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Us TOO® PROSTATE CANCER EDUCATION & SUPPORT

HOTSHEET

March 2005

THE ORIGIN OF SUPPORT GROUPS FOR PROSTATE CANCER SURVIVORS AND THEIR FAMILIES

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Edward Kaps has been fighting prostate cancer for 23 years. First diagnosed in 1978 he elected radiation therapy treatment; in 1988 he had a radical prostatectomy; and in 1992 he went to hormone therapy. In the spring of 2001 he elected to stop hormone therapy and currently has an undetectable PSA. A retired General Motors manager, Edward sits on several national Boards of Directors including the American Foundation for Urologic Disease, Inc. (AFUD) Board of Directors.

John Moenck is a prostate cancer survivor and activist.

Gerald Chodak, M.D., is Director of the Midwest Prostate and Urology Health Center and a Professor of Surgery at the University of Chicago.

In early 1990, Dr. Gerald Chodak, a Chicago urologist, wrote a letter to his prostate cancer patients indicating that several of his patients had expressed an interest in forming a support group for men with prostate cancer. This notion was similar to the Y-ME National Breast Cancer Organization (Y-ME) that was formed for women with breast cancer.

On February 27, 1990, 22 people responded to Dr. Chodak's invitation and attended an initial meeting at his office. Mr. Ed von Holst, prostate

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Us TOO 15th ANNIVERSARY 1990-2005

US TOO CELEBRATES 15 YEARS OF PEER TO PEER SUPPORT

Us TOO International Prostate Cancer Education and Support Network reaches a milestone this year as we celebrate our 15th anniversary of providing peer-to-peer support among prostate cancer patients.

Throughout the entire year, we will be recognizing our founders, our accomplishments and the many volunteers who have made such a difference in the lives of prostate cancer patients and their families via our chapter support group network.

We are working on other special activities and plans as part of our anniversary celebration, so watch www.ustoo.org and your Hot-Sheets for more information!

Do you have information, materials or a story you'd like to share from the early days of Us TOO? If so, please send an email, letter or fax with your remembrances, and details of dates, events or participants to:

Us TOO 15 Year Memories
Us TOO International
5003 Fairview Avenue
Downers Grove, IL 60515-5286

Fax: 630-795-1602
Email: ustoo@ustoo.org
Use subject line:
<Your Name> Us TOO memories

US TOO PUBLICATIONS

In addition to the Hotsheet, Us TOO offers a FREE e-mail based service called *NEWS You Can Use* sponsored by Sanofi, providing updates on the latest prostate cancer related news. To subscribe or link to the archives, simply visit the Us TOO website www.ustoo.org.

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 loved ones and personal physician before deciding on **any** course of action.

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AstraZeneca

ORIGIN OF US TOO

(Continued from page 1)

cancer survivor, and two other men spoke on behalf of starting a support group. After considerable discussion, the group decided they wanted to start a support group for prostate cancer patients and their families.

Dr. Chodak asked them to indicate their interest in helping facilitate future meetings. The following men agreed to help: John DeBoer, Edward von Holst, Edward Kaps, John Moenck and Vincent Young. These volunteers became the co-founders of the country's first prostate cancer support group.

Shortly thereafter, the following officer positions were accepted by the support group members: Edward Kaps, Chairman/Treasurer; John DeBoer, Vice Chairman; Edward von Holst, Vice Chairman; John Moenck, Secretary; and Vincent Young, Assistant Secretary.

In early March 1990, Ed von Holst and Edward Kaps planned the second meeting of the larger group. Arrangements were made by Dr. Chodak to have Dr. Nicholas J. Volgelzang address the group to discuss radiation therapy for prostate cancer.

Through August of 1990, meetings were held at the University of Chicago Hospital every month and each of the officers took turns conducting the meeting. Several names were proposed for the group and Edward Kaps suggested 'Us TOO' thinking this name might work for prostate cancer as well as the name Y-ME did for breast cancer.

In August 1990, Dr. Flanigan from Loyola University Medical Center in Chicago asked Dr. Chodak if his group would come and help him start a support group at Loyola. John Moenck and Ed Kaps met with Dr. Flanigan and on September 25, 1990 the second Us TOO support group was initiated. A hospital in Hinsdale, Illinois became number three and the fourth was Northwestern University, which was started in late December 1990.

Dr. Chodak made arrangements for the Us TOO leaders to meet with representatives of ICI Pharmaceuticals, today known as AstraZeneca. ICI indicated that they had been active in supporting breast cancer support groups and wanted to be involved with prostate cancer support groups as well. Today, AstraZeneca is still a major contributor to Us TOO.

The officers decided that Us TOO should apply for 501(c)(3) status. On June 8, 1990 Us TOO was issued a certificate from the Secretary of the State of Illinois for its incorporation. On November 7, 1990, Us TOO was officially recognized as a 501(c)(3) organization under the Charitable Trust Act and the Illinois Solicitation Act.

In the fall of 1990, through the efforts of Dr. Chodak, Edward Kaps met with Dr. C. Eugene Carlton, Jr., a member of the boards of the American Urological Association (AUA) and AFUD. Dr. Carlton was told of the support group's work and asked Mr. Kaps if he would consider a position on the AFUD Board of Directors. In October 1990 the officers of Us TOO approved Edward Kaps to sit on AFUD's board of directors.

In January 1991, Edward Kaps attended his first meeting of AFUD and was challenged to expand his support group efforts into other areas of the United States. To help US TOO accomplish this task, AFUD mailed letters to all AUA urologists informing them of the Us TOO program. Edward Kaps traveled throughout the country to discuss the support group program. He also went to Canada and Turkey as part of this effort.

During this time of growth, the workload was overwhelming the 5 founders and in 1991 AFUD hired an administrator, Brooke Moran, to run the support group program.

ORIGIN OF US TOO

(Continued from page 2)

Many of the funds required to administer the growing efforts were donated by ZENECA (AstraZeneca) and the remainder came from other AFUD sources.

By the end of 1992, Regional Directors were appointed to be responsible for all areas of United States and Canada. By June 1993, barely three years after its inception, there were more than 170 active prostate cancer support groups as a result of efforts made by AFUD and Us TOO.

Throughout this process, the Us TOO officers worked as a team. Uncountable hours were spent by each of the five founders to raise awareness and to help survivors and their families.

From February 1990 through June 1993 the name Us TOO was recognized as a leader in support groups for prostate cancer survivors and their families. Concurrently, there was another significant effort being headed by Mr. Jim Mullen of Sarasota, Florida. In April 1990 Jim Mullen formed Man to Man, a prostate cancer support group. The first group in Sarasota Florida is still in existence today. Many who attended Jim Mullen's support groups were vacationing in Florida and upon returning home they started groups all over the U.S. and Canada. Today, the large Man to Man support group network is administered by the American Cancer Society. Many prostate cancer organizations have formed since February 1990.

Additionally, the American Cancer Society (Man to Man), The National Prostate Cancer Coalition, (an advocate for more prostate cancer research), Cap Cure and AFUD are among the larger organizations that are continuously supporting prostate cancer research and treatment through education and advocacy at the state and national levels. Prostate cancer can be an important learning experience. We must remember that no matter how old we are, cancer is still frightening. Through participating in support groups, men of all ages and their families can find friends to share the journey. Together we are learning to cope through knowledge and hope.

RADIATION SEEDS MAY BE ENOUGH FOR PROSTATE CANCER

Implanting tiny radioactive "seeds" in the prostate, a treatment called brachytherapy, may be all that is needed to combat low-risk forms of prostate cancer, new research suggests.

Additional treatments, such as radiation from an external source, known as external beam radiotherapy (EBRT), or reducing testosterone levels, known as androgen deprivation therapy (ADT), may only be necessary for severe forms of the disease. The findings appear in the January first issue of the International Journal of Radiation Oncology, Biology, Physics.

"The most important part of the work is that low-risk patients do not require (EBRT) or ADT," Dr. Gregory S. Merrick from Wheeling Hospital, in West Virginia told Reuters Health.

"Based on preliminary findings, it also appears that (EBRT) will be proven unnecessary in intermediate-risk patients and once again, ADT is unnecessary in intermediate-risk patients," Merrick said.

Merrick and colleagues evaluated the benefit of adding EBRT and/or ADT to seed therapy in 227 patients with low-risk prostate cancer, 251 with intermediate-risk prostate cancer, and 190 with high-risk prostate cancer.

As noted, the authors found no evidence that adding EBRT or ADT to seed therapy improved survival in the low-risk group of patients and probably not in the intermediate-risk group either.

For high-risk patients, however, these added therapies did seem to offer a benefit beyond that achieved with seed therapy and the researchers plan to look at this issue further in an upcoming study.

Reuters Health, 26 January 2005

NEW POLICY CALLS FOR NIH-FUNDED STUDIES TO BE PUBLICLY ACCESSIBLE

The NIH has announced a new policy calling for increased public access to research articles resulting from NIH-funded studies.

The policy, which is the first of its kind for the NIH, calls on scientists to publicly release their manuscripts within 12 months of publication at the latest. As part of the agency's proposal, the peer-reviewed, NIH-funded articles will be available through an internet-based archive managed by the National Library of Medicine, a component of the NIH.

"With the rapid growth in the public's use of the internet, the NIH must take a leadership role in making available to the public the research that we support," said NIH Director Elias Zerhouni. "While this new policy is voluntary, we are strongly encouraging all NIH-supported researchers to release their published manuscripts as soon as possible for the benefit of the public. Scientists have a right to see the results of their work disseminated as quickly and broadly as possible, and the NIH is committed to helping our scientists exercise this right. We urge publishers to work closely with authors in implementing this policy."

Beginning May 2, the policy requests that NIH-funded scientists submit an electronic version of the author's final manuscript, upon acceptance for publication, resulting from research supported in whole or in part by the NIH.

FDAnews.com, 15 February 2005

NEW OPTIONS FOR INCONTINENCE

There are tens of million of people who experience incontinence and the number is rapidly growing due to the Baby Boomers aging and the high ratio of men diagnosed with prostate problems. We live in a very active society where many people enjoy physical activities like golfing, tennis, hiking and jogging. Wearing adult diapers can limit a person's ability to perform certain activities, both physical and social, without the fear of an embarrassing urinary leak or odor. This can cause a person to suffer emotionally.

Many men who are incontinent from prostate cancer are unsatisfied with the various methods available for managing their incontinence. Traditional methods of using absorbent pads, condom catheters with adhesives, leg bags, and tubes, and clamps all have their problems. Two new options for incontinence are now on the market, and are presented here.

The External Collection System (ECS) is an alternative to wearing adult diapers. The ECS consists of a leg bag, tube and condom catheter. The ECS can be found in medical supply companies, some pharmacies, mail order and on the Internet. There are numerous companies that manufacture the ECS. The leg bags are currently sold with leg straps to hold the leg bag in place. Leg straps may constrict the circulation of the lower leg when worn too tight. In some cases a person will develop open leg ulcers caused by the abrasion of the leg straps against the skin. When the leg straps are not tight, the leg bag may fall during physical activities and the tube may become unattached to the leg bag causing a urinary accident.

Urology companies continue to develop products to improve the ECS and give the user a higher level of physical activities, non-constriction to the lower leg and a higher quality of life. Some of these products include leg bag holders (Bard, JT Posey, Tytex and Urocare) that function as a sleeve over the leg bag and around the leg. This eliminates the problems associated with using leg straps, but it does not give the user the ability to perform some physical activities without the leg bag falling down the leg. Another leg bag holder one-leg pant made by LL Medico is designed with a holder for the leg bag that is attached to the waist for greater support.

Better Pant™ is a new urology undergarment designed to provide significantly more comfort and security to people who suffer from the inconveniences associated with incontinence. Better Pant is used with ECS including condom catheters, ileoconduit and nephrostomy systems and some Foley catheters. The knee-length urology undergarment has an internal pouch that conceals and holds a 500ml or 1000ml leg bag in place without leg straps. Better Pant has been market tested and shown to permit a higher level of physical activity by wearers when compared to using leg straps. Ambulatory, paraplegic, quadriplegic and non-ambulatory persons have used the product. To learn more about Better Pant, visit www.betterpant.com or call 310-457-8350.

Another incontinence management solution for men is the AlphaDry™ system. AlphaDry is a combination one-piece condom catheter, one-way valve, and reservoir that tucks neatly into any Jockey style underwear. The sheath portion attaches to the penis. The urine passes directly from the penis through the one-way valve into a reservoir that lies in your underwear. This allows men to function normally again without having to wear pads, leg bags, and or clamps. The AlphaDry sheath has grippers inside and a Velcro strap that prevents any slipping and leaking. No adhesives are required. Learn more about AlphaDry at www.alphadry.com or call 1-877-235-9379 (Toll Free).

The urology and incontinence are fast growing markets. There are many new products being developed to improve a person's quality of life. As Us TOO become aware of new products, we will continue to inform our readers.

EXERCISE MAY HELP CANCER PATIENTS RECUPERATE

Low blood counts, lack of sleep, pain and stress often leave cancer patients with overwhelming fatigue during therapy. As medical editor Mary Ann Childers explains, resting to conserve energy may not be the best remedy.

When Dick Yolevich is not poolside having coffee with his wife, he is inside working hard to fight fatigue. "I hope that my experience is indicative of what it's going to do for other people, he says.

The prostate cancer patient is in a study to see if exercise helps patients avoid fatigue during radiation treatments. Doctors typically tell weary cancer patients to relax, take it easy. Now new research suggests the opposite.

What we actually see is if you can get up and get moving even just a little bit, there are some positive things that occur systemically in the body which actually can help alleviate some of that fatigue, says Karen Mustian, PhD.

Along with some resistance training, even a little workout boosts his energy says Dick Yolevich. This is a fatigue that doesn't go away with sleep. It just hangs on and fortunately, I didn't experience any of that.

Previous studies have shown that cancer patients with fatigue who are inactive can actually feel worse. As always, if you think you want to start an exercise program ask your doctor for guidelines.

CBS2Chicago.com, 27 January 2005

STUDY PROVIDES INSIGHTS ON WHY SOME PROSTATE CANCER BECOMES RESISTANT TO HORMONE WITHDRAWAL THERAPY

A new study by scientists at Fred Hutchinson Cancer Research Center provides insight into why some men develop aggressive prostate cancer that becomes resistant to hormone-withdrawal therapy, a common form of treatment.

Researchers found that certain mutations in a protein called the androgen receptor cause advanced and invasive prostate cancer when put into otherwise healthy mice. The androgen receptor's normal function is to control growth of the prostate gland in response to cues from male androgens, which have long been thought to stimulate prostate tumors.

Because similarly defective androgen receptors have been found in prostate-cancer patients whose disease is resistant to hormone withdrawal, the finding sheds light on why most men with advanced prostate cancer treated with hormone-withdrawal therapy fail to be cured. The work opens the door to discovery of new, more effective therapies, according to Norman Greenberg, Ph.D., a member of Fred Hutchinson's Clinical Research Division.

The study is published in the Jan. 25, 2005 issue of the *Proceedings of the National Academy of Sciences*. Dr. Guangzhou Han and colleagues led the study.

Greenberg said that despite these and other earlier findings indicating a strong relationship between the androgen receptor and prostate cancer, no group had proved that it could be a key driver of disease.

"Our study is the first to demonstrate that if the androgen receptor acquires certain mutations, it can cause prostate cancer in otherwise healthy mice," he said. "Because very similar mutations have been found in androgen receptors from prostate-cancer patients whose disease is resistant to hormone-withdrawal therapy, we think this is a very significant finding."

The results suggest that prostate-cancer prevention trials involving drugs that lower a man's androgen levels should proceed cautiously, since complete androgen withdrawal seems to provide an environment that favors the development of the cancer-causing mutations. In addition, the work is the first to show that a class of proteins called steroid receptors, of which the androgen receptor is a member, can become cancer-causing genes known as oncogenes. The estrogen and progesterone receptors--two receptors that become defective in many breast cancers--are also members of this protein family.

The androgen receptor is a protein produced by prostate cells that binds to androgens, a family of chemically related hormones that includes testosterone. Although the binding of androgens to the receptor is important for healthy prostate development, the hormones may, under some conditions, stimulate the prostate-tumor cells to divide. For that reason, many men with advanced prostate cancer are treated with drugs that either block the production of androgens or the ability of the androgens to interact with their receptor.

About 90 percent of the time, prostate tumors shrink after hormone deprivation, but in most cases, it is believed that a small percentage of the tumor cells become resistant. Eventually, these resistant cells grow to become the predominant cancer, and no successful therapies have yet been developed for men with the hormone-withdrawal-resistant form of the disease.

In their study, researchers identified several mutations that impair the ability of the androgen receptor to interact with proteins called co-regulators. Co-regulators help the receptor to carry out its functions at the proper time; therefore, lack of interaction between the receptor and the appropriate co-regulators is thought to spur cancer development. Analogous mutant receptors also have been found in human prostate cancers.

Researchers wondered what would happen if they put the mutant receptors into otherwise healthy mice that also contained a normal version of the androgen receptor. They found that 100 percent of the time, the addition of one particular mutant receptor cause rapid development of a precancerous condition that progressed to advanced disease. In contrast, mice with extra copies of a normal receptor, as well as mice with the normal receptor and an unrelated type of mutant receptor, did not cause cancer.

"This demonstrates a causal role for certain androgen receptor mutations in prostate cancer," Greenberg said. Not all men with hormone-withdrawal-resistant disease develop such mutations, Greenberg said. Yet hormone-deprivation treatment can create a situation in some prostate tumors in which such mutations give a growth advantage to cancer cells.

Such mutant receptors might prove to be good drug targets, Greenberg said. Because androgen deprivation has numerous side effects--including bone loss and sexual dysfunction--drugs that specifically attack the cancer-causing protein would be much more desirable than existing therapies.

Since the mutations Greenberg's lab studied appear to affect one specific function of the androgen receptor, it may also be possible to develop drugs that target other proteins in this pathway. Greenberg's lab is now studying this pathway, with the hope of providing more insight into the drug discovery process.

Fred Hutchison Cancer Center
25 January 2005

DON'T RELY ON PSA SCREENS TO DETECT PROSTATE CANCER IN OBESE MEN

Testing for high levels of prostate-specific antigen is enough to detect cancer, right? Wrong -- and obese men may be paying the price.

Obese men produce almost 30 percent less PSA than men of normal weight, according to a study conducted by researchers at the University of Texas Health Science Center in San Antonio and published in the Jan. 24 issue of *Cancer*.

While high levels of PSA typically signal prostate cancer, obese men's increased levels may still fall below the high-risk line and go unnoticed. "This tells us it's likely or it's possible that prostate cancer detection may be delayed in overweight or obese men," associate professor of epidemiology Jacques Baillargeon told the *Associated Press*.

Lesson Learned: Experts suggest obese men have a biopsy along with the traditional PSA test to ensure prostate cancer is detected as early as possible.

Lab Line, 28 January 2005

OBESITY RAISES PROSTATE CANCER RISK

Obesity not only raises the risk of heart disease, diabetes and blood pressure, but also makes the likelihood of developing prostate cancer more likely, say Portuguese researchers.

Abdominal obesity has long been associated with an increase in heart-related conditions and some types of cancers but until now, it has not been possible to establish a relationship between prostate cancer and weight, even if evidence supports the idea that environmental factors, such as western diet and life style, affect the incidence of the disease.

But a new study, published in the December issue of *Obesity Research* (pp 1930-5), shows that visceral fat, or the fat found around organs, is associated with increased danger of prostate cancer.

The finding has major implications given today's rise in obesity. Almost one third of people living in the European Union are overweight and more than one in ten is obese, according to European Association for the Study of Obesity.

The study also shows that risk of obesity-related disease depends on types of fat.

Different types of fat tissue, because they possess different types of metabolism that produce different biochemical substances, affect the body in very different ways.

Adipose tissue in the human body comes in two types: subcutaneous fat which is located just below the skin, and visceral fat, which is located, unnoticed, below the muscles surrounding vital organs.

This fat is considered much more harmful than subcutaneous adiposity as it is known to predispose to cardiovascular and metabolic problems, although the mechanism(s) by which these complications appear is still not known.

Pedro Von Hafe, Henrique Barros and colleagues from the Faculty of Medicine of Porto and the Hospital of São João, Porto, Portugal used computerized axial tomography, a technique that employs advanced x-ray technology and allows to distinguish, and individually measure, different types of adipose tissue.

They compared 63 prostate cancer male patients with the same number of healthy controls from the same ethnical background and with similar age, height and weight.

It was found that higher quantities of visceral fat, but not of subcutaneous fat, were associated with prostate cancer. The quantity of visceral fat, however, did not correlate with the disease stage, indicating that once established, other factors contribute to the evolution of disease.

The different results found between visceral and subcutaneous fat, probably result from different biochemical substances produced by each of the adipose tissue, which will affect the body in different ways.

Furthermore, the researchers note that visceral fat tends to be metabolized by the liver into fatty acids and released into the blood, ultimately leading to an increase of insulin.

Insulin is known to be capable of inducing the growth of carcinogenic cells, including cells from prostate tumors.

NUTRAingredients.com
4 February 2005

NWBT TO INITIATE PHASE III TRIAL FOR PROSTATE CANCER

Northwest Biotherapeutics (NWBT) has received clearance from the FDA to begin assessment of its cell-based dendritic cell product candidate, DCVax-Prostate, in a Phase III clinical trial.

This trial is based on promising clinical data from a previously conducted Phase I/II clinical trial. The double-blinded, placebo-controlled, Phase III clinical trial is expected to enroll roughly 600 patients at 30 to 50 sites throughout the U.S.

Northwest Biotherapeutics previously received clearance through the FDA for a Phase II clinical trial for DCVax-Brain, a promising new treatment for Glioblastoma Multiforme which is the most common, and lethal form of brain cancer. The company intends to begin this multisite clinical trial later this year. In addition, the DCVax platform can be used for multiple cancer indications, and NWBT has completed preclinical work targeted for a Phase I clinical trial for non-small cell lung cancer and head and neck cancer.

FDA News, 3 February 2005

PHASE III PILOT STUDY OF DOSE ESCALATION USING CONFORMAL RADIOTHERAPY IN PROSTATE CANCER: PSA CONTROL AND SIDE EFFECTS

Dearnaley DP, et al

BJC 92: 488-98, 2005

Radical radiotherapy is a standard form of management of localized prostate cancer. Conformal treatment planning spares adjacent normal tissues reducing treatment-related side effects and may permit safe dose escalation. We have tested the effects on tumor control and side effects of escalating radiotherapy dose and investigated the appropriate target volume margin.

After an initial 3-6 month period of androgen suppression, 126 men were randomized and treated with radiotherapy using a 2 by 2 factorial trial design. The initial radiotherapy tumor target volume included the prostate and base of seminal vesicles (SV) or complete SV depending on SV involvement risk. Treatments were randomized to deliver a dose of 64 Gy with either a 1.0 or 1.5 cm margin around the tumor volume (1.0 and 1.5 cm margin groups) and also to treat either with or without a 10 Gy boost to the prostate alone with no additional margin (64 and 74 Gy groups). Tumor control was monitored by prostate-specific antigen (PSA) testing and clinical examination with additional tests as appropriate. Acute and late side effects of treatment were measured using the Radiation Treatment and Oncology Groups (RTOG) and LENT SOM systems.

The results showed that freedom from PSA failure was higher in the 74 Gy group compared to the 64 Gy group, but this did not reach conventional levels of statistical significance with 5-year actuarial control rates of 71% (95% CI 58-81%) in the 74 Gy group vs. 59% (95% CI 45-70%) in the 64 Gy group. There were 23 failures in the 74Gy group and 33 in the 64 Gy group (Hazard ratio 0.64, 95% CI 0.38-1.10, P=0.10). No difference in disease control was seen between the 1.0 and 1.5 cm margin groups (5-year actuarial control rates 67%, 95% CI 53-77% vs. 63%, 95% CI 50-74%) with 28 events in each group (Hazard ratio 0.97, 95% CI 0.50-1.86, P=0.94).

Acute side effects were generally mild and 18 weeks after treatment, only four and five of the 126 men had persistent $\geq$ Grade 1 bowel or bladder side effects, respectively. Statistically significant increases in acute bladder side effects were seen after treatment in the men receiving 74 Gy (P=0.006), and increases in both acute bowel side effects during treatment (P=0.05) and acute bladder sequelae (P=0.002) were recorded for men in the 1.5 cm margin group. While statistically significant, these differences were of short duration and of doubtful clinical importance. Late bowel side effects (RTOG $\geq$ 2) were seen more commonly in the 74 Gy and 1.5 cm margin groups (P=0.02 and P=0.05, respectively) in the first 2 years after randomization. Similar results were found using the LENT SOM assessments.

No significant differences in late bladder side effects were seen between the randomized groups using the RTOG scoring system. Using the LENT SOM instrument, a higher proportion of men treated in the 74 Gy group had Grade $\geq$ 3 urinary frequency at 6 and 12 months. Compared to baseline scores, bladder symptoms improved after 6 months or more follow-up in all groups. Sexual function deteriorated after treatment with the number of men reporting some sexual dysfunction (Grade $\geq$ 1) increasing from 38% at baseline to 66% at 6 months and 1 year and 81% by year 5. However, no consistent differences were seen between the randomized groups.

In conclusion, dose escalation from 64 to 74 Gy using conformal radiotherapy may improve long-term PSA control, but a treatment margin of 1.5 cm is unnecessary and is associated with increased acute bowel and bladder reactions and more late rectal side effects. Data from this randomized pilot study informed the Data Monitoring Committee of the Medical Research Council RT 01 Trial and the two studies will be combined in subsequent meta-analysis.

NEW PRESCRIBING INFORMATION FOR ZOMETA® AND AREDIA® REGARDING SAFETY

Zometa® (zoledronic acid) Injection is indicated for the treatment of documented bone metastases from solid tumors, in conjunction with standard antineoplastic therapy. Prostate cancer should have progressed after treatment with at least one hormonal therapy. Zometa, and a related drug, Aredia (pamidronate disodium injection) are also approved for hypercalcemia of malignancy.

Recent changes were made to the prescribing information for these drugs. These changes include:

(1) Recommendation on lower Zometa doses for patients whose baseline creatinine clearance is 60 mL/min or lower, and

(2) Information about osteonecrosis of the jaw (ONJ), in patients who have received either Zometa or Aredia® as a component of their therapy.

These changes were instituted as a result of adverse effects with Zometa and Aredia reported to the FDA. Full prescribing information, including dosing and contraindications is available at

www.fda.gov/cder/foi/label/2005/021223s009,010lbl.pdf

publicpolicy@asco.org
7 February 2005

RESEARCHERS IN QUEST OF OSTEOPOROSIS PREVENTION FIND VITAMIN B12 BENEFITS

It can't be said enough: an ounce of prevention is worth a pound of bone. An estimated 40% of women and 13% of men are at high risk of an osteoporotic fracture in their lifetime. When these fractures occur in older individuals, quality of life can decrease, sometimes dramatically. Osteoporosis is also associated with higher mortality. New research conducted by Katherine Tucker, PhD, director of the Dietary Assessment and Epidemiology Research Program at the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts, examined dietary factors in relation to osteoporosis and uncovered a positive association between vitamin B12 and bone health. In other words, the authors conclude that vitamin B12 deficiency may be an important modifiable risk factor for osteoporosis.

"Osteoporosis is becoming a much greater issue now that people are living so much longer," said lead author Tucker, also a professor at the Friedman School of Nutrition Science and Policy at Tufts. "Our study provides support for a way in which people can actively lower their risk of osteoporosis and help to preserve quality of life."

Tucker and her colleagues measured bone mineral density--a measure of bone quality--and vitamin B12 level in more than 2,500 men and women participating in the Framingham Osteoporosis Study. They found that both men and women with low vitamin B12 levels had on average lower bone mineral densities--putting them at greater risk of osteoporosis--than men and women with higher levels. The men exhibiting low vitamin B12 levels had significantly lower bone density in several areas of the hip, and the women exhibiting low vitamin B12 levels had particularly low bone density in the spine.

KOSAN INITIATES PHASE II TRIAL OF KOS-862 (EPOTHILONE D) FOR PROSTATE CANCER

Kosan Biosciences Incorporated (Nasdaq: KOSN) announced today the start of a multi-center Phase II clinical trial to evaluate the safety and efficacy of KOS-862 (Epothilone D) as monotherapy for prostate cancer. KOS-862 is a polyketide that inhibits cancer cells by the same mechanism as paclitaxel, and preclinical models show the compound to be effective against paclitaxel-resistant tumors.

"Based on encouraging data from preclinical and clinical trials, we are initiating a Phase II monotherapy trial to evaluate the antitumor activity and clinical benefit of KOS-862 in prostate cancer patients," said Robert G. Johnson, Jr., M.D., Ph.D., Executive Vice President, Development and Chief Medical Officer, Kosan Biosciences. "In the fourth quarter of 2005, we expect to be able to take an interim look at data acquired during the first stage of the study."

According to the Phase II trial design, KOS-862 will be administered weekly by intravenous administration for three of four weeks at a dose of 100 mg/m^2. The trial is expected to enroll between 20 and 50 patients in hormone refractory patients who have progressed with a docetaxel-based treatment. Changes in PSA and tumor response will be assessed to determine clinical activity.

For additional information, please visit the Company's website at www.kosan.com.

PR Newswire/NewsEdge Corporation
14 February 2005

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