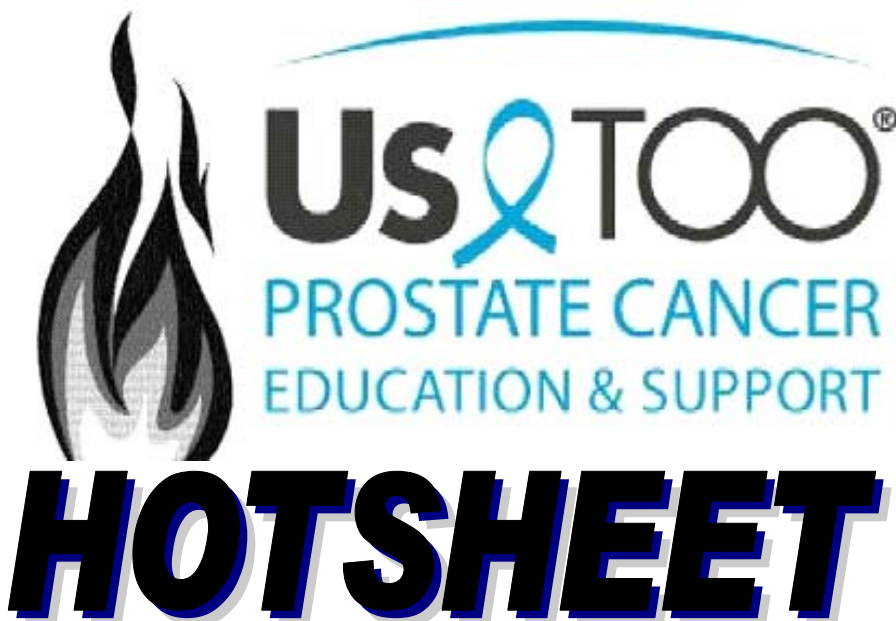


INSIDE THIS ISSUE

- RT Shown Beneficial for Prostate Cancer Subset
- Denosumab Extends Time to Bone Events
- Us TOO Seeks Board Member Applications
- High-Intensity Focused Ultrasound (HIFU) Non-Inferior to EBRT for Prostate Cancer
- Cabazitaxel Benefit Confirmed in Prostate Cancer Now FDA Approved (Jevtana®, sanofi-aventis)
- Doc Moyad's "No Bogus Science" Column – "Exercise Ups Cialis®, Levitra® & Viagra®"
- Pelvic RT Increases Hip Fracture Risk in Men
- Bevacizumab (Avastin®) Fails to Prolong Survival in Resistant Prostate Cancer
- PSA Misses the Mark in Active Surveillance
- Ask Doctor Snuffy Myers
- Doctor Chodak's Bottom Line



JULY 2010

KEY ARTICLES FROM THE 2010 AUA & ASCO MEETINGS

RT SHOWN BENEFICIAL FOR PROSTATE CA SUBSET

Men with advanced prostate cancer lived significantly longer when treated with RT and hormonal therapy (HT) compared with HT alone, data from a multinational clinical trial showed.

Combination therapy reduced overall mortality by 23% and disease-specific mortality by 43% versus HT alone. The benefits accrued with no increase in toxicity, Pdraig Warde, MBChB, reported at the 2010 American Society of Clinical Oncology (ASCO) meeting.

"We're confident that RT should be part of the treatment package in this group of patients," said Warde, of the University of Toronto and Princess Margaret Hospital. "It's interesting to note that it's possible that we underestimated the benefit of RT, as with the changes in technology over the past decade, radiation oncologists have been able to put much higher doses of RT into the prostate than used in this study."

Though widely used in the treatment of prostate cancer, RT had an undetermined impact on survival in men with locally advanced disease. To address that void, investigators in Canada, Europe, and the US conducted a randomized, controlled clinical trial of HT with or without RT.

(Continued on page 4)

DENOSUMAB EXTENDS TIME TO BONE EVENTS IN PROSTATE CANCER

The monoclonal antibody denosumab (Prolia®) appears to significantly increase the time before a patient with castration-resistant prostate cancer (CRPC) suffers a skeletal fracture, researchers reported in an oral presentation at the 2010 Annual ASCO meeting.

The median time until a fracture occurred in men treated with denosumab was 20.7 months, compared with 17.1 months for those treated with zoledronic acid (Zometa®, ZA) (P=0.008).

In the trial, Karim Fizazi, MD, PhD, head of the department of medical oncology at Institut Gustave Roussy, Villejuif, France, noted that the primary endpoint was to prove that denosumab was noninferior to ZA. The secondary endpoint was to show superiority.

"Denosumab was superior to ZA in preventing or delaying the first skeletal-related events and in preventing or delaying multiple skeletal events," Fizazi said. Fizazi explained that denosumab, a RANKL (Receptor Activator for Nuclear Factor κB Ligand), interrupts the cascade of molecular events that leads to prostate cancer metastatic bone lesions.

The trial enrolled 945 patients who were

(Continued on page 8)

US TOO SEEKS BOARD MEMBER APPLICATIONS

Us TOO is seeking nominations to the Us TOO International Board of Directors (BOD). In addition to the two seats that will become vacant beginning January 1, 2011, there are also seats currently available now.

The Board Membership Committee, chaired by Carl Frankel, Esq., will review and evaluate nominees and submit recommendations to the full Board for approval throughout the remainder of this year, as well as at its December 2010 Board meeting.

The Us TOO International BOD is made up of 15 seats, one third of which are up for re-election annually. Two Board members who will be ending their terms of service this December 2010 are Greg Bielawski and Carl Frankel, Esq.

Retiring Board Secretary Carl Frankel exclaims, "What a wonderful experience and opportunity it has been to serve on the Board of Us TOO, International! For Directors, the "dividend" is the knowledge that we have contributed meaningfully and in our own individual way to the goal of providing support, education and a voice to prostate cancer patients and their families. It is how we fight

(Continued on page 2)

THIS ISSUE OF THE US TOO PROSTATE CANCER
HOT SHEET IS MADE POSSIBLE BY
CHARITABLE CONTRIBUTIONS FROM

Genentech
IN BUSINESS FOR LIFE

AND PEOPLE LIKE YOU!

ITEMS CONTAINED IN US TOO PUBLICATIONS ARE OBTAINED FROM VARIOUS NEWS SOURCES AND EDITED FOR INCLUSION. WHERE AVAILABLE, A POINT-OF-CONTACT IS PROVIDED.

REFERENCES TO PERSONS, COMPANIES, PRODUCTS OR SERVICES ARE PROVIDED FOR INFORMATION ONLY AND ARE NOT ENDORSEMENTS. READERS SHOULD CONDUCT THEIR OWN RESEARCH INTO ANY PERSON, COMPANY, PRODUCT OR SERVICE, AND CONSULT WITH THEIR LOVED ONES AND PERSONAL PHYSICIAN BEFORE DECIDING ON ANY COURSE OF ACTION.

THE INFORMATION AND OPINIONS EXPRESSED IN THIS PUBLICATION ARE NOT RECOMMENDATIONS FOR ANY MEDICAL TREATMENT, PRODUCT SERVICE OR COURSE OF ACTION BY US TOO INTERNATIONAL, INC., ITS OFFICERS AND DIRECTORS, OR THE EDITORS OF THIS PUBLICATION. FOR MEDICAL, LEGAL OR OTHER ADVICE, PLEASE CONSULT PROFESSIONAL(S) OF YOUR CHOICE.

HOT SHEET EDITORIAL TEAM:

JONATHAN McDERMED, PHARM D
PAMELA BARRETT
THOMAS N. KIRK

US TOO INTERNATIONAL STAFF:

THOMAS N. KIRK, PRESIDENT AND CEO
PAMELA BARRETT, DEVELOPMENT DIRECTOR
TERRI GIBBONS, CHAPTER SERVICES PROGRAM
MANAGER
JAQUELINE KONIECZKA, OFFICE MANAGER
RYAN MAGUIRE, COMMUNICATIONS
COORDINATOR

US TOO BOARD OF DIRECTORS:

EXECUTIVE COMMITTEE/OFFICERS

FRED MILLS, CHAIRMAN
KAY LOWMASTER, MSW, LCSW, VICE-CHAIR
CARL FRANKEL, ESQ., SECRETARY
DAVID P. HOUCHEMS, PH.D, TREASURER
RIDGE TAYLOR, ASSISTANT TREASURER/SECRETARY

DIRECTORS:

GREG BIELAWSKI
JERRY HARDY
JEAN JEFFRIES
DAVID M. LUBAROFF, PH.D
RICK LYKE, APR
THOMAS N. KIRK, PRESIDENT AND CEO

US TOO INTERNATIONAL, INC. IS INCORPORATED
IN THE STATE OF ILLINOIS AND RECOGNIZED
AS A 501(C)(3) NOT-FOR-PROFIT
CHARITABLE CORPORATION

**DONATIONS / GIFTS TO US TOO
ARE TAX DEDUCTIBLE**

5003 FAIRVIEW AVE. DOWNER'S GROVE, IL 60515
PHONE: (630) 795-1002 / FAX: (630) 795-1602

WEBSITE: WWW.USTOO.ORG

COPYRIGHT 2010, US TOO INTERNATIONAL, INC.

HIGH-INTENSITY FOCUSED ULTRASOUND NONINFERIOR TO EXTERNAL BEAM RT FOR PROSTATE CANCER

New data presented here at the 2010 American Urological Association (AUA) Annual Meeting show that high-intensity focused ultrasound (HIFU) as primary therapy for prostate cancer can produce outcomes equal to external beam radiation therapy (EBRT).

A series of 880 consecutive patients showed steadily improving results as HIFU technology improves, according to Sebastien Crouzet, MD, Edouard Herriot Hospital, University of Lyon, Lyon, France. "We have followed some patients as long as 10 years and are reaching results very similar to EBRT," stated Dr. Crouzet. "The main issue is that you can repeat HIFU if you see evidence of disease. And if the disease continues to progress, you can add salvage RT to achieve very good control."

Starting in 1997, all patients with prostate cancer with localized disease who received whole gland ablation and at least 1 year of follow-up were included in the study cohort. Follow-up included serial PSA measurements and systematic control biopsies at 6 months.

Men with a rising PSA were biopsied and if recurring cancer was evident, they were offered additional treatments and repeat biopsies. Those with a positive biopsy after follow-up HIFU were offered EBRT or androgen deprivation.

The study included a total of 880 men. Their mean age was 70 years and their mean PSA at first HIFU was 8.4 ng/mL. Of the group, 36% had low-risk disease, 48% had intermediate-risk disease, and 16% had high-risk disease. Patients received a mean of 1.4 HIFU treatments.

The mean PSA nadir was 0.45 ng/mL and 69% of men reached ≤ 0.3 ng/mL. Mean follow-up was 41 months. The overall 7-year survival rate was 90% and the 7-year cancer-specific survival rate was 98%. Fully 96% of patients were free of metastases 7 years after HIFU. The 5-year biochemical survival rate was 75%, 59%, and 45% for low-, intermediate-, and high-risk patients. The 7-year biochemical survival rate

(Continued on page 3)

NEW BOD MEMBERS NEEDED

(Continued from page 1)

back against the disease that has invaded all our lives."

Frankel continues, "The last few years have been especially challenging, but Us TOO has responded well, and we look forward to our 20th anniversary celebration in just a few months. As for the future, I see opportunities to provide new and improved services to what promises to be a growing patient base and, importantly, to secure the necessary resources to fund those services. Though I enjoyed and profited emotionally from my two terms on the Board, I do envy the successor Directors who will share in this upcoming adventure."

Greg Bielawski will also end his term of service this December. He has served as Board Treasurer, and Co-Chair of the Annual SEA Blue Prostate Cancer Walk & Run event in Chicago, IL.

Greg comments: "Us TOO International is celebrating its 20th birthday this year. Over the last seven years as a board member, I am proud to have been part of the maturing and growth of Us TOO from primarily a prostate cancer education and support organization into that of a leader in the prostate cancer advocacy world whose perspective is sought out and respected. If you wish to see Us TOO become even more influential in the next decade, and have the passion and desire to help that happen, please consider applying to join the BOD."

Selection criteria include items such as the candidate's relationship to Us TOO's purpose, its membership criteria ("...any man diagnosed with prostate cancer, a member of such a man's family or significant other, or any person involved in or interested in support or treatment of any such patients..."), familiarity with an Us TOO chapter, ability to think globally, skills or experience deemed beneficial to the work of Us TOO and commitment to Us TOO's purpose and mission.

Letters of nomination with a vita or resume can be sent now to Thomas Kirk, President/CEO, Us TOO International, 5003 Fairview Avenue, Downers Grove, IL 60515 or e-mail <tom@ustoo.org>.

CABAZITAXEL BENEFIT CONFIRMED IN PROSTATE CANCER

Final results of the TROPIC study confirmed that the investigational taxane cabazitaxel extends survival among castration-resistant prostate cancer (CRPC) patients whose cancers progressed despite docetaxel (Taxotere®), researchers reported at the 2010 ASCO meeting.

The multinational phase III study found that cabazitaxel reduced mortality risk by 28% vs. mitoxantrone (Novantrone®; P<0.0001), reported Johann De Bono, MD, DSc, PhD, senior lecturer at Royal Marsden Hospital, London. “Cabazitaxel is the first treatment to show a survival benefit to patients with metastatic castrate-resistant prostate cancer after failure of docetaxel based therapy.”

The trial randomized 378 patients with CRPC to receive cabazitaxel 25 mg/m² and 377 to receive mitoxantrone 12 mg/m², both intravenously every 3 weeks. All participants got prednisone 10 mg per day for 10 cycles of chemotherapy.

Overall, CRPC patients survived a mean of 15.1 months on cabazitaxel and 12.7 months on mitoxantrone, for a hazard ratio of 0.72. He also reported that patients receiving cabazitaxel showed statistically significant improvement in progression-free survival, tumor response rates, and in time to disease progression.

Grade 3 or higher neutropenia occurred in 58% of patients in the mitoxantrone group vs. 82% of those on cabazitaxel. Prophylactic use of white blood cell growth factors was permitted, except for the first treatment cycle.

In his discussion of the trial, Ian Tannock, MD, PhD, senior scientist at the Ontario Cancer Institute, Princess Margaret Hospital, Toronto, suggested that the rate of toxic deaths – about 5% of the patients – might have been mitigated if the researchers had used a lower dose

of the drug, which was found to have fewer side effects in breast cancer.

He added “cabazitaxel significantly improved survival when compared to mitoxantrone in men who received prior docetaxel and will likely become standard of care. There is no FDA-approved treatment after docetaxel.”

De Bono J, et al, J Clin Oncol 2010; 28: 344s
MedPage Today, 9 June 2010

Editor’s note: On 17 June 2010, the US FDA approved cabazitaxel (Jevtana® Injection, sanofi-aventis) for use in combination with prednisone for treatment of patients with metastatic CRPC previously treated with a docetaxel-containing regimen. The approval is based primarily on the results of the study described in the above article.

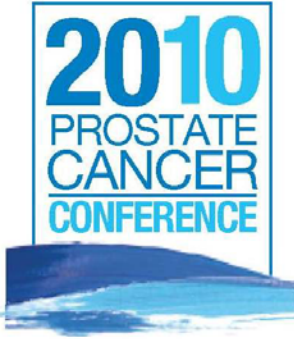
HIFU VS. EBRT

(Continued from page 2)

was 62%, 50%, and 39% for low-, intermediate-, and high-risk patients (P=0.0001). A total of 239 patients had biopsy-proven local relapse after a second HIFU treatment. Of this group, 156 patients had salvage EBRT and 83 patients had androgen deprivation therapy.

“Disease control and survival rates with HIFU are very encouraging,” Dr. Crouzet said. “You also have the advantage that HIFU is very minimally invasive. You don’t touch the nerve or the sphincter, therefore you avoid the side effects of more invasive treatment.”

Crouzet S, et al, AUA 2010; abstract 1953
<www.docguide.com>, 3 June 2010



SAVE THE DATES!

SEPTEMBER 11-12, 2010
MARRIOTT LOS ANGELES AIRPORT HOTEL, CALIFORNIA
Making a Positive Impact on Quality of Life
MODERATED BY: MARK MOYAD, MD

Register Early and Save!
www.pcri.org


Join us in Los Angeles for the Prostate Cancer Conference. The 1 ½ day conference features an impressive line-up of clinicians and researchers who will tackle subjects ranging from diet and nutrition, sexual health, erectile dysfunction, active surveillance, hormone treatments, radiation, chemotherapy and much more!

There will be plenty of opportunity to ask your questions and get answers – **Meet the Speakers, Ask the Experts, Roundtable Discussion, Support Group Meetings, and Exhibits.** Plus we will host a gala night and organize a couple of Los Angeles excursions.


FACULTY


William Aronson, Duke Bahn, Marc Botnick, Richard Lam, Mark Moyad
 John Mulhall, Charles Myers, Dean Ornish, Mack Roach III, Mark Scholz,
 Stephen Strum and Nicholas Vogelzang


Proudly produced by:





Working together for a cure


















SEA
BLUE



6TH ANNUAL CHICAGO
 prostate
 cancer
 walk/run

SUPPORT EDUCATE ADVOCATE

Sunday, September 19, 2010
 Lincoln Park, Chicago, IL

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

**"Exercise makes Cialis®, Levitra®, & Viagra® work better!
Maybe the drug itself should come with a free treadmill?"**

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

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

Bottom Line: There is now a randomized trial to demonstrate that when you are taking a prescription drug for erectile dysfunction and you also begin to exercise regularly there is a potential further benefit in the area of sexual desire and erectile function that does not occur with the drug alone.

This is fabulous information! However, you are not going to see the results of this study advertised on TV or the radio or in the newspaper. There have been several past studies to suggest that exercise can improve erectile function. However, a group from Italy decided to do a randomized trial.

Patients that accomplished 3 or more hours a week of exercise (only about 30 minutes on average a day for most days of the week) while also taking an erectile dysfunction pill demonstrated significant improvements in erectile function compared to men that just took the pill by itself. The type of exercise did not really matter but just the commitment to exercise.

For example, men in the intervention group did any of the following activities: jogging, biking, walking briskly, soccer, tennis and swimming. The average age of the participants was 50 and the average body mass index (BMI) was 27, which means that the average man in this study was overweight (similar to the US). Research suggests that exercise causes an increase in blood flow to numerous parts of the body, and causes the release of a compound that helps to maintain an erection.

The most amazing thing about this study is that many people do not realize that the erectile dysfunction drugs have never been shown to significantly increase sex

drive (also known as "libido"). They do a good job of improving erections and they do come with side effects and cost too much money, but they do work, but just not in the area of improving sex drive. In this study, over 3 months, there was no increase in sex drive for the men that took the drug alone and did NOT exercise. However, the men that took the medications and exercised did have a significant increase in sex drive!

So, this study makes me wonder how well exercise by itself would have done compared to taking the pill alone or taking the pill and exercising. In other words, it is interesting that there was no third group of men studied in this clinical trial that just exercised (no pills)! I wonder, would that group have beaten the pill? We are left to wonder-dang! However, what we are not left to wonder is that if you take any prescription drug for erectile dysfunction and you do not exercise...well you are not getting the most of your investment my friends. Heart health=penile health! Sorry, just decided to cut to the chase because I am running out of writing room!

Maio G, Saraeb S, Marchiori A, J Sex Med, 30 March 2010, Epub ahead of print

PELVIC RADIATION BOOSTS HIP FRACTURE RISK IN MEN

External beam radiation therapy (EBRT) for prostate cancer increased the risk of hip fracture by almost 70% compared with radical prostatectomy (RP) according to a study reported at the 2010 AUA meeting by Sean Elliott, MD, of the University of Minnesota in Minneapolis.

Elliott and colleagues researched the Surveillance, Epidemiology and End Results (SEER) and Medicare data related to prostate cancer therapy for 1992 to 2005 for men who were at least 66 at diagnosis. Using RP as reference, they examined fracture risk in men who had EBRT alone, EBRT+ androgen deprivation (ADT, 6 to 36 months), or ADT alone (no duration limit). A total of 55,448

RT+HT BENEFICIAL

(Continued from page 1)

Enrollment was limited to patients with locally advanced or high-risk prostate cancer, defined as bulky disease or a high PSA level, or Gleason score of 8 or greater. Warde said the subgroup constitutes 15% to 25% of prostate cancer patients and accounts for a substantial proportion of prostate cancer deaths.

All patients underwent bilateral orchiectomy or received lifelong androgen deprivation therapy. Patients randomized to RT received a total dose of 69 Gy to the prostate and seminal vesicles with or without 45 Gy to the pelvic lymph nodes. The primary objective was to determine the effect of RT on overall survival. Secondary endpoints were disease-specific survival, time to disease progression, and quality of life.

The study involved 1,205 patients, whose baseline characteristics did not differ significantly between the groups. After a median follow-up of seven years, 74% of patients in the combined-therapy group remained alive, compared with 66% in the control group. The difference translated into a mortality hazard ratio of 0.77 in favor of combination therapy (P=0.033).

Also at seven years, more than twice as many patients in the control group had died of prostate cancer, 21% versus 10% in the combination arm, a difference that resulted in a hazard ratio of 0.57 for prostate cancer-specific mortality (P=0.001).

The quality-of-life assessment focused primarily on toxicity. Warde said the two treatment groups did not differ significantly with respect to the frequency of adverse events, including late grade 2+ gastrointestinal toxicity, which occurred in 1.3% of the control group and 1.8% of patients who received RT.

"We feel that we've shown that patients treated with combined treatment, RT and HT, live longer and are less likely to die of prostate cancer," said Warde. "RT gave very little in side effects."

Warde PR, et al, J Clin Oncol 2010; 4504s
MedPage Today, 8 June 2010

(Continued on page 8)

BEVACIZUMAB FAILS TO PROLONG SURVIVAL IN RESISTANT PROSTATE CANCER

The addition of bevacizumab (Avastin®) to chemotherapy in treating metastatic castrate-resistant prostate cancer fell short of providing a survival benefit to patients, researchers said here.

Patients who received the antiangiogenesis target agent bevacizumab, along with standard taxane-based therapy, achieved a 9% decreased risk of mortality in the study, but that difference in overall survival failed to achieve statistical significance ($P=0.181$), said William Kevin Kelly, DO, associate professor of medicine at Yale University.

“The role of antiangiogenesis therapeutics in metastatic castrate-resistant prostate cancer remains to be defined,” said Kelly, who reported the results at the annual meeting of the American Society of Clinical Oncology on behalf of the Cancer and Leukemia Group B (CALGB) and Eastern Cooperative Oncology Group investigators.

He noted that treatment with bevacizumab added to docetaxel (Taxotere®), with pretreatment dexamethasone, and prednisone did improve progression-free survival to 9.9 months compared with 7.5 months ($P<0.001$) for patients who did not receive bevacizumab.

The researchers also noted that an objective response was observed in 53.2% of the bevacizumab patients, compared with 42.1% of the patients not receiving bevacizumab ($P=0.0113$). About 69.5% of patients taking bevacizumab achieved a greater than 50% decline in prostate-specific antigen levels, compared with 57.9% of the patients who only received the docetaxel-based therapy ($P=0.0002$).

But despite those favorable results among these widely-accepted surrogate markers for treatment success, these secondary endpoint outcomes did not translate into a survival benefit in the trial. However, the investigators noted that median overall survival in the docetaxel/prednisone group was longer than reported in other trials.

Doctors recruited 1,050 patients who were diagnosed with progressive, metastatic castration-resistant prostate cancer and randomized 524 of the men to receive docetaxel 75 mg/m² by intravenous infusion over one hour every 21 days, plus prednisone 5 mg orally twice a day with bevacizumab 15 mg/kg given intravenously every three weeks. The other 526 men received the same dosing of docetaxel and prednisone. All pa-

tients received dexamethasone 8 mg prior to receiving docetaxel.

Kelly noted that patients receiving bevacizumab experienced a worse adverse effect profile with patients having more fatigue, more febrile neutropenia, more hypertension, and more gastrointestinal perforation and hemorrhage.

In his discussion of the study, William Dahut, MD, chief of the genitourinary/gynecological clinical research section of the National Cancer Institute, Bethesda, Md., suggested that despite the negative findings in the CALGB 90401 study, there still may be a role for antiangiogenesis agents in advanced prostate cancer.

“Angiogenesis remains a target worthy of exploration in metastatic castrate-resistant prostate cancer,” he said. “Questions of appropriate populations, treatment duration, and the need for combination therapy need to be answered in order to validate this as a target. Bevacizumab combinations cannot be recommended at this time outside a clinical trial.”

Kelly W, et al, *J Clin Oncol* 2010; 34:4s
MedPage Today, 9 June 2010

PSA MISSES THE MARK IN ACTIVE SURVEILLANCE (AS)

An evaluation of commonly used prostate specific antigen (PSA) parameters showed the tests would have led to treatment recommendations for as many as 84% of low-risk patients, data from an ongoing study showed. Moreover, PSA-based decision-making had the potential to expose some men to multiple interventions, according to Laurence Klotz, MD, of Sunnybrook Health Sciences Centre and the University of Toronto.

“There is a critical need for a trigger that strikes a balance between recommending treatment for patients at high risk of progression and minimizing treatment for those at low risk,” Klotz told attendees at the 2010 Annual AUA meeting. At an AUA press briefing, Klotz acknowledged that the search for a more accurate alternative to PSA-based testing has yet to uncover any can’t-miss prospects. He characterized the search as the “\$64,000 question of AS.”

Despite consistent evidence of overtreatment, AS (or watchful waiting or observation) has yet to catch on as a primary approach to managing low-risk prostate cancer, particularly in the US. That’s in part because of uncertainty about how to determine when a prostate tumor has begun to progress, said J. Brantley Thrasher, MD, of the University of Kansas in Kansas City, who moderated the press briefing.

To shed light on the accuracy of PSA-based measures for decision-making in AS, Klotz and his colleagues applied various PSA parameters to a cohort of men with low-risk prostate cancer, some of whom have been followed for as long as 20 years. Their analysis involved 452 men enrolled in the Sunnybrook Active Surveillance Program at Toronto’s Sunnybrook Medical Center. Median age at enrollment was 69 years and ranged from 49 to 84 years.

The patients had stage T1b-T2b organ-confined disease. Almost 80% of them had pathology-confirmed Gleason 6 or less prostate cancer, and all men with higher Gleason values were 70 years or older. Klotz said 84% of the men had PSA values less than 10 ng/mL, and the remaining patients had values that were less than 15 ng/mL.

The entire cohort had a 10-year survival of 68%, and prostate cancer accounted for only five of 97 deaths, resulting in a 10-year cause-specific survival of 97%. Klotz said 70% of the cohort remained on surveillance and 62% remained free of intervention at 10 years.

Comparing cause-specific versus non-prostate cancer survival resulted in a hazard of 18.6, meaning that men in the study were 19 times more likely to die of a cause other than prostate cancer.

A subgroup of 315 men with stable,

(Continued on page 8)

ASK DOCTOR SNUFFY MYERS

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

Several American oncologists, including you, have suggested that some of their patients go to the Netherlands for a Combindex scan to aid in determining which lymph nodes might be involved with their prostate cancer in order that clinical decisions can be made regarding follow-up radiation or other therapeutic approaches.

It appears that Combindex scans may no longer be available. Do you consider this a setback to accurately determining nodal involvement?

A group of other physicians and I have had a chance to see Combindex results on our patients. The images are quite stun-

ning in the clarity with which the cancer in the lymph nodes can be seen. I have sent these patients for radiation therapy, largely to Dr. Dattoli in Sarasota, FL. Dr. Roach, a radiation therapist at University of California San Francisco, has also had extensive experience using this approach, but most of my patients are on the East Coast and have been treated by Dr. Dattoli. I have a group of men with cancer recurrent after surgery or radiation to the prostate gland that are now disease-free because of Combindex-guided radiation therapy. Both Marc Scholz and Stephen Strum have had similar positive experiences.

The agent continued to be available in Nijmegen, Netherlands for a period of time. However, the company making the imaging agent used by the Nijmegen group stopped manufacturing the agent.

Why was this agent not approved in the US? The company that had the responsibility to carry the Combindex through the FDA approval process followed a strat-

egy that was poorly thought out and destined to fail. In the end, the information they presented to the FDA did not come close to satisfying requirements for approval. The FDA really had no choice in the matter.

Right now, nothing available in the US even remotely replaces the missing Combindex scan. Both the ProstaScint scan and PET scans can pick up lymph node involvement often missed on CT scan, but are not nearly as useful as the Combindex scan was.

So yes, I do consider this a setback to accurately determining nodal involvement with prostate cancer.

Efforts are now ongoing to see if the Nijmegen group can find an alternate source of the imaging agent. Also, a number of concerned physicians in the United States are working to find a substitute for the Combindex scan.

Editors' note: See the April/May 2010 issue of the Us TOO Chapter NEWS for a cover story on a meeting re: Combindex developments.

From Passion To Action : Us TOO at 20

The Us TOO International Summit, Symposium & Celebration

for Men and their Families Battling Prostate Cancer

AUGUST 20 - 21, 2010 • CHICAGO, ILLINOIS

Join the Fun and Excitement!!!!

- A Pre-symposium **Advocacy Summit**: moving beyond the confusion on prostate cancer screening guidelines & updates on research priorities in imaging.
- 2-day **Educational Symposium**: with respected MDs, active survivors & family members addressing the latest on treatment approaches & critical research, status of new or potential breakthroughs & examples of citizen action.
- Exhibits & "Meet the Authors."
- 20th Anniversary Dinner & Awards Celebration.
- Quality Hotel! Great Rate! Easy Location!
- **Pints for Prostates** – Gourmet Beer-Tasting Fundraiser.



To Learn More and Register
www.ustoo.org/2010symposium

or Call

1-800-808-7866

Space is Limited

REGISTER TODAY!

Early Bird Discounts

DOCTOR CHODAK'S BOTTOM LINE

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*. Our desire is to enrich the content of the *HotSheet* to empower the reader. Each piece contains the opinions and thoughts of its author and is not necessarily those of Us TOO International.

This month's *HotSheet* contains articles from the recent ASCO and AUA annual meetings. As you read through them keep in mind that, on average, Less than 20% of presentations at medical meeting will not get published in the next five years, although that is less common for randomized studies. For that reason, some caution is needed in interpreting the results of some of these reports.

Over the past 15 years, radiotherapists have done several randomized studies assessing the value of radiation in prostate cancer. Some of those studies found that giving hormones for 28 to 36 months along with radiation significantly improved survival in men with locally advanced or high risk disease.

None of those studies, however, proved that the radiation was necessary. That proof is now available. A large randomized study gave all men continuous hormone therapy but only about one-half also received radiation.

After 7 years, there was a 8% higher survival in men getting the combination and a 10% lower risk of dying from this disease. Fortunately, the side effects were low. Although the survival benefit is not huge, keep in mind that the dose of radiation used in the study was only 69 Gy, which is known to be less effective than doses of 76 -80 Gy used today.

The questions still needing answers are whether hormone therapy needs to be permanent and whether higher doses of radiation will further increase survival.

The Bottom Line: The best way to maximize survival for men with locally advanced or high risk prostate cancer is to use radiation and hormone therapy rather than either alone.

Despite the clear benefit of this combination, the long term risks are less well studied. Hormone therapy increases osteoporosis and bone fractures. A new study using Medicare data suggests that

radiation to the prostate increases the risk of pelvic fractures compared to men having a prostatectomy. That rate appears even higher when radiation is combined with hormone therapy. The risk also could be higher in men now getting much higher doses of radiation. The problem with this study is that the data may be misleading because of age differences in the different groups.

The Bottom Line: Few men getting prostate radiation are informed about the possible risk of a pelvic fracture years later. This risk must be further evaluated so that men can get accurate information when weighing their treatment options.

Fortunately, the risk of fractures and other bone related events can be prevented. Zoledronic acid (Zometa®) is one drug approved for reducing this risk. A new drug, Denosumab (Prolia®), has been compared to Zoledronic acid in a large phase III randomized study. The results show that Denosumab delayed the time to first bone fracture or other bone related events by three months in one-half of the men.

This study will need further scrutiny when published due to the high percentage of men withdrawing from the study and the higher incidence of side effects. Although Denosumab has been approved with restrictions for postmenopausal women, the FDA has not yet approved it for prostate cancer.

The Bottom Line: Men with metastatic prostate cancer are at risk for fractures and should be offered treatment with Zoledronic acid until other drugs are approved.

The article on High Intensity Focused Ultrasound is a good example of the need for caution from an uncontrolled study presented at a medical meeting. This large study is very misleading. According to the presenter, the advantages of HIFU are it can be repeated and "you don't touch the nerve or the sphincter." If anything, the results argue against the use of HIFU to treat this disease. What do we really know from this report?

Without giving the definition of a PSA failure, 38% of men with low risk disease had a PSA recurrence at seven years and 27% had cancer present on biopsy after two courses of treatment.

These results alone are very inferior to surgery and radiation. Finally, no quality of life data are presented but other studies show high rates of impotence.

The Bottom Line: HIFU has a high failure rate, no long term survival data and limited information about side effects. Since it is not approved in the US, men should make sure they are properly counseled about its strengths and weaknesses if considering going to another country to get this treatment.

A study evaluated the ability of Bevacizumab (Avastin®) to improve survival of men with metastatic disease who were receiving docetaxel chemotherapy. This drug is already FDA approved to treat other types of cancer. Although preliminary studies suggested a benefit in prostate cancer, the phase III randomized trial did not show significantly improved survival with this drug. This happened even though it delayed time to progression or more often reduced the PSA by at least 50%. New studies will be needed to determine if either can play any role in helping men with this disease.

The Bottom Line: Once again, randomized phase III studies are the only way to confirm a possible benefit from a new drug and Bevacizumab failed to benefit men with metastatic prostate cancer receiving chemotherapy. These studies provide additional evidence that a drug's PSA-lowering effect might not translate into a survival benefit.

Another study involving men who progressed while on docetaxel tested a new drug called Cabazitaxel. In a randomized phase III trial, all men were given prednisone and either Mitoxantrone or Cabazitaxel. The experimental drug increased the average survival by 2.4 months. This is the first evidence of a drug improving survival in very advanced disease after primary chemotherapy failed. The problem is the side effects were very significant with a severe drop in the white blood cell count in 80% of patients and 5% died of side effects.

The Bottom Line: Cabazitaxel could become a new therapy that helps improve survival of men with very advanced disease but more work is needed to reduce the severe side effects.

PSA MISSES THE MARK

(Continued from page 5)

untreated cancer formed the basis for the analysis Klotz reported. Investigators applied seven PSA-related measures to the cohort to determine what proportion of men likely would have gotten recommendations for treatment as a result of PSA findings.

The PSA triggers for intervention were a PSA threshold of 10 or 20 ng/mL, two measures of PSA doubling time, and three measures of PSA velocity. The results showed that treatment would have been recommended for the following proportion of men:

- PSA threshold 10 ng/mL: 38%
- PSA threshold 20 ng/mL: 14%
- PSA doubling time: 37% to 50%
- PSA velocity: 42% to 84%

“These results show that a transient rise in PSA should be interpreted with caution in men on active surveillance,” said Klotz. “Almost all of these commonly used PSA triggers would have resulted in high rates of recommendations for treatment, on repeated occasions.”

Klotz L, et al, AUA 2010; abstract 245
MedPage Today, 2 June 2010

DENOSUMAB

(Continued from page 1)

treated with ZA 4 mg intravenously, and 943 patients who were assigned to denosumab 120 mg injected subcutaneously. Eligible patients had diagnosed CRPC and bone metastases. Their average age was 71 years and over 90% had good performance status.

About 80% of the patients in both arms of the trial discontinued treatment, but only about 5% discontinued due to an adverse event. Approximately 20% of patients experienced skeletal-related events that required radiation therapy or surgery to the bone and about 30% in each arm died. Osteonecrosis of the jaw was observed in about 1.3% of patients on ZA and 2.3% on denosumab. Hypocalcemia was seen in 12.8% of patients on denosumab and 5.9% on ZA.

“Denosumab continues to be studied as a potential treatment option for bone metastases,” he said. Among its advantages, he noted, are its subcutaneous route of administration, no acute phase reactions or need for renal monitoring. Remaining questions are its possible need for life-long treatment and if the drug can prevent or delay bone metastases.

Fizazi K, et al, J Clin Oncol 2010; 28: 343s
MedPage Today, 8 June 2010

EBRT+RT

(Continued from page 4)

patients were identified for the analysis – 9,463 men who had RP, 13,701 who had EBRT, 7,239 who had EBRT+ADT and 19,455 who had ADT alone.

As expected, treatment varied by age group – 55% of men 60 to 69 had RP while older patients were more likely to receive ADT alone. Compared with RP, EBRT alone was associated with an adjusted hazard for hip fracture of 1.67. EBRT+ADT doubled the hip fracture hazard (HR 2.01), and ADT alone further increased the HR to 2.52. The addition of ADT to EBRT increased the wrist fracture risk by almost 30% versus RP, and the risk jumped to almost 70% higher in patients treated solely with ADT (HR 1.69).

“The cumulative incidence of hip fracture in elderly prostate cancer patients was 10% at 10 years,” Elliott said. “EBRT increases the risk of hip but not wrist fracture versus RP.”

While acknowledging some limitations to the analysis, Elliot concluded that “These findings suggest a need to consider osteoprotective interventions in men receiving pelvic EBRT.”

Elliott S et al, AUA 2010; abstract 48
MedPage Today, 30 May 2010

**US TOO INTERNATIONAL:
OUR MISSION**

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



US TOO INTERNATIONAL

See blue. SEA Blue.

**SUPPORT
EDUCATE
ADVOCATE**

US TOO INTERNATIONAL Tax Deductible Donation

Name: _____ Company: _____

Address: _____

City: _____ State: _____ ZIP: _____

Phone: () _____ Fax: () _____ e-mail: _____

Please accept my enclosed tax-deductible donation to Us TOO a not-for-profit 501(c)(3) organization.

Amount: _____ \$25 _____ \$50 _____ \$75 _____ \$100 Other: \$ _____ Check # _____

VISA/MasterCard # _____ Expiration Date: ____ / ____

Signature _____

US TOO INTERNATIONAL, Inc., 5003 Fairview Ave., Downers Grove, IL 60515