Us TOO® PROSTATE CANCER EDUCATION & SUPPORT

HOT SHEET

SEPTEMBER 2004

JOHN PAGE STEPPING DOWN AS US TOO PRESIDENT/CEO

Us TOO International announced that its President and CEO, John A. Page, will be leaving this fall to pursue other interests and spend more time with his family.

"I've been with Us TOO for more than four years and in that time there have been significant advances in the prostate cancer arena – and in our

(l to r) *Fred Gersh*, Us TOO State Coordinator and Secretary of the Virginia Prostate Cancer Coalition, *Mac Showers*, Walter Reed Army Medical Center & Department of Defense Center for Prostate Disease Research Representative, and *John Page*, President & CEO Us TOO International Prostate Cancer Education & Support at recent Men's Health Conference

ability to help men with the disease, as well as their companions and families." said Page. "We have strengthened our local chapter network while also improving our ability to serve those in need outside the chapter structure – both in the U.S. and Internationally. With nearly

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LINK ESTABLISHED BETWEEN KEY PROTEIN AND AGGRESSIVENESS OF PROSTATE CANCER

Prostate cancer is much more likely to be aggressive if a key protein called Stat5 is found activated and in abundance in the cancer cells, report researchers from Georgetown University's Lombardi Comprehensive Cancer Center. By inhibiting this protein, called Stat5, doctors are exploring how to develop a new treatment strategy for advanced prostate cancer.

The new findings, reported in Cancer Research, show that active Stat5 protein is particularly plentiful in high-histological-grade human prostate cancer. High-histological-grade prostate cancers have often already metastasized by the time of diagnosis and are typically more aggressive in growth.

"Currently, there are only few treatment options available for advanced prostate cancer," said Marja Nevalainen, MD, PhD, assistant professor of oncology at Georgetown University Lombardi Comprehensive Cancer Center. "If we can find a way to stop Stat5 from turning on in prostate cancer cells, we may be able to devise a new strategy for treating this disease."

Previous studies by Nevalainen show that when the "telephone line" that

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COMBINATION THERAPY FOR PROSTATE CANCER SHOWS PROMISE

Doctors were able to cut the death rate of prostate cancer patients nearly in half and spare them several serious drug side effects by combining radiation therapy with a limited course of hormone therapy, according to a new study.

The finding could have a significant impact on the treatment of men whose cancer is thought to be localized but who are at higher risk because of higher prostate lab test scores. As many as 125,000 men, or about half of all newly diagnosed cases each year, fall into that category, according to lead author Anthony D'Amico, a radiation oncologist at Brigham and Women's Hospital and the Dana-Farber Cancer Institute in Boston.

"This is really the first study to show you can prolong life by adding hormone therapy to local therapy (radiation) ... for men with localized prostate cancer," said D'Amico, also a professor of radiation oncology at Harvard Medical School.

Men getting the combined therapy had an overall five-year survival rate of 88 percent, compared with 78 percent for those who got just radiation.

"That's a huge survival benefit,"

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US TOO PUBLICATIONS

In addition to the Hot Sheet, ***Us TOO*** also publishes a FREE e-mail based news service 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

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FOCAL CRYOTHERAPY MAY OFFER BENEFITS OVER CURRENT TREATMENTS

Physicians are adopting a new cryosurgical procedure for prostate cancer using focal, freezing technologies, which early evidence suggests causes fewer side effects than the current surgical treatments for the disease.

Clinical results of this new focal procedure called the "male lumpectomy" were presented by Gary Onik at the recent annual meeting of the Society of Uroradiology. Onik's study examined 21 patients aged 58 to 70 with prostate cancer who underwent focal cryosurgery, and 20 had no evidence of cancer in follow-up examinations between 2 and 8 years later.

Onik said, "Essentially 95% of the patients had stable prostate specific antigens (PSA) at an average of 4 years. This demonstrates that patients are responding to the procedure."

Impotency and incontinence are the two most common complications associated with any prostate surgery, but Onik and colleagues found about 80% of men receiving focal cryosurgery remained potent and none became incontinent.

Endocare Inc., the manufacturer of the Cryocare system used for the procedure estimates that the number of focal procedures has doubled each year in recent years. A recent survey cited in Physicians Weekly said approximately 60% of the 150 centers that perform cryosurgery in the U.S. now offer some form of focal cryotherapy.

Additionally, targeted cryosurgery is the most effective treatment for men with recurrent prostate cancer (after failed radiation treatment) whose PSA levels again rise.

Aaron Katz of Columbia Presbyterian presented compelling 6-year clinical data at the national AUA conference where he showed 71% of failed patients still had undetectable PSA values 5 years after undergoing targeted cryosurgery.

COMBINING RADIATION MODALITIES INCREASES PROSTATE CANCER CURE RATES

High-risk prostate cancer patients who undergo a combination of hormonal therapy, radioactive seed implant (also called brachytherapy) and external beam radiation therapy are shown to have an increased chance of cancer cure, according to a new study published in the August 1, 2004, issue of the International Journal of Radiation Oncology*Biology*Physics, the official journal of ASTRO, the American Society for Therapeutic Radiology and Oncology.

Historically, high-risk prostate cancer has been a therapeutic challenge for physicians, despite their efforts to cure patients by aggressively treating them with either surgery, brachytherapy or external beam radiation. Previous studies have shown the 5-year freedom from recurrence rates for high- risk patients treated with just one of these treatments to be between 0 and 50 percent, with up to half of these failures occurring where the original tumor was found.

To see if combining therapies would decrease recurrence rates for men with high-risk prostate cancer, 132 patients with high Gleason scores, with high prostate-specific antigen (PSA) scores or who were at an advanced clinical stage of prostate cancer were studied. A three-pronged approach that included brachytherapy, external beam radiation therapy and hormonal therapy produced an 86 percent rate of freedom from recurrence after five years. In addition, 47 of the original 132 patients in the study had a prostate biopsy performed two years after the end of treatment and 100 percent of them showed no evidence of the cancer recurring.

"This is a very exciting study because it shows that this new approach of combining brachytherapy, external beam radiation and hormonal therapy to cure prostate cancer can be very effective for men with aggressive forms of the disease," said Richard G. Stock, M.D., lead author of the

study and Chairman of the Department of Radiation Oncology at the Mount Sinai School of Medicine in New York. "The data also supports the theory that enhanced local control can improve overall disease control."

NEW EVIDENCE SHOWS HER-2/NEU RECEPTOR CORRELATES WITH PROSTATE CANCER RISK

New evidence shows that the Her-2/neu receptor correlates with an increased risk of developing prostate cancer.

According to a study from Italy, "Development of prostate cancer and progression to androgen-independent disease is correlated with increased expression of growth factors and receptors capable of establishing autocrine and/or paracrine growth-stimulatory loops.

"A thorough review was made of the current literature and recent abstract presentations at scientific meetings focusing on the role of the HER-2/neu (c-erbB2) receptor in prostate cancer and the potential clinical usefulness of its specific inhibitors."

"In the past 10 years," wrote G. DiLorenzo and coworkers, "conflicting results on HER-2/neu expression in prostate cancer have been reported. More recently, four studies have shown experimental evidence of HER-2/neu in the development of prostate cancer and, more specifically, in the progression to a hormone-refractory clinical behavior."

"Furthermore," the authors continued, "it has been proposed that HER-2 family and androgen receptors function synergistically in the absence of androgen, which suggests a crosstalk between the HER-2/neu and androgen receptor pathways."

DiLorenzo concluded, "Finally, clinical trials are in progress in prostate cancer patients to test novel agents that selectively interfere with HER-2/neu activity."

DiLorenzo and colleagues published their study in Tumori (Her-2/neu receptor in prostate cancer development and progression to androgen independence. Tumori, 2004;90(2):163-170).

For more information, contact G. DiLorenzo, Dipartimento di Endocrinologia e Oncologia Molecolare e Clinica, Universita degli Studi Federico II, Naples, Italy, Via S Pansini 5, I-80131 Naples, Italy.

PROSTATE CANCER AND CORONARY HEART DISEASE SHARE SOME RISK FACTORS

Reducing risk factors for cardiovascular disease will help patients with prostate cancer.

According to recent research published in the journal Urologic Clinics of North America, "Cardiovascular disease (CVD) is the leading cause of death in men in the United States and most countries worldwide, the leading cause of death in most cancer prevention trials, and the primary or secondary cause of death in most prostate cancer patients."

"Some risk factors for prostate cancer are similar to the risk factors for CVD, and some methods to reduce the risk for are similar to the methods to reduce the risk for prostate cancer. Recent evidence suggests a correlation between CVD and prostate cancer, but more research is needed," wrote M.A. Moyad and colleagues, University of Michigan, Medical Center.

"Regardless, reducing the risk for CVD could reduce the primary or secondary cause of mortality in men with or without prostate cancer," the researchers concluded.

Moyad and colleagues published their study in theUrologic Clinics of North America (Prostate cancer and coronary heart disease: Correlation or coincidence? Urol Clin North Am, 2004;31(2):207).

For additional information, contact M.A. Moyad, University of Michigan, Medical Center, Department of Urology, 1500 E. Medical Center Dr., Ann Arbor, MI 48109 USA.

ZOLEDRONIC ACID PREVENTS SREs IN HORMONE-REFRACTORY PROSTATE CANCER

Zoledronic acid prevents skeletal-related events (SREs) in hormone-refractory prostate cancer.

According to recent research published in the Journal of the National Cancer Institute, "In a placebo-controlled randomized clinical trial, zoledronic acid (4 mg via a 15-minute infusion every 3 weeks for 15 months) reduced the incidence of skeletal-related events (SREs) in men with hormone-refractory metastatic prostate cancer."

"Among 122 patients who completed a total of 24 months on study," reported F. Saad and colleagues, "fewer patients in the 4 mg zoledronic acid group than in the placebo group had at least one SRE (38 versus 49%, difference=-11.0%, 95% confidence interval [CI]=-20.2 to -1.3%; p=.028), and the annual incidence of SREs was 0.77 for the 4 mg zoledronic acid group versus 1.47 for the placebo group (p=.005)."

"The median time to the first SRE was 488 days for the 4 mg zoledronic acid group versus 321 days for the placebo group (p=.009). Compared with placebo," said investigators, "4 mg of zoledronic acid reduced the ongoing risk of SREs by 36% (risk ratio=0.64, 95% CI=0.485 to 0.845; p=.002).

"Patients in the 4 mg zoledronic acid group had a lower incidence of SREs than did patients in the placebo group, regardless of whether they had an SRE prior to entry in the study."

The authors concluded, "Long-term treatment with 4 mg of zoledronic acid is safe and provides sustained clinical benefits for men with metastatic hormone-refractory prostate cancer."

Saad and colleagues published their

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ZOLEDRONIC ACID

(continued from page 3)

study in Journal of the National Cancer Institute (Long-term efficacy of zoledronic acid for the prevention of skeletal complications in patients with metastatic hormone-refractory prostate cancer. J Nat Cancer Inst, 2004;96(11):879-882).

For additional information, contact F. Saad, University of Montreal, Center Hospital, Hop Notre Dame, 1560 Rue Sherbrooke E, Montreal, PQ H2L 4MI, Canada.

GET VITAMINS THE TRADITIONAL WAY - FROM GOOD FOOD

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FOOD FACTS

When you ask folks, "Where is the best place to get vitamins?" most will suggest a local pharmacy or health food store. Actually, the best place to get vitamins is from food.

Science is always trying to duplicate nature, but when it comes to finding good sources of nutrients you need for good health, food is hard to duplicate. While it is true you can purchase just about any vitamin and/or mineral in a pill, nature still seems to do it better. Despite current research, the natural interaction of nutrients and compounds found in foods is not completely understood.

Phytochemicals are a perfect example. These deep, rich, colorful compounds found in foods have various health benefits. While their functions are very important, they don't provide energy or building properties like nutrients. Over 1,000 phytochemicals have been identified, and one food could contain as many as 50 different phytochemicals. The combinations of different phytochemicals can provide protection from cancer, heart disease and eye diseases. One phytochemical and/or one vitamin can not take care of you, that's why it is so important to consume a healthy and colorful diet to get all you need in the recommended amounts.

Plants use these wonderful phytochemical pigments for protection. Plants are at risk from damaging sunlight, drought, insects and disease. So, these same phytochemicals that protect plants can also defend us from health risks like cancer, and heart and eye diseases. All we have to do is eat them to reap the benefits.

Fresh produce is the best place to find these cancer-protecting compounds. According to research, you can cut your cancer risks in half with a large consumption of fruits and vegetables. You'll receive maximum benefit when you limit peeling and prepare by steaming, broiling or microwaving.

The following is a list of some phytochemicals, with source and purported health benefits:

Lycopene: Found in tomatoes, red grapefruit, watermelon and pink guavas. May lower risk of digestive cancers such as: mouth, pharynx, esophagus, stomach, prostate, colon, and rectum.

Ellagic acid: Found in berries, nuts, fruits, vegetables, grapes. May show great promise as a cancer preventer.

Anthocyanins: Found in red cabbage, red grapes, berries, red onions, eggplant, plums, olives, black beans, most plants with pink, blue and purple pigmentation. May play a role in coronary heart-disease protection and inhibition of a variety of carcinogens.

Liminoids: Found in citrus oils, rinds of citrus fruits, kumquats, marmalade and the fruits of citrus. Currently being researched for prevention and possibly the treatment of breast cancer.

Isoflavones: Found in soybeans, tofu, textured vegetable protein, soy flour. Soy foods in amounts providing 20 to 40 grams of soy protein per day may effectively reduce serum cholesterol levels. Soy foods may offer protection against breast and prostate cancer.

Capsaicin: Found in peppers (mild to hot; the more capsaicin, the hotter the chili). This antioxidant may be capable of disarming damaging chemicals such as nitrosamines that are found in cured and barbecued meats.

Beta-carotene: Found in dark green and yellow vegetables. May reduce the risk of cancers, especially lung.

Allium compounds: Found in onions, chives, garlic, scallions, shallots and leeks. Protect against cancer, especially of the stomach and gastrointestinal tract. Reduces the risk of heart disease. Garlic may reduce blood cholesterol.

Organic isothiocynates: Found in cruciferous vegetables (mustard greens, turnips, horseradish, cabbage, broccoli, and watercress). Decreases cancer risk.

Polyphenols, including flavonoids and catechins: Found in vegetables, fruits, tea and wine. Decrease in death from coronary heart disease. May be linked to reduced incidence of cancer.

Lutein and zeaxanthin: Found in dark green vegetables like kale, collard greens, spinach, watercress, okra, Romaine lettuce and broccoli. Play a crucial role in preventing age-related macular degeneration and cataracts.

There may be times during your life you need to supplement your diet with purchased vitamins and minerals, but nature has designed the best place to receive the nutrients you need in food, especially fruits and vegetables. Be sure to eat a variety of different fruits and vegetables, because they contain various phytochemicals. They are perfectly designed to give you what you need in the right amounts.

NEW MOLECULAR TEST FOR PROSTATE CANCER MAY HELP ADDRESS LIMITATIONS OF TRADITIONAL TESTING

Molecular testing for a new, highly specific prostate cancer marker may help address some of the well- known

limitations of current prostate cancer detection, according to a 517- patient study published in the journal UROLOGY.

In the multi-center study, an investigational molecular test called uPM3 gave a correct positive or negative result for the presence of prostate cancer 81% of the time. The uPM3 test detects the presence of a new prostate cancer gene marker called PCA3 in urine. In contrast, traditional prostate cancer detection by measuring total prostate specific antigen levels, or tPSA, had an overall accuracy of 43% or 47% in the study, depending on the cut-off level used.

"The uPM3 test is an exciting new urine test to help men make critical decisions regarding early detection for prostate cancer", said Alan Partin, M.D., Ph.D., Professor of Urology at Johns Hopkins Medical Institute. Dr. Partin was not involved in the study.

In the UROLOGY study, the researchers collected urine samples following a digital rectal exam from 517 men undergoing prostate biopsies. The uPM3 test had a positive predictive value of 75%, compared to 38% for tPSA. This means that 75% of patients actually had prostate cancer (as confirmed by biopsy) when the uPM3 test was positive. In addition, the uPM3 test had a negative predictive value of 84%, compared to 80% for tPSA at a cut-off of 4.0 ng/ml, which means that 84% of patients did not have cancer when the test was negative.

David Bostwick, Medical Director of Bostwick Laboratories, and a noted expert on the pathology of prostate cancer, stated: "Previous studies have shown that the PCA3 gene is one of the most specific genes yet found to be associated with prostate cancer. It is over-expressed in 95% of cancers tested, at a median level 66 times greater than in adjacent non-cancerous tissue. This study shows that identifying this gene in cells from the urine of men undergoing biopsy may be an important new tool for determining which men have this all-too-common disease."

The UROLOGY study was conducted by researchers at Universite Laval, Universite de Montreal, McGill University, Cite de la sante and DiagnoCure Inc. Lead author Yves Fradet, M.D. is Chairman of the Department of Surgery and Professor of surgery/urology at Universite Laval, CHUQ - L'Hotel-Dieu de Quebec and also Senior Vice President and Chief Scientific Officer at DiagnoCure Inc.

The uPM3 assay was developed by DiagnoCure Inc., of Quebec City, Canada, which holds worldwide exclusive rights to the diagnostic and therapeutic applications of the PCA3 gene. Last November, DiagnoCure and Gen-Probe Incorporated entered into an exclusive, worldwide license and collaboration agreement under which they will jointly develop on Gen-Probe's proprietary technology, and Gen-Probe will market, an innovative urine test to detect the highly specific PCA3 gene for prostate cancer.

STATIN USE ASSOCIATED WITH DECREASED RISK OF PROSTATE CANCER AND ELEVATED PSA

* Data from Veterans Administration (VA) study
* Case-control design

Summary of Key Conclusions
* Statin use appears to be associated with a reduced risk of prostate cancer
* Longer use and higher doses of statins appear to correlate with the greatest benefit
* Larger prospective studies, controlling for other risk factors, needed to confirm these results

Background
* 1 in 7 men over age 60 will be diagnosed with prostate cancer
* Better screening and diagnostic tools have helped identify high-risk patients
* No established preventive therapy exists
* Recent evidence indicates that HMG CoA reductase inhibitors (statins) may induce apoptosis and cell death in certain tumor types

Summary of Study Design
* Case-control analyses of data collected as part of a larger VA study of diet and prostate cancer
* Cases recruited upon referral for prostate biopsy
  - 72 with prostate cancer
  - 224 with prostate-specific antigen (PSA) > 4.0 ng/mL
* Controls (n = 208) with normal PSA, identified from VA primary care clinic
* Statin use (type, duration, dose) obtained through record review
* Statin use categorically defined as:
  - Duration > or ≤ 3 years
  - Dose > or ≤ 40 mg/day
* Age, race, and body mass index (BMI) data also collected

Main Findings
* After adjustment for age, race, and BMI, any statin use was associated with
  - 58% decreased risk of prostate cancer
  - 55% decreased risk of elevated PSA
* Decrease in risk was greatest among those with highest statin use: > 40 mg/day associated with odds ratio .51 (95% CI, .22-1.18)
* Longer duration of statin use associated with increased benefit: Patients with longest duration of use (> 3 years) and higher dose (> 40 mg/day) had 65% lower risk compared with nonusers (odds ratio, .35; 95% CI, .12-1.0)

Reference
Shannon J, Garzotto M, Palma AJ. Statin use and prostate cancer risk. Program and abstracts of the 40th Annual Meeting of the American Society of Clinical Oncology; June 5-8, 2004; New Orleans, Louisiana. Abstract 4596

Statin Use (Average Daily Dose, mg)	Odds Ratio (95% CI) Prostate Cancer	Odds Ratio (95% CI) Elevated PSA
Nonuser	1.0	1.0
0-9.3	.59 (.25-1.45)	.79 (.45-1.40)
9.3-19.0	.34 (.12-.93)	.38 (.20-.73)
19-38.0	.34 (.12-.93)	.31 (.16-.62)
> 38.0	.45 (.18-1.11)	.34 (.18-.66)

COMBINATION THERAPY SHOWS PROMISE

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D'Amico said. "Most cancer advances give you a couple percentage points. They don't give you 10 (percentage points)."

During the study, six of the patients in the radiation group died of prostate cancer and 17 from other causes, compared with no prostate cancer deaths in the combined therapy group and 12 from other causes.

In addition, 43 of the men in the radiation group had disease progression, compared with 21 in the combination therapy group.

Equally important, D'Amico said, was the fact that the men in the combined therapy group were spared many of the ill effects of long-term hormone therapy, which often lasts three years. Long-term hormone therapy can cause osteoporosis, muscle loss, irregular heartbeat, memory loss and other cognitive problems, impotence and breast enlargement. Hormone therapy drugs block the production of testosterone.

However, by limiting androgen suppression therapy to six months, many of those side effects can be limited, although breasts still can become enlarged and there may be temporary erectile dysfunction, he said.

The study, which appears in the August 18, 2004 issue of the Journal of the American Medical Association, involved 206 men aged 49 to 82 who received either two months of radiation therapy alone or in combination with six months of androgen suppression therapy.

While biopsies suggested that their cancer was confined to the prostate, they were at a somewhat higher risk because of prostate specific antigen, or PSA, scores of 10 or more, or of a Gleason score - a grading system for cancerous prostate tissue - of at least 7. They also may have had radiographic evidence that the cancer had spread beyond the prostate.

Already, doctors are using combination therapy to treat men with more aggressive prostate cancer, said Theodore DeWeese, chairman of radiation oncology at Johns Hopkins University Medical School. Now there is sound evidence that it can be beneficial for men at intermediate risk, said DeWeese, who also wrote an editorial in JAMA accompanying the study.

"I think it's a very significant development," he said in an interview.

The JAMA study used a lower dose of radiation, DeWeese said. What is not known is how the survival rates would have been affected had the researchers used a higher dose. It is possible that survival would have improved in both groups or the radiation group alone, he said.

Either way, the research is likely to change the way doctors treat prostate cancer, he said.

The study also gives doctors confidence about using a shorter course of hormone therapy in men who are at intermediate risk, said Robert Donnell, an associate professor of urology at the Medical College of Wisconsin.

That's important, he said, because some men are less able to endure two or three years of hormone therapy.

"It (the study) gives some rationale for using hormones for a shorter period of time," Donnell said.

What still is needed, Donnell said, is a large study over the course of 10 to 20 years comparing radiation alone and in combination with hormone therapy.

In a separate project, teams of researchers from several institutions said they were close to finding a gene that may strongly influence prostate cancer risk.

Reporting in the Journal of the National Cancer Institute, the scientists said they found a region on chromosome 17 that appears to have a strong link to prostate cancer.

Coincidentally, chromosome 17 is the location of one of two genes that greatly increase the risk of breast cancer.

One in six men eventually will be diagnosed with prostate cancer. Having a family history of the disease or being African-American increases the risk.

Already, three genes that seem to modestly increase prostate cancer risk have been identified, said John Carpten, senior investigator with the Translational Genomics Research Institution, a Phoenix non-profit research group.

The other researchers involved in the study were from Wake Forest University, Johns Hopkins, the University of Michigan, the National Institutes of Health and two Scandinavian universities.

The chromosome 17 gene was identified by doing a genetic analysis of more than 2,000 people and 400 families in the United States and Sweden with a history of prostate cancer.

PROTEIN LINKED TO PCA AGRESSION

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sends signals to turn Stat5 on is blocked, human prostate cancer cells die. When the line remains open for communication, allowing Stat5 to send cellular signals, prostate cancer cells stay alive and thrive. Nevalainen's work is focused on finding ways to short-circuit the signals that turn on Stat5, thus killing prostate cells before they flourish.

In this study, human prostate cancer specimens, which are routinely collected during prostate cancer surgeries for analysis of the histological grade of each prostate cancer, were analyzed for activation of Stat5. Activation of Stat5 was then correlated statistically with the histological grade of each specimen.

Nevalainen sees dual possibilities for where the future of Stat 5 research may one day lead: development of potential treatments and identifying whether Stat5 could serve as an effective sign for diagnosing cancer. "We are in the process of determining whether

activation of Stat5 in prostate cancer would serve as an effective prognostic biomarker. Development of additional diagnostics, beyond the PSA test, may help physicians on the frontlines of cancer detection" (Li H, Ahonen TJ, Alanen K, et al., Activation of signal transducer and activator of transcription 5 in human prostate cancer is associated with high histological grade. Cancer Res, 2004;64(14):4774-82)

INTERMITTENT ANDROGEN SUPPRESSION FOR LOCALLY ADVANCED AND METASTATIC PROSTATE CANCER

Sato N, Akakura K, Isaka S, Nakatsu H, Tanaka M, Ito H, Masai M; Chiba Prostate Study Group.
Urology. 2004 Aug;64(2):341-5

OBJECTIVES: To clarify the effect of intermittent androgen suppression on the time to androgen-independent progression and changes in quality of life (QOL).

METHODS: Patients with locally advanced or metastatic prostate cancer were treated with a combination of leuprolide acetate and flutamide for 36 weeks. When the serum prostate-specific antigen (PSA) levels at 24 and 32 weeks were less than 4.0 ng/mL, treatment was withheld until the PSA level reached 15 ng/mL or the pretreatment level. This cycle of on-treatment and off-treatment was repeated until PSA failure (three consecutive increases in PSA level greater than 4.0 ng/mL during the on-treatment period) or symptomatic progression was observed. Changes in QOL were assessed by a self-assessment questionnaire.

RESULTS: Forty-nine patients (26 with T3N0M0, 8 with T2-T3N1M0, 2 with T4N0M0, and 13 with T2-T3N0M1) were enrolled. The mean follow-up period was 136.5 weeks. Thirty-one patients finished cycle 1, six finished cycle 2, and three finished cycle 3. The mean off-treatment duration in cycles 1, 2, and 3 was 46.1, 36.9, and 23.3 weeks, respectively. In the off-treatment period, statistically significant improvements in the QOL score were observed in the categories of potency (11.4 versus 2.4) and social/family well-being (20.3 versus 16.1) compared with those in the on-treatment period. PSA failure occurred in 6 patients (3 with T3N0M0 and 3 with T2-T3N1M0), and all patients were alive at last follow-up.

CONCLUSIONS: Our interim analysis indicated that QOL is remarkably improved during the off-treatment period. Intermittent androgen suppression would be a viable option for treatment of advanced prostate cancer, although a randomized controlled study is required to determine whether intermittent androgen suppression prolongs the time to androgen-independent cancer. We will continue follow-up in this study to a minimum of 3 years.

EXERCISE MAY BEAT FATIGUE IN PROSTATE CANCER

Reuters Health

Staying active through moderate walking may help prevent fatigue in men undergoing radiation therapy for prostate cancer, a UK study shows.

Cancer patients commonly develop fatigue as the stress of the illness and the physical effects of treatment take their toll. It's common for patients undergoing treatment to be told to take it easy, and some may self-impose limits on their daily activities, according to the study's lead author Dr. Phyllis M. Windsor.

But in her team's study of 66 men with cancer confined to the prostate gland, those who were physically active during their month of radiation treatment showed no substantial increase in fatigue. The same was not true of patients in the non-exercising "control" group, according to findings published in the August issue of the journal Cancer.

The findings are in line with research with women undergoing radiation and chemotherapy for breast cancer, noted Windsor, a cancer specialist at Ninewells Hospital in Dundee, Scotland. It's thought, she told Reuters Health, that such results "potentially apply to all groups of patients with cancer."

While rest may be the intuitive response to fatigue, too much inactivity can make the problem worse. Long periods of rest, Windsor said, may de-condition muscles and roll back a person's capacity for exercise, making even routine daily tasks tough to tackle.

Exercise, on the other hand, keeps muscles conditioned, so that everyday activities require less effort and are less taxing on the body. In addition, Windsor pointed out, research suggests that exercise combats depression, which can alter patients' perceptions of fatigue.

For the current study, the researchers randomly assigned 66 men with localized prostate cancer to either an exercise group or a control group. The exercisers walked at a moderate pace for 30 minutes, three days per week; patients in the control group were not discouraged from performing their usual activities, but were told to rest if they became tired.

After four weeks of radiation therapy, men in the control group were had greater fatigue than they did before treatment; and one month later, these patients were still showing signs of weariness.

In contrast, exercisers showed no significant increase in fatigue at any point during the study, according to the researchers.

Windsor said she and her colleagues are planning a larger study to see if walking or, for patients who cannot walk, chair-based exercises can counter fatigue in patients with a range of cancers, including prostate, cervical, uterine, bladder and kidney cancers.

SOURCE: Cancer, August 2004

NATURAL HISTORY OF EARLY, LOCALIZED PROSTATE CANCER.

Johansson JE, Andren O, Andersson SO, Dickman PW, Holmberg L, Magnuson A,

CONTEXT: Among men with early prostate cancer, the natural history

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a quarter million men a year being diagnosed in the U.S. alone there is a growing need for the education and support services that Us TOO has to offer."

"John has been instrumental in elevating Us TOO and enhancing our ability to better serve men with prostate cancer, their families and men at risk", stated Lewis Musgrove, Us TOO Chairman of the Board. "He has left a lasting impression on this organization and on the men we serve. He will be missed."

"I will pass the baton of an organization which is stronger and more energized then when I arrived. We have a broad and committed volunteer base and staff. That is important because there is a great amount of work yet to be done. I am confident that Us TOO will continue to be a force for positive change and collaboration within the prostate cancer community." said Page.

"John has been a great advocate for the prostate cancer community", said Jim Kiefert, Us TOO Treasurer, "and as a result Us TOO has made great strides in diversifying our ability to obtain funding from sources such as the CDC."

"I've always particularly enjoyed the patient interaction this job afforded me." Said Page. "That patient contact always reminded me why we work in an organization like Us TOO. I'll particularly miss that aspect of the job."

"We will sorely miss John's compassion for the patient and passion for the job." said Us TOO Board Executive Committee Member Jo Ann Hardy. "His leadership has helped to establish Us TOO as one of the most well respected groups in the cancer community and that has allowed us to achieve so much that is measurable in both quality and quantity. It has been his personal touch that has made so much of that happen."

Page will continue to serve through October 31 while the organization goes through a recruitment for and transition to a new CEO.

EARLY, LOCALIZED PCA

(continued from page 7)

without initial therapy determines the potential for survival benefit following radical local treatment. However, little is known about disease progression and mortality beyond 10 to 15 years of watchful waiting.

OBJECTIVE: To examine the long-term natural history of untreated, early stage prostatic cancer.

DESIGN: Population-based, cohort study with a mean observation period of 21 years.

SETTING: Regionally well-defined catchment area in central Sweden (recruitment March 1977 through February 1984).

PATIENTS: A consecutive sample of 223 patients (98% of all eligible) with early-stage (T0-T2 NX M0 classification), initially untreated prostatic cancer. Patients with tumor progression were hormonally treated (either by orchiectomy or estrogens) if they had symptoms.

MAIN OUTCOME MEASURES: Progression-free, cause-specific, and overall survival.

RESULTS: After complete follow-up, 39 (17%) of all patients experienced generalized disease. Most cancers had an indolent course during the first 10 to 15 years. However, further follow-up from 15 (when 49 patients were still alive) to 20 years revealed a substantial decrease in cumulative progression-free survival (from 45.0% to 36.0%), survival without metastases (from 76.9% to 51.2%), and prostate cancer-specific survival (from 78.7% to 54.4%). The prostate cancer mortality rate increased from 15 per 1000 person-years (95% confidence interval, 10-21) during the first 15 years to 44 per 1000 person-years (95% confidence interval, 22-88) beyond 15 years of follow-up (P =.01).

CONCLUSION: Although most prostate cancers diagnosed at an early stage have an indolent course, local tumor progression and aggressive metastatic disease may develop in the long term. These findings would support early radical treatment, notably among patients with an estimated life expectancy exceeding 15 years.

SOURCE: JAMA. 2004 Jun 9;291(22):2713-9.

TURP SAFE AFTER BRACHYTHERAPY FOR PROSTATE CANCER

After an interval of 6 months or longer, transurethral resection of the prostate (TURP) can be safely conducted in men who have undergone brachytherapy as the sole treatment for localized prostate cancer, according to French researchers.

Brachytherapy has become a popular alternative to radical prostatectomy and external radiation therapy in prostate cancer patients, Dr. Thierry A. Flam of Hopital Cochin, Paris and colleagues note in the July issue of the Journal of Urology.

The researchers evaluated 600 patients who underwent brachytherapy without adjuvant treatment at their institution between 1998 and 2003. Of these patients, 19 (3.1%) subsequently underwent TURP.

Urinary retention developed in these patients a median of 2 months after brachytherapy, but TURP was not performed for at least 6 months after the implant. The median interval was 7 months and the range was from 6 to 41 months.

The median weight of the resected tissue was 8 gm, and from 1 to 11 seeds were removed during the procedure.

At a median follow-up of 28 months after brachytherapy, no patient had clinical or biochemical evidence of disease progression. Moreover, median prostate specific antigen values (0.38 ng/mL) were lower than those before the procedure (0.5 ng/mL).

The researchers conclude that when TURP is performed at least 6 months after seed implantation it "can be done safely" without impairing the results of brachytherapy.

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