April
Biomarkers Predict Prostate Cancer Progression	June
Bone Density May Predict Prostate Cancer	September
Cabazitaxel – New Approach for Prostate Cancer	November
Cabazitaxel (Jevtana®) Now Approved for Refractory CRPC	August
Cabazitaxel Benefit Confirmed in Prostate Cancer	July
Calypso Dynamic Edge Gating Receives FDA Clearance	December
Clinically Localized Cancer Treated With Brachytherapy	September

Name of Article	Month
Coffee May Cut Risk of Prostate Cancer	February
Comorbidity & Entry in Controlled Cancer Therapy Trials	March
Comorbidities Key in Prostate Cancer Treatment Decisions	October
Cost Should Enter Effectiveness Equation	December
Degarelix as Second-Line Therapy for Prostate Cancer	June
Degarelix vs. Leuprolide in Advanced Prostate Cancer	January
Dendreon Receives FDA Complete Response for Provenge	January
Dendreon's $93K Price Must Be Paid by US	September
Denosumab Extends Time to Bone Events	July
Discussing Provenge with Cancer Patients	June
Doc Moyad – Statins & Low Cholesterol	January
Doc Moyad – Treatments for ADT-Induced Hot Flashes Work	February
Doc Moyad – Weight Loss Supplements Are a Problem Part 2	March
Doc Moyad – Weight Loss Supplements Are a Problem Part 1	April
Doc Moyad – L-Theanine Anti-Stress Amino Acid in Tea	May
Doc Moyad – Provenge® Receives FDA Approval	June
Doc Moyad – Exercise Ups Cialis®, Levitra® & Viagra®	July
Doc Moyad – Too Much Vitamin D3 Is Not a Good Thing	August
Doc Moyad – Too Much Folic Acid May Not Be Good	September
Doc Moyad – Let's Walk the Talk This Month!	October
Doc Moyad – Need More Signatures on the CMS Petition!	November
Doc Moyad – Mega-Dose Vitamins	December
Doctor Chodak's Bottom Line	Feb. – Dec.
Drug Eases ADT Side Effect in Men	January
Drug Extends Survival in Prostate Cancer	December
ERSPC Screening Reduced Prostate Cancer Deaths 20 Percent	February
Exercise May Prevent Incontinence from Prostatectomy	March
FDA Approves Prostate Cancer Vaccine	June
FDA Scrutiny of GnRH Agonists Continues	June
First National Research Study Recruitment Registry	January
Gat's Hypothesis for the Cause of Prostate Cancers	February
Genetic Variations in Japanese Linked to Prostate Cancer	September

INDEX OF MEDICAL ARTICLES PUBLISHED IN US TOO'S *HOTSHEET* DURING 2010

Name of Article	Month
Gen-Probe Files PMA for PROGENSA® PCA3	November
Guidelines from Multiple Organizations Confuse Screening	April
Higher Dose Radiation Better in Prostate Cancer	April
High-Fiber Foods Block Cancer Pathways	April
High-Intensity Focused Ultrasound & Radiation Therapy	July
Holiday Giving? Remember Us TOO	December
Immunotherapy Benefits Prostate Cancer	September
Index of Articles Appearing in the 2009 HotSheets	January
Infertility & Prostate Cancer May Have a Common Cause	May
Information about the READY Trial	September
J&J Drug Helps in Last-Ditch Prostate Cancer Fight	April
Leather Wristbands Help Raise Awareness, Funds	August
MDV3100 "Substantial Activity" in Advanced Cancer	June
Medicare to Review Provenge® Coverage	August
Nanosensors Used to Measure Cancer Biomarkers	February
NCCN Stresses Careful Consideration of Active Surveillance	February
New ACS Screening Guidelines – Dr. Len Lichtenfeld	April
New Study to Improve Prediction of Prostate Biopsy Results	August
New Warnings on Prostate Cancer Drugs	December
Nitroglycerin to Treat Prostate Cancer Shows Promise	April
No Prostate Cancer Indication for Sunitinib	November
NRC Meeting on Prostate Brachytherapy	August
Options Similarly Effective for Low-Risk Prostate Cancer	March
PAF's Additional Co-Pay Support for Prostate Cancer	September
Patients Face Yearlong Rationing of Provenge	August
Pelvic RT Increases Hip Fracture Risk in Men	July
POM Wonderful vs. Federal Trade Commission	November
Positive Results for Sanofi-Aventis Drug	May
Prostate Biopsy Can Cause Urinary and Erectile Problems	October
Prostate Cancer Diagnosis Raises Risk of Suicide	March
Cancer Progresses More Quickly in African-American Men	June
Prostate Cancer Risk & Native and Foreign Born Blacks	November
Prostate Cancer Roadmap – New Cancer Resource	October

Name of Article	Month
Prostatectomy Performed by Surgeons with Little Experience	January
Protein Array Accurate for Prostate CA	November
PSA & the PSA Test: What the Public Needs to Know	May
PSA 2 Years Post-RT Predicts Long-Term Cancer Survival	February
PSA Misses the Mark in Active Surveillance	July
PSA Screening Can Lead to Overtreatment	September
PSA Screening Should Be Offered to Older Men	January
PSA Test Does Cut Prostate Cancer Deaths	August
PSA Test Reduces Risk of Spread if Prostate Cancer Strikes	December
PSA Velocity Helps Identify Insignificant Prostate Cancer	February
Public-Private Divide in Prostate Cancer Treatment	March
Radiation for Prostate Cancer Lacks Data	June
Radio Ablation Safe & Effective for Painful Bone Metastases	February
Robot-Assisted Surgery Is Not Better for Prostate Cancer	April
RT Shown Beneficial for Prostate Cancer Subset	July
Sex & Masturbation in 20s/30s Linked to Prostate Cancer Risk	March
Soy May Protect Against Prostate Cancer	March
Stand Up to Cancer Is Back	September
Statins Reduce PSA Spikes After Surgery	August
Suicide Risk in Men with PSA-Detected Cancer	March
Super Molecule That Kills Prostate Cancer Cells	February
Teva's Phase III Study Compares Radiation Treatments	November
Understanding Diagnostic Testing for Prostate Cancer	October
Unexpected Cell Causes Prostate Cancer	September
Us TOO Board Welcomes 2 New Members	November
Us TOO Names New Board Reps for 2010	January
Us TOO's Summit, Symposium & 20th Anniversary Celebration	October
VA Begins Paying Benefits for New Agent Orange Exposure	December
Volunteer for Congressional Medical Research Review Panels	April
What Men Are Told About Cancer Treatment Options	October
Which Men Should Take Finasteride?	April
ZERO's "Prostate Polar Plunge"	March