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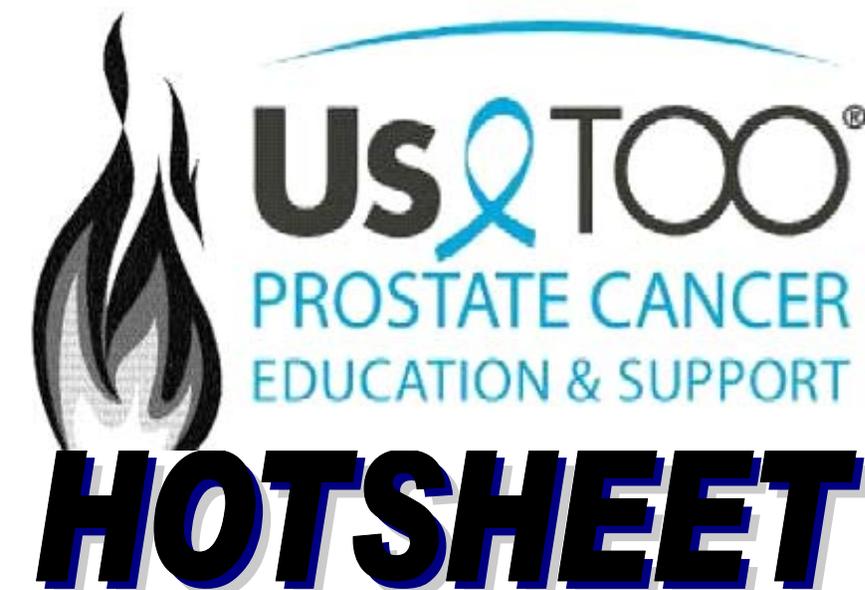
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NEW ANALYSIS OUT ON CANCER DRUG

Patient advocates said Thursday they would continue to press Congress for action, a day after a congressional committee declined to hold hearings on the Food and Drug Administration's decision to delay approval of a prostate cancer drug made by Dendreon Corp. The Seattle Company, meanwhile, released a positive analysis of the drug's effect on patient survival at the 2008 ASCO Genitourinary Conference. Dendreon's stock jumped more than 8 percent, or 49 cents, to close at \$6.17 on the Nasdaq stock market.

Provenge, Dendreon's prostate cancer treatment, is a therapy that attempts to stimulate an immune system response against prostate cancer cells. In its analysis released Thursday, Dendreon said there was a statistically significant correlation between use of the therapy and patient survival, even when data were adjusted to compensate for other factors. "The results today are supportive of the drug's action and tie a specific potency metric to the efficacy in a patient," said Dendreon Chief Financial Officer Greg Schiffman in an e-mail. However, he said that while the company was "very excited by the findings ... they do not provide the required support to enable us to amend our filing with the FDA."

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April 2008

GTx's TOREMIFENE CITRATE 80 MG MEETS PRIMARY AND KEY END- POINTS IN PHASE III TRIAL IN ADVANCED PROSTATE CANCER PATIENTS ON ANDROGEN DEPRIVATION THERAPY (ADT)

GTx, Inc. (NASDAQ:GTXI) today announced Phase III clinical data for toremifene citrate 80 mg, the Company's investigational therapy for the treatment of multiple side effects of ADT for advanced prostate cancer. Results show that toremifene citrate 80 mg reduced vertebral fractures and met other key endpoints, including bone mineral density, lipid profiles, and gynecomastia.

Based on these findings, GTx plans to file a New Drug Application (NDA) with the US Food and Drug Administration (FDA) by the summer of 2008. In addition, GTx plans to present the full data set at an upcoming medical meeting.

"The toremifene citrate 80 mg Phase III ADT clinical trial is the first fracture prevention study in men receiving ADT for prostate cancer. The study confirms that men receiving ADT are at high risk for fractures. The rate of vertebral fracture in the placebo group

(Continued on page 7)

TREATMENT DECISION- MAKING FOR PROSTATE CANCER NOT AN EASY MATTER

A new review prepared for the Agency for Healthcare Research and Quality and published online February 4th in the *Annals of Internal Medicine* reports that available evidence provides minimal assistance.

"Until high-quality studies — especially randomized controlled trials — are completed, patients and providers must make treatment decisions based on limited and inadequate information," stated lead author Timothy Wilt, MD, from the Minneapolis VA Center for Chronic Disease Outcomes Research, in Minnesota.

To compare the effectiveness and harms of various therapies, investigators reviewed randomized trials and observational studies that evaluated treatments and reported clinical or biochemical outcomes in localized prostate cancer. Using Medline, the Cochrane Library and the Cochrane Review Group in Prostate Diseases registry, they identified 18 randomized and 473 observational studies.

Researchers found little high-quality evidence that established the superiority of one therapy over another. All treatments, including androgen deprivation

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THIS ISSUE OF THE US TOO PROSTATE CANCER
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NEW ANALYSIS OUT ON PROVENGE *(continued from page 1)*

In May, the FDA said that Dendreon had to provide additional clinical data demonstrating Provenge's impact on patient survival before it approved the therapy. The company has since completed enrollment in a trial that Dendreon hopes will generate the additional data the FDA has asked for. Interim results are expected later this year.

FDA's decision to delay Provenge's approval was controversial because an FDA advisory committee had previously determined that the drug was safe and effective. Patient advocates argued that two of the members of the committee who opposed the drug's approval and later wrote critical letters to the FDA had conflicts of interest.

In mid-December, three members of Congress asked a congressional committee to hold hearings to determine whether there had been ethical lapses in the way the FDA reviewed the drug. But on February 13th, the chairman of the Committee on Energy and Commerce and the chairman of the subcommittee on health wrote in a letter that such a hearing would be inappropriate, in part, because the FDA had yet to make a final decision and the two members of the committee whose conflicts were being questioned had been granted conflict of interest waivers.

Members of a patients group that has urged the FDA to reconsider its deci-

sion said Thursday they were disappointed by the committee's decision. Scott Riccio, the founder and director of A Right to Live, said that the congressional committee's response ignored that it was up to members of advisory committees themselves to outline their conflicts -- a process in which there was little or no oversight. He added that there was also little transparency over what went on between the times an advisory committee met and when the FDA made a decision.

Charles Bennett, a member of A Right to Live, said that it was possible that another committee or subcommittee could examine what happened. "I don't think that the Energy and Commerce committee is the only game in town," Bennett said, adding that it was possible that a committee that handled veteran's issues could examine the issue. "There are other avenues that some of these congressmen want to pursue."

Schiffman, Dendreon's CFO, said the company did not have a comment on the congressional committee's decision. "We always (felt) the best way to get the drug to market (was) to work with the FDA to complete our current study," he said. FDA has indicated that positive interim results could be enough to take a second look at Provenge.

Seattle Post Intelligencer
14 February 2008

THE POWER OF WORDS FOR CANCER PATIENTS

When my mother was first diagnosed with cancer, she did something she had never done before. She started to write down her feelings. My mother had always been too busy for something she felt was as indulgent as keeping a journal, but in the early days of her cancer diagnosis, she found that writing down her thoughts helped her cope with the prospect of dying.

This month, a medical journal confirms what many cancer patients intuitively know. Expressive writing, which involves writing down your deepest thoughts and feelings, may improve the quality of life for cancer patients, according to a new report in *The Oncologist*. Previous research conducted in controlled laboratory experiments has suggested that expressive writing helps physical and psy-

chological well-being. However, the recent study was a real-world experiment, conducted in the waiting rooms of an oncology practice.

Researchers from the Lombardi Comprehensive Cancer Center in Washington, D.C., studied the effects of expressive writing on 71 adults with leukemia or lymphoma who journaled their thoughts while waiting for their regular oncology appointments. The patients were asked to write their thoughts in answer to the question: How has cancer changed you, and how do you feel about those changes?

After the writing assignment, about half of the cancer patients said the exercise had changed their thinking about their illness, while 35 percent

(Continued on page 8)

APRIL BRINGS A NEW LOOK TO SEA BLUE FOR NATIONAL MINORITY CANCER AWARENESS WEEK

It has been almost 22 years since a congressional joint resolution designated the full third week in April as National Minority Cancer Awareness Week. The purpose of the resolution was to draw attention to the cancer disparities that have had a disproportionately severe impact on minorities and the economically disadvantaged.

Early in our history, the Us TOO International Board responded to the growing awareness of special at-risk populations, in which the incidence of prostate cancer is extraordinarily high, yet education and awareness have been disproportionately low.

In 2002, then Us TOO Board Chairman Lew Musgrove called for action to better serve these special at-risk populations. Jim Raby, Jamal Rasheed, Ralph Valle, Rex Zeiger and Jim Kiefert created the program design which eventually became a new partnership between Us TOO and the Centers for Disease Control (CDC).

Five years later, this partnership is a thriving program, the Minority and Underserved Program, or "MUP." The multi-year partnership with the CDC is significant, having reached over 300,000 men and their families. What began in 2003 with four high-incidence states and areas, or pilot sites, focused primarily on the African-American population has now expanded to (eighteen states plus Washington DC). The program now is also reaching into the Hispanic and Native American populations.



Jamal Rasheed and students at Lancaster High School during a presentation on prostate cancer in the Health Science Class

Through trained volunteers, this program reaches people through non-traditional locations, such as churches, community events, retail sites, employer sites, barbershops, family reunions, and sporting events. The program has also reached students and young adults through health science classroom visits in the high schools.

In Mississippi, Emily Washington coordinates the "Take Your Love One to the Doctor, Daddy Checkup Day" which has successfully reached families with critical information and screening. Held each year around Father's Day, the event features activities for the entire family, as well as health screening for dad, such as PSA and DRE.

Not only has this program brought important information into countless at-risk lives, it has also deeply touched those delivering the message. Bob Jelks, of Decatur, IL, puts it this way:

"This program has given me an outlet to release my passion in helping families. I've touched many lives and have been touched in return. Words can't express the joy of being a 10-year prostate cancer survivor."



Bob Jelks, ten-year cancer survivor and MUP participant, with his grandson

While there are many, many success stories and terrific progress, the need for emphasis on cancer disparities is even more pressing than ever. Your efforts are vital for bridging the gap.

THE NEW LOOK FOR SEA BLUE

At Us TOO, we recognize this glaring disparity will not change without focused **attention** and **action**. In response to April's National Minority Cancer Awareness Week, Us TOO is pleased to launch our special SEA Blue campaign:

SEA Blue Awareness Campaign – **S**upport, **E**ducate, **A**dvocate.

"As pink is to breast cancer, blue is to prostate cancer."

The focus of our campaign is to reach out to those at risk in minority and underserved populations, promote prostate cancer screening, and give a voice in the community to the issue of prostate cancer awareness.

WHAT CAN YOU DO?

SEA Blue Campaign posters, information, and convenient, easy-to-use "window-clings" can be obtained by visiting our website <www.ustoo.org> or by calling 1-800-808-7866.

It is simple. It is important. And it could save lives.

Please help bridge the gap. Your efforts matter.

GENETIC VARIANTS FOUND TO BE ASSOCIATED WITH PROSTATE CANCER

A recent study published in the *New England Journal of Medicine* reveals that genetic variants located in five different chromosomal regions have been associated with prostate cancer.¹

Other than skin cancer, prostate cancer is the most common form of cancer diagnosed in men. Factors influencing the risk of prostate cancer include age, race, and family history. Prostate cancer is more common among older men, African-American men, and men with a family history of prostate cancer. Some of these differences in risk may be explained by inherited genetic variation.

Looked at individually, specific genetic variants have tended to show only moderate associations with prostate cancer. It's possible, however, that when looked at in combination, a stronger link will emerge.

To explore relationships between a combination of genetic variants and risk of prostate cancer, researchers in Sweden conducted a study in 2,893 men with prostate cancer and 1,781 men without prostate cancer. The final analysis focused on 5 genetic variants (a single genetic variant at each of five chromosomal regions), as well as family history of prostate cancer.

- Men with a greater number of genetic variants had a higher risk of prostate cancer.
- Men with either 5 genetic variants with or without a family history or four genetic variants with a family history were more than 9 times more likely to develop prostate cancer than men with no genetic variants and no family history.
- Together the 5 genetic variants and family history were thought to account for 46% of the prostate cancer cases in this population.

Researchers conclude that genetic variants at 5 chromosomal locations, plus family history appear strongly linked with prostate cancer risk.

The specific mechanism by which the genetic variants affect the risk of pros-

(Continued on page 5)

NEW HOPE FOR CHEMO HOLIDAYS FOR MEN WITH ADVANCED PROSTATE CANCER

Oregon Health & Science University Cancer Institute researchers, in a first-of-its-kind study, have found that even men with advanced prostate cancer can take a much-needed safe break, or holiday, from chemotherapy.

The double-blind, randomized study, led by principal investigator Tomasz Beer, MD, recently was published in the journal *Cancer*. Beer is the Grover C. Bagby Endowed Chair for Cancer Research, director of the OHSU Cancer Institute Prostate Cancer Program, and associate professor of medicine (hematology/medical oncology), OHSU School of Medicine.

Beer and his team wanted to know if men with metastatic, androgen-independent prostate cancer that has spread from the prostate and is not affected by the male hormone, androgen could take a break from docetaxel, an intravenous chemotherapy delivery drug that is the gold standard treatment for androgen-independent prostate cancer. Docetaxel works by killing cancer cells and slowing cell growth. However, the drug also can cause side effects, such as hair loss, nausea, loss of appetite and increased chance for infections. Chemo holidays can be a much-needed vacation from these side effects.

Prior to this study, it wasn't known whether stopping chemotherapy would lead to treatment resistance.

"We wanted to see if we could improve the quality of life for these patients by giving them time away from chemotherapy and possibly extend the time their cancer is controlled. Essentially, what we proved is that in selected subjects, chemotherapy holidays are feasible and provided meaningful breaks from treatment," said Beer.

This is the first multi-institutional trial to examine outcomes from intermittent chemotherapy. A total of 250 men participated. Of those, 18 percent entered the intermittent arm of the study. These men previously had responded well to chemotherapy.

The median duration of the first chemo holiday was 18 weeks. On resumption of chemotherapy, the majority of subjects responded to treatment. Spe-

cifically, 45.5 percent of participants responded with a greater than 50 percent reduction in prostate specific antigen (PSA) from their post-holiday baseline; of those, 45.5 percent had stable PSAs for at least 12 weeks; and 9.1 percent developed disease progression. Prostate-specific antigen is a protein produced by the cells of the prostate gland and is present in small quantities in the serum of healthy men, and it often elevates when prostate cancer is present. Most men have less than 4 nanograms. Anything higher can indicate prostate cancer.

The next step, said Beer, is to study the addition of immunotherapy, treating the cancer by working with the immune system, during the chemotherapy holidays.

"Because we know holidays are a good thing, we want to find ways to make them even longer," Beer said. OHSU and Beer have significant financial interest in Novacea, Inc., a company that has a commercial interest in the results of this research and technology. This potential conflict was reviewed and a management plan approved by the OHSU Conflict of Interest in Research Committee and the Integrity Program Oversight Council was implemented.

Other authors include: Christopher Ryan, MD, Division of Hematology/Medical Oncology OHSU Cancer Institute; Peter Venner, MD, Cross Cancer Institute, Alberta, Canada; Daniel Petrylak, MD, Division of Hematology and Medical Oncology, Columbia Presbyterian Medical Center; Gurkmal Chatta, MD, Pavillion Hellman Cancer Center; J. Dean Ruether, MD, Tom Baker Cancer Centre, Calgary, Alberta, Canada; Kim Chi, MD, Division of Medical Oncology, University of British Columbia, Vancouver, British Columbia, Canada; James Young, MS and W. David Henner, MD, PhD, Novacea Inc., San Francisco, CA.

"Intermittent Chemotherapy in Patients with Metastatic Androgen-Independent Prostate Cancer."

Adapted from materials provided by OHSU via EurekAlert!

ScienceDaily, 25 February 2008

NERVE-SPARING PROSTATECTOMY IMPROVES SUBSEQUENT CONTINENCE

A nerve-sparing approach to radical prostatectomy (RP) shortens the period until continence is regained and improves long-term continence rates, new research shows.

Previous studies show that preserving the neurovascular bundle can improve post-RP potency rates, but whether nerve-sparing surgery improves incontinence was unclear, senior author Dr. Craig D. Zippe, from the Cleveland Clinic Foundation, and colleagues note in the December issue of the journal *Urology* (*Urology*, Vol. 70, pp. 1127-30, 2008).

To investigate, the researchers assessed incontinence rates in 152 patients who underwent RP with unilateral or bilateral nerve sparing or with no nerve sparing. During an average follow-up of 7.8 years, 27 patients (18%) were incontinent. Eighteen of 61 (30%) patients treated with non-nerve-sparing RP were incontinent compared with just 6 of 66 (9%) treated with bilateral nerve-sparing RP ($p < 0.05$). By contrast, unilateral nerve sparing offered no benefit over non-nerve sparing.

In addition to the type of surgery, patient age also affected incontinence rates; subjects older than 65 years were significantly more likely to become incontinent than were younger patients.

"This study suggests that all patients, irrespective of potency status and age, would benefit from nerve-sparing procedures when this is clinically feasible," the authors conclude.

Reuters Health, 31 January 2008

GENETIC VARIANTS

(Continued from page 4)

tate cancer has not been identified, and future research will be needed to test the value of these findings in determining the risk of prostate cancer in individual men.

¹ Zheng SL, Sun J, Wiklund F et al. Cumulative association of five genetic variants with prostate cancer. *New England Journal of Medicine* [early online publication]. *www.nejm.org online*, 16 January 2008

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

"Ouch! High-dose vitamin E supplements have been taking more hits than Mike Tyson, Rocky Balboa & Roger Clemens combined!"

Mark A. Moyad, MD, MPH

University of Michigan Medical Center, Department of Urology

*To order Dr. Moyad's new "No Bogus Science Diet Book" just call toll-free 1-877-722-2264 to reserve a copy now or in a few minutes!

Bottom Line: Yo Adrian!! High-dose vitamin E supplements may increase the risk of lung cancer, especially in smokers! Remember, the forest over the tree if you have or had prostate cancer, so I would stay away from these things for now!

Poor vitamin E supplements! Man, it is almost as if everyone is starting to pile on right now! It is almost as if these pills are the Britney Spears of the supplement world. Do you remember how just a few years ago there were lots of "experts" recommending vitamin E supplements for men with and without prostate cancer?! The interesting thing about this research that got a lot of people excited was that the dose used in the clinical trial in 1998 was only 50 IU of vitamin E. Why did "experts" start recommending higher doses and why did we forget to look at the forest over the tree?! Vitamin E supplements have now failed to reduce the risk of cardiovascular disease in men and women in so many clinical trials, and there is some suggestion that in higher doses they may even be harmful, so I do not see many doctors recommending them anymore. There was even one large trial (Hope-Too) for example, which suggested that 400 IU of vitamin E increased the risk of heart failure?! Wow! Now, there is this latest large study from

the state of Washington to suggest that 400 IU of vitamin E or more increases the risk of lung cancer, especially in smokers! Look, I am not going to B.S. the readers of this wonderful newsletter. Let me let you in on a little secret and that is, I have no idea if vitamin E supplements really do anything good for you!? All I know is that vitamin E has not followed Moyad's rule which is heart healthy = prostate healthy. In other words, the overall research suggests that vitamin E supplements may either do nothing, help in one or a few areas of medicine, or may really harm you in a bad way in most areas of medicine. Since this is the latest overall data that adds to the "forest" of knowledge, I suggest you walk away from the "tree" and stop taking vitamin E supplements or at least do not get more than 30 to 50 IU in a multivitamin. And, if you are a smoker and worried about vitamin E supplements, well it is kind of like asking me if the cup of coffee in your hand is okay to drink while you are driving right toward a large rock at 200 miles an hour! Are you feeling me on this one dawg? (Note: it is important for me to use my teenage son's vernacular every once in a while in order to get him to read this column and this newsletter!)

Reference

Am J Respir Crit Care Med 177: 524-30, 2007



May 30, 2008 -
June 30, 2008

DONATE ITEMS FOR 3RD ANNUAL US TOO ONLINE AUCTION

The 3rd Annual Us TOO International Online Auction will open on Friday, May 30th, and will continue through Monday, June 30th. We need your help! We are seeking as many appealing items as possible in order to make the auction as successful as ever. To donate an item, please visit the following link: <www.ustoo.org/Donate_Item>. We are looking for electronics, sports memorabilia, jewelry, art and more. If you have questions or comments, please feel free to contact Dan Reed at dan@ustoo.org or at 630-795-1002. Thank you!

REVIEW OF PROSTATE CANCER LEAVES MEN IN A MUDDLE

A diagnosis of prostate cancer is scary enough — but just as scary is that nobody knows the best way to treat it.

This month, the Agency for Healthcare Research and Quality issued a sweeping review of prostate cancer treatments, including surgical removal, radiation, hormone therapy and so-called watchful waiting. Because none of these treatments emerged as superior, the agency came to the troubling conclusion that it could not recommend one over the others.

“Having been involved in this area for a long time, it was not shocking, but it is disappointing,” said Dr. Timothy J. Wilt, lead researcher on the report, from the Minneapolis Veterans Affairs Center for Chronic Disease Outcomes Research. “Information is really lacking to determine whether over all one treatment is more effective and preferred.”

The reasons behind the lack of data include a lack of financing and advocacy but also due the fact that research studies can take more than 10 years to complete. This is a disincentive for the drug industry, which typically has patent protection for 7 years or so.

“Men don’t go into the clinical trials,” said Dr. Daniel P. Petrylak, director of the genitourinary oncology program at the Columbia University Medical Center. “That’s the whole problem. Patients ask me all the time, ‘What is the best treatment?’ And I can’t give them an evidence-based approach for that, because we don’t have the data.”

Prostate doctors and patient advocates often compare their cause with that of the other major sex-specific disease: one of the largest prostate cancer support groups is called Us TOO, a play on the Y-ME National Breast Cancer Organization. Funding for prostate cancer research pales in comparison to the campaign against breast cancer.

“We’re at least a decade behind where breast cancer awareness is,” Thomas Kirk, president of Us TOO, said. “We need to catch up. The lessons learned by breast cancer are the ones we’re trying to apply to prostate cancer.”

Read the full story by going to:
<www.nytimes.com/2008/02/26/health/26well.html?_r=1&st=cse&sq=MEN+IN+A+MUDDLE&scp=1&oref=slogin>.

New York Times, 26 February 2008

TREATMENT DECISIONS

(Continued from page 1)

vation, radical prostatectomy, and radiotherapy, caused adverse events, but the severity varied among treatments. Adverse events primarily were urinary incontinence, bowel problems and erectile dysfunction. The chances of bowel problems or erectile dysfunction are similar for surgery and external radiation. Urinary incontinence is at least six times more likely among surgery patients than those treated by external radiation.

“Few existing trials assessed between-treatment rather than within-treatment category differences,” the authors write. And “few randomized trials were adequately powered to assess overall or disease-specific survival or metastatic spread.”

“This report is a reminder that patient outcomes may vary according to treatment settings” said AHRQ Director Carolyn M. Clancy, MD “But this analysis also underscores a broader message: when it comes to prostate cancer, we have much to learn about which treatments work best, and patients should be informed about the benefits

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HARRY PINCHOT

July 11, 1940 - January 23, 2008



The Prostate Cancer community lost a champion and friend with the passing of Harry Pinchot on January 23, 2008. Although I knew Harry for only a few short years, he made a huge impression on me. I first met Harry Pinchot

when I joined him on the Board of Us TOO International in 2003. He readily shared his immense knowledge and passion about prostate cancer with me. Harry could engage in thoughtful and fun discussion on almost any topic and it was an honor and privilege to have known him.

My wife, Ann, and I were grateful to have had the opportunity to remember Harry at a Mass and Memorial in Camarillo, California on February 23, 2008. The Mass was celebrated by Father R. Janowski and Offerings were given by Harry’s grandchildren Genevieve, Emily, Judy and Donovan. Bob Each, a survivor and long-time friend of Harry, read the wonderful eulogy written by Dr. Steven Strum. Harry’s lovely granddaughter, Genevieve (who looked to be in her early teens), gave an emotional piano performance of Chopin’s Nocturne in E Flat as part of the service in the beautiful and inspiring

Padre Serra Catholic Church.

Following the Mass, Harry’s wife, Dee, their children and grandchildren hosted a reception and remembrance luncheon at the Sterling Hills Golf Club. Among those attending were many prominent oncologists: Dr. “Snuffy” Myers and his wife, Rose, flew in for the occasion and Dr. Mark Scholz drove up from Marina del Rey. Numerous friends, associates and Harry’s brother all shared stories of Harry’s dedication to his fellow man and his devotion to his family. There was a remarkable and touching outpouring of gracious and loving words from doctors, friends and fellow survivors. We will all miss him.

Harry was and will always remain my inspiration and hero.

*Tom Hiatt
Board of Directors
Us TOO International*

TOREMIFENE

(Continued from page 1)

in this study was about 10 times greater than that expected for men of a similar age not receiving ADT, as reported in other studies,” said Matthew R. Smith, MD, PhD, Director, Genitourinary Medical Oncology, Massachusetts General Hospital Cancer Center and Lead Principal Investigator of the Phase III ADT clinical trial.

“ADT is the cornerstone treatment for men with advanced prostate cancer, but has been associated with serious side effects. The results from this exciting study demonstrate that toremifene citrate 80 mg reduced fractures and other side effects in men taking ADT,” added Dr. Smith.

ADT has also been associated with increased risk of cardiovascular disease and death. There are no drugs approved by the FDA to treat multiple side effects of ADT for prostate cancer. Men with prostate cancer of a similar age who are not on ADT have a vertebral fracture rate of approximately 0.3% over two years.

The two year double-blind, placebo-controlled study randomized 1,389 ADT patients at approximately 150 clinical sites in the United States and Mexico. The primary endpoint was new morphometric vertebral fractures read by an independent third party. Other key endpoints included bone mineral density (BMD), lipid changes, hot flashes, and gynecomastia.

In a modified intent to treat analysis which included all patients with at least one evaluable study radiograph and a minimum of one dose of study drug or placebo, toremifene citrate 80 mg demonstrated a 50% reduction in morphometric vertebral fractures ($p < 0.05$; 5% fracture rate in the placebo group). The estimated two year fracture rate for new morphometric vertebral fractures in the placebo group was 6.2%.

In an intent to treat analysis which included all patients randomized into the trial, toremifene citrate 80 mg demonstrated a 53% reduction in new morphometric vertebral fractures ($p = 0.034$; 3.6% fracture rate in the placebo group).

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THE DOCTOR’S NOTE

By Gerald W. Chodak, MD

This issue presents many important matters. Possibly most important is the finding that no randomized trial to date recommend one local therapy over another. Without randomized trials this problem will not resolve soon, so patients must obtain adequate information on all options to weigh the pros and cons. This means if your doctor is pushing one local therapy over another, there is very little scientific data to support its superiority.

Some randomized trials are occurring but they do not always lead to a clear direction for patients. One example is Toremifene, which found benefits to patients with advanced disease in preventing bone fractures. Yet, here is an interesting finding: the relative benefit was a 50% reduction in fractures but only 3 out of 100 men benefited while side effects occurred more often. So, the drug does work, but whether or not it will be worth the expense and risks is a question that patients will have to weigh if the drug gets approved.

Another case in point relates to a randomized trial in Europe on the use of early hormone therapy for men with lymph node metastases. The study contradicted another trial published a decade ago. The first study found a survival benefit with early treatment and the recent study did not. Both studies have methodological weaknesses that prevent a clear answer to the question. Unfortunately the problem probably will never be resolved because of difficulty finding patients

to enroll. Consequently it may be right for some men and not others; those wanting aggressive therapy will do it, especially because of improvements in reducing long-term side effects.

One example where randomized studies help resolve controversies is discussed by Dr. Moyad in his review of Vitamin E’s role in men with prostate cancer. Despite publicity regarding its probable health benefit, The fact is, no real benefit was found when properly studied and there are some alarming adverse consequences. Before filling up your medicine closet with this and other supplements that are supposedly beneficial, be aware there is a downside to taking things that have not been properly studied.

Another article on radiation therapy after radical prostatectomy warrants our attention because considerable debate has surrounded this topic and many men are advised to have it. The article seems to support its role but the author properly stresses that no firm conclusions can be made without conducting a prospective randomized trial.

Lastly, I want to take this opportunity to make patients aware of a forthcoming new educational endeavor of mine—a unique website in which all the various aspects of prostate cancer will be discussed in a concise video format. This service will be free to patients and should be ready for launch this month. More information follows in the next *HotSheet*.

NOTE NEW DATE!

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TREATMENT DECISIONS

(Continued from page 6)

and harms of treatment options.”
 “Treatment decision-making may be based in part on differences in the importance that individuals assign to estimated effectiveness and convenience vs earlier and potentially persistent adverse events,” the authors write. Despite the limits of treatment and subsequent adverse effects, Dr. Wilt said, most men report being very satisfied with their choice of treatment.

The report entitled, “Comparative Effectiveness of Therapies for Clinically Localized Prostate Cancer” is the newest analysis from AHRQ’s Effective Health Care program. This AHRQ program represents an important federal effort to compare treatments for significant health conditions and make the findings public.

The Effective Health Care program also translates reports into plain-language guides for clinicians, patients and policymakers. Information on the program, including reports and summaries can be found at <www.effectivehealthcare.ahrq.gov>.

Adapted from information provided by: PRNewswire-USNewswire, 4 February 2008 Medscape Medical News, 7 February 2008

POWER OF WORDS

(Continued from page 2)

reported that writing changed the way they felt about their illness. Three weeks after the writing exercise, the effect had been maintained. Writing had the biggest impact on patients who were younger and recently diagnosed. While a change in the way a patient thinks or feels about a disease may not sound like much, the findings showed that the brief writing exercise led to improved quality of life.

“Thoughts and feelings, or the cognitive processing and emotions related to cancer, are key writing elements associated with health benefits,” said Nancy P. Morgan, director of the center’s Arts and Humanities Program. “Writing about only the facts has shown no benefit.”

Researchers also analyzed the content of the patient writings. Most patients noted that cancer had been life-changing. Many patients wrote that the changes were positive and that cancer had altered their views about family, spirituality, work and the future. One patient wrote: “Don’t get me wrong, cancer isn’t a gift, it just showed me what the gifts in my life are.”

New York Times, 28 February 2008

TOREMIFENE

(Continued from page 7)

Patients treated with toremifene citrate 80 mg compared to placebo demonstrated statistically significant increases in BMD in the lumbar spine, hip, and femur sites (p< 0.0001 at each site). Treatment compared to placebo also resulted in a decrease in total cholesterol (p=0.011), LDL (p=0.018), and triglycerides (p<0.0001), and an increase in HDL (p=0.001).

The most common adverse events with toremifene citrate 80 mg occurring in >2% of study subjects were joint pain (treated 7%, placebo 12%), dizziness (treated 6%, placebo 5%), back pain (treated 6%, placebo 5%), and extremity pain (treated 5%, placebo 4%). Venous thromboembolic events (VTEs) were 17 (2%) in the treated group and 7 (1%) in the placebo group.

“GTx has successfully reached an important corporate milestone event by meeting the primary and key secondary objectives of the Phase III ADT clinical trial,” said Dr. Mitchell Steiner, CEO of GTx. “We now can move forward with our plans to prepare and submit the NDA for toremifene citrate 80 mg.”

BUSINESS WIRE, 25 February 2008

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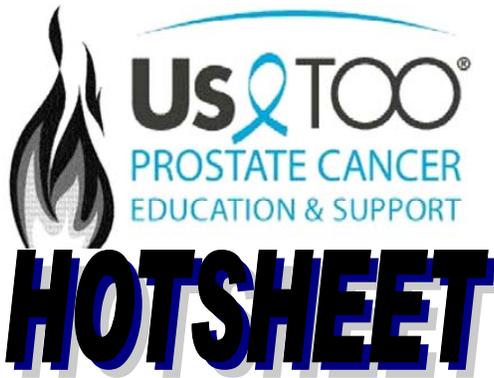
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HIGHLIGHTS FROM ASCO'S 2008 GENITOURINARY CANCERS SYMPOSIUM—SAN FRANCISCO, CA, FEBRUARY 14-16, 2008

DENDREON PRESENTS DATA CORRELATING THE CUMULATIVE POTENCY OF PROVENGE® TO OVERALL SURVIVAL

Researchers from Dendreon Corporation presented data demonstrating the correlation of a measure of the cumulative potency of PROVENGE (sipuleucel-T), an investigational active cellular immunotherapy for hormone-refractory prostate cancer, with overall survival. This is the first time that an association between higher potency of an active immune therapy and increased patient survival has been reported. The correlation appeared to be independent of other important baseline prognostic factors.

In two Phase 3 trials, D9901 and D9902A, researchers evaluated cumulative product release parameters of PROVENGE, including CD54 upregulation (a measure of product potency defined as the increase of CD54 molecules expressed on Antigen Presenting Cells [APC] after incubation with the PROVENGE Antigen Delivery Cassette™ and the number of total nucleated cells (TNCs) among patients treated with sipuleucel-T (n=146).

(Continued on page 2)

CELL GENESYS REPORTS ASSOCIATION BETWEEN IMMUNE RESPONSE AND PATIENT SURVIVAL IN PHASE 2 TRIAL OF GVAX IMMUNOTHERAPY FOR PROSTATE CANCER

Cell Genesys, Inc. (Nasdaq: CEGE) reported the results of an analysis examining the potential association between immune responses to GVAX immunotherapy for prostate cancer and increased patient survival in a Phase 2 trial in patients with metastatic, hormone refractory prostate cancer (HRPC). More than 400 patient-specific GVAX-induced antibody responses were identified in the sera of the treated patients by three different biochemical techniques confirming, as previously reported, that GVAX treatment results in a broad, multi-antigen immune response.

An ongoing analysis of these GVAX-induced antibody responses has shown that at least two of the antibody responses are associated with patient survival, an association that is independent of the dose and number of treatments administered. These data was presented by Dr. Thomas Harding

(Continued on page 2)

LOW RISK SEEN IN MONITORING, NOT TREATING, SOME PROSTATE CANCERS

The vast majority of older men diagnosed with localized prostate cancer who initially forego treatment will die of something other than prostate cancer, researchers said last week. The finding supports the view that actively monitoring the cancer's progression until such time as treatment is needed - a strategy called watchful waiting - is a reasonable response to a diagnosis of early-stage disease for some men.

Using data from NCI's Surveillance, Epidemiology, and End Results (SEER) program, Dr. Grace Lu-Yao of The Cancer Institute of New Jersey and her colleagues asked what happened to 9,000 men who chose active surveillance rather than treatment in an era when screening with the prostate-specific antigen test increased.

After 10 years, 3 to 7 percent of those with low- or moderate-grade disease had died of prostate cancer, compared with 23 percent of men with high-grade cancers. The men were diagnosed between 1992 and 2002 and did not have treatment in the first 6 months after diagnosis. Half were over age 75.

Of the approximately 2,600 men who eventually underwent treatment for the disease, about half delayed therapy for more than a decade. Prostate cancers detected by screening tend to progress slowly, and many older men die with the disease, not of it.

(Continued on page 2)

Co-Sponsors of the 2008 Genitourinary Symposium



PATIENT SURVIVAL WITH GVAX *(Continued from page 1)*

and colleagues from Cell Genesys at the American Society of Clinical Oncology's Genitourinary Cancer Symposium held in San Francisco, CA.

Cell Genesys previously reported the results of two multicenter Phase 2 trials of GVAX immunotherapy for metastatic HRPC. The second of these two trials enrolled 80 patients. The serum of 65 patients (the total number for whom adequate sera were available) were examined to determine each patient's immune response to two specific antigens, HLA-A24 and FLJ14668, after GVAX treatment.

Thirty-four of 65 patients demonstrated an FLJ14668-specific antibody immune response. These 34 patients had a median survival of 43 months, compared to a median survival of 21 months achieved by the patients who did not generate anti-FLJ14668 antibodies ($p=0.002$). Twenty-two of these 65 patients received a dose of GVAX immunotherapy for prostate cancer comparable to that being evaluated in ongoing Phase 3 clinical trials. Of these 22 patients, 16 patients (73 percent) mounted an immune response to FLJ14668. These 16 patients achieved a median survival of 44.9 months. As previously reported, the median survival for all 22 patients in this treatment group was 35.0 months. Finally, of the 58 patients who were HLA-A24 genotype negative and therefore potentially able to mount anti-HLA-A24 specific antibody responses, 30 patients were found to be anti-HLA-A24 antibody positive. These 30 patients had a median survival of 43 months, compared to a median survival of 18 months in the patients who did not generate anti-HLA-A24 antibodies ($p=0.05$). Importantly, the apparent associations between the presence of these two specific antibody responses and survival were shown by multivariate analysis to be independent of both dose and duration of treatment.

"The findings reported today indicate a potential association between two specific GVAX-induced antibody responses and patient survival, an association consistent with the proposed mechanism of action for this product. We look forward to expanding these findings in a prospective analysis of the sera of patients treated in our two

randomized controlled Phase 3 trials," stated Peter K. Working, Ph.D., senior vice president of research and development at Cell Genesys. "Since GVAX immunotherapy for prostate cancer is a multi-antigen product that can induce a broad immune response, we believe we have a unique opportunity to identify the widest possible array of specific antibody responses that may be associated with clinical benefit."

Cell Genesys is currently evaluating GVAX immunotherapy for prostate cancer in two Phase 3 multicenter, randomized, controlled clinical trials.

VITAL-1, which is fully enrolled with 626 patients, is designed to compare survival duration with GVAX cancer immunotherapy against Taxotere® (docetaxel) chemotherapy plus prednisone in asymptomatic patients with metastatic HRPC.

VITAL-2, which the company expects to fully enroll with approximately 600 patients in the first half of 2009, is designed to evaluate the safety and efficacy of GVAX immunotherapy for prostate cancer used in combination with Taxotere chemotherapy compared to the use of Taxotere chemotherapy and prednisone in symptomatic patients with metastatic HRPC. The primary endpoint again is an improvement in survival.

Abstract #261 "Identification of antibody responses induced in patients with metastatic hormone-refractory prostate cancer (mHRPC) treated with GVAX immunotherapy for prostate cancer." T. Harding.

ASCO 2008 Genitourinary Symposium PRNewswire-FirstCall, 15 February 2008

WATCHFUL WAITING

(Continued from page 1)

This study provides additional support for the use of active surveillance of localized prostate cancer in older men, particularly among those with lower grade tumors, commented Dr. Howard Sandler of the University of Michigan at the meeting.

Abstract #10 "Disease trajectory of untreated localized prostate cancer in elderly men: A population-based study." G. Lu-Yao, M.J. Barry, A. Zietman, et al.

ASCO 2008 Genitourinary Symposium NCI Cancer Bulletin, 19 February 2008

PROVENGE®

(Continued from page 1)

CD54 is a costimulatory molecule which serves as a marker for APCs. Its expression is increased when APCs become activated and this upregulation of CD54 serves as a potency release assay for PROVENGE.

Results showed that PROVENGE patients experienced improved survival if they received more cells across the three doses of PROVENGE (higher cumulative TNC count ($p=0.019$)) or higher cumulative CD54 upregulation values ($p=0.009$). The effect on survival for TNCs appeared to reflect in part the patients' baseline prognostic factors. However, the CD54 upregulation ratio appeared to be an independent predictor of survival in patients who received PROVENGE, as the correlation remained strong even after adjusting for baseline prognostic factors ($p=0.022$).

"We have been able to show a correlation between patient survival and a measure of the cumulative potency of PROVENGE; such a correlation between product potency and clinical outcome has not been previously demonstrated with an active immunotherapy," said Mark Frohlich, MD, chief medical officer of Dendreon. "These data provide further evidence that sipuleucel-T is actively engaging the immune system in a clinically meaningful way that prolongs patient survival."

PROVENGE may represent the first product in a new class of active cellular immunotherapies (ACIs) that are uniquely designed to use live human cells to engage the patient's own immune system with the goal of eliciting a specific long-lasting response against cancer. In clinical studies, patients typically received three doses of PROVENGE over a one-month period as a complete course of therapy.

For more information about Dendreon and its programs, visit their website <<http://www.dendreon.com>>.

Abstract #21 "Cell Number and CD54 Expression in Sipuleucel-T Correlate with Survival in Metastatic Androgen Independent Prostate Cancer." R.B. Sims, N.M. Provost, D.L. Urdal, Y. Xu, M.W. Frohlich.

ASCO 2008 Genitourinary Symposium PRNewswire-FirstCall, 14 February 2008

RADIATION REDUCES MORTALITY RISK OF RECURRENT PROSTATE CANCER

Ten-year prostate cancer survival was substantially higher for men given salvage radiotherapy alone or with hormonal therapy than for those who received no salvage therapy (86%, 82%, and 62%, respectively, P<0.0001), reported Bruce Trock, M.D., of Johns Hopkins University, and colleagues.

The advantage extended even to those who waited for up to two years after biochemical recurrence to start radiotherapy, Dr. Trock told attendees at the American Society of Clinical Oncology Genitourinary Cancers Symposium. Early salvage treatment was critical; salvage radiotherapy improved prostate cancer-specific survival only if given 2 years after biochemical recurrence.

Currently only about a quarter of men with biochemical recurrence receive radiation and about half are not treated, commented Howard M. Sandler, M.D., of the University of Michigan Health System in Ann Arbor, who moderated a press conference where the results were presented. "By showing that there's a survival advantage to salvage radiotherapy, this study might increase the utilization of that particular androgen strategy after surgery," he said.

When adjuvant radiation therapy is given, Dr. Trock said, it is often done immediately after their surgery for men with high-risk features because trials have shown that doing so can prolong survival. If the findings of the retrospective study are validated, it may be safe to hold off on adjuvant radiation until recurrence, Dr. Trock said. "It could eventually support a way to determine who should get immediate adjuvant radiation and who could wait until the time of recurrence to have salvage therapy," he said.

Previous studies had been too small with not enough follow-up to answer the question of survival, and none looked at the benefit of waiting until overt metastasis developed, he said. So his group analyzed survival among 635 men treated at Johns Hopkins who developed prostate cancer recurrence after radical prostatectomy. Most (397) received neither salvage radiotherapy nor hormonal therapy, 160

underwent salvage radiotherapy alone, and 78 got both. Over the median follow-up of six years after recurrence, 18% of the men died from prostate cancer.

The effect of salvage radiotherapy appeared to differ by PSA doubling time (P<0.0001). Nearly all the men with a PSA doubling time of six months or more survived to five years regardless of radiotherapy after recurrence (98% for both). Men at higher risk with a doubling time of less than six months had just as good five-year survival if they had salvage radiotherapy (95%) (HR 0.14, 95% CI 0.05-0.39), but survival fell substantially -- to 60% -- among those who did not get radiation.

Ten-year survival showed a similar benefit for radiation: it was more pronounced among those with faster doubling times (86% versus 75% for doubling time of six months or longer and 82% versus 30% with doubling time of less than six months). Although it would be expected that prognostic factors would be different for men who received treatment compared with those who did not, the results were not changed after adjustment for Gleason score, year of surgery, and time from surgery to recurrence.

Survival also differed by PSA response to salvage radiotherapy with the highest survival rates among those with a stable drop in PSA compared with those whose PSA did not fall after treatment or who did not receive treatment. Surprisingly, though, there was still a survival benefit for men whose PSA fell initially and then rose again, Dr. Trock said.

However, he emphasized repeatedly, the findings were preliminary because of the retrospective nature of the study. He said a clinical trial is needed to validate the results.

Abstract #85 "Prostate cancer-specific survival in men with biochemical recurrence after radical prostatectomy: impact of salvage radiotherapy vs. observation." B. Trock, M. Han, S.J. Freedland, E.B. Humphreys, T.L. DeWeese, A.W. Partin, P.C. Walsh.

ASCO 2008 Genitourinary Symposium MedPage Today, 14 February 2008

BISPHOSPHONATE EFFECTIVE LONG TERM IN PROSTATE CANCER HORMONE THERAPY

Zoledronic acid (Zometa®, ZA) significantly increased T scores in both hips and the lumbar spine (P<0.05) over more than a year of use in older high-risk men, according to a small randomized trial presented at the American Society of Clinical Oncology Genitourinary Cancers Symposium. This was true even when the drug was started later in the course of therapy, reported William R. Broderick, MD, of Loyola University Medical Center in Maywood, IL, and colleagues.

Starting ZA later may allow men to avoid the drug's side effects of bone pain and renal impairment until bone mineral density (BMD) changes appear, Dr. Broderick said. Men who are at lower risk based on comorbidities and annual screening of BMD may be able to first pursue lifestyle modification, including exercise and smoking cessation, said co-author Nirmala Bhoopalani, MD, of Loyola and the VA Hospital in Hines, IL.

Longer-term use among men on androgen deprivation therapy (ADT) has not been studied; nor was there proof it would prevent bone loss if not started at the same time as ADT, the researchers noted. So, they randomized 93 men with nonmetastatic prostate cancer treated at VA medical centers to receive a double blind intravenous infusion every three months of 4 mg ZA or placebo. Men in both groups were also started on calcium, vitamin D, and weight-bearing exercise. Mean age was 70.5 years; 55% were Caucasian, 41% were African-American, and 4% were Hispanic, and mean BMI was 29.4. None of the men had osteoporosis at baseline, defined as a BMD T score of -2.0 or less as measured by dual energy X-ray absorptiometry. Follow-up scans were done at six and 12 months.

Overall, T-score percent change was significantly better with active treatment than placebo for the left and right hip (both P<0.05) and most dramatically so for the lumbar spine (6% increase versus more than 1% de-

(Continued on page 4)

WHICH MEN ARE LIKELY TO HAVE PERSISTENT PROSTATE CANCER?

“Radiotherapy offers the chance of a cure for most patients,” explained Mark K. Buyyounouski, MD, MS, attending physician in the radiation oncology department at Fox Chase Cancer Center. “For some, however, an elevated PSA level after treatment indicates the cancer is still around or has come back. Our new study shows how we can use biopsy information prior to treatment to help us predict which patients are most likely to still have disease after treatment. With this knowledge, we can better tailor treatment.”

In the study presented by Buyyounouski, researchers compared prostate biopsies taken before treatment with those taken again two years after treatment. All the study volunteers had cancers that were intermediate or high risk. “Larger tumors are believed to be more likely to persist after treatment, but what defines a larger tumor has been controversial,” said Buyyounouski. “What we found was that a high percentage of cancer observed in the biopsy before treatment correlated with a higher probability of a positive biopsy afterwards. This information is important because locally persistent cancer may result in later spread of the disease and possibly death.”

Buyyounouski explained that other researchers have explored the use of biopsy information to identify higher risk of recurrence for men with prostate cancer. Using a percentage of positive biopsy cores has been advocated by some, but these types of studies compared the cores to PSA level after treatment and not post-treatment biopsies. “This study is important because the percentage of cancer seen in the biopsy before treatment is directly correlated with cancer seen in the biopsy in the same location two years after treatment,” he explained.

Buyyounouski said current sophisticated radiation technologies such as IMRT could allow physicians to tailor treatment for these patients.

Abstract #88 “Predicting local persistence of prostate cancer using percentage of adenocarcinoma in pretreatment biopsy tissue.” M.K. Buyyounouski, T. Li, T. Al-Saleem, E. Horwitz, A. Pollack.

ASCO 2008 Genitourinary Symposium ScienceDaily, 19 February 2008

IMMEDIATE ANDROGEN SUPPRESSION QUESTIONED FOR NODE-POSITIVE PROSTATE CANCER

Neither overall nor disease-specific survival were significantly higher for men who held off than for those who started androgen suppression (AS) immediately, said Fritz H. Schröder, MD, PhD, of Erasmus Medical Center in Rotterdam, The Netherlands and colleagues. The issue of timing remains unresolved, though, because the large randomized trial was underpowered, he added. The power of the study to show a 50% difference between treatment groups was only 80%.

Nevertheless, the findings may challenge early endocrine therapy as the standard, commented Bruce J. Roth, MD, of Vanderbilt-Ingram Cancer Center in Nashville, TN, who chaired the conference program committee. “Now it’s really a toss-up,” he said. “It needs to be driven by patient decision after a lengthy discussion of what the implications of a longer duration of hormonal therapy are.” The benefits in biochemical recurrence and potentially survival from early AS come at the price of increased cardiovascular mortality from additional years of hormonal therapy, Dr. Roth noted.

Early hormone therapy became the gold standard in the US primarily based on an Eastern Cooperative Oncology Group (ECOG) trial published in the New England Journal of Medicine in 1999 that showed a survival benefit with 7 years of follow-up. “Unfortunately, what most people don’t realize was the study was heavily underpowered and unable to make those conclusions definitively,” Dr. Roth said. The trial was designed to be a 230-patient trial but was stopped at 97 patients for lack of accrual.

Dr. Schröder’s group undertook the European Organization for Research and Treatment of Cancer study 30846 to answer the same question of timing. Like the ECOG trial, it faced slow accrual and was closed in 1998 with 234 patients who had non-metastatic T2 to T3 prostate cancer and one to three positive nodes. Participants received no treatment for their primary prostate cancers. They were randomized to immediately start endocrine therapy with monthly injections of goserelin (Zoladex®) plus cyproterone acetate during the first four weeks or to the

same regimen only upon disease progression. Nearly all patients in the delayed-treatment group started AS within four years. Delayed therapy offered a quality-of-life window of 18 months, Dr. Schröder said.

After a median 13 years of follow-up, there were no significant differences between the immediate and delayed treatment groups in overall survival (median 7.6 vs. 6.1 years, $P=0.166$). Causes of death were similar between groups, although prostate cancer-specific mortality was slightly higher with delayed than immediate endocrine therapy (60.9% vs. 58%).

“Without a larger study, which may be impossible to conduct at this point, one has to just take that data for what it is — not definitive,” he added.

Abstract #5 Early versus delayed endocrine treatment of pN1-3 M0 prostate cancer without local treatment of the primary tumor: results of European Organization for the Research and Treatment of Cancer protocol 30846 after 13 years of follow-up -- a phase III study.” F.H. Schröder.

*ASCO GU Meeting 2008
MedPage Today, 15 February 2008*

ZOMETA®

(Continued from page 3)

crease, $P<0.05$). Among the 50 patients who had been on ADT for less than a year at baseline, BMD increased 5.95% with ZA but decreased 3.2% with placebo ($P=0.0044$).

Among the 43 patients entering the study more than a year after initiating ADT, BMD increases were greater with ZA (6.1% vs. 1.6%, $P=0.0005$).

BMD in left and right hips also increased in both groups with active treatment ($P<0.05$), which is important, Dr. Bhoopal said, because hip fractures are the type most worrisome to patients. However, the study was not of long enough duration to see an impact on fracture incidence.

Abstract # 177 “A phase III trial of zoledronic acid (Z) to prevent osteoporosis in men on early and prolonged androgen deprivation therapy (ADT) in a high risk VA population.” W.R. Broderick.

*ASCO 2008 Genitourinary Symposium
MedPage Today, 18 February 2008*