



PROSTATE CANCER HOT SHEET

Us Too! INTERNATIONAL **FEBRUARY 2003**

MEN SEEK 'THE TRUTH' ON PROSTATE TREATMENTS

By Anne Barnard
Boston Globe Staff

At a robust 56, he faced surgery for prostate cancer, terrified that it would leave him impotent. He made the rounds, visiting top urologists at Harvard hospitals. He chose a surgeon who told him that 80 percent of his patients end up able to have sex without the help of devices.

Last week, unable to get an erection and suffering from incontinence, he went to a support group at Beth Israel Deaconess Medical Center, where he learned that the vast majority of the group have significant trouble with sexual function, even years after surgery or radiation treatment.

It turns out that the 80 percent success rate may be more hope than reality, achieved only by a few highly practiced surgeons on selected patients. One large-scale study of prostate cancer survivors found that, 18 months after treatment, 60 percent could not get an erection firm enough for intercourse.

As a result, many men, including some in the (*Us Too!*) Beth Israel support group, feel they were misled about the sexual side effects of their treatment.

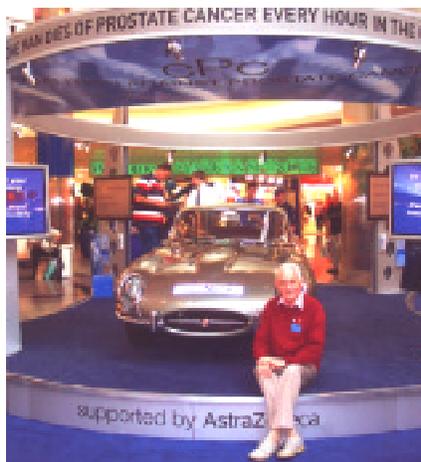
"Why can't we get good solid information?" said the Boston man at Beth Israel, who, at four months after surgery, still hopes for improvement and did not want his name used for fear of alienating his doctor. "If people knew the truth, if there was more - I hate to use the word honesty - but I think people could deal with this disease a little bit better."

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DRIVING HOME THE AWARENESS MESSAGE IN THE UK

By David G. Rowlands
Chairman, PCaSo
Prostate Cancer Support Organization
and Us Too! Regional Director

In the knowledge that men tend to care and look after their car more than their health, a Classic 'E' Type Jaguar has proved to be a real crowd puller



Us Too! UK Regional Director David G. Rowlands helps to drive home the awareness message - with a little help from a Classic 'E' Type Jaguar.

in the Road Show, touring major cities in the United Kingdom.

The Road Show is being driven by **cPc**, *Coalition against Prostate Cancer*, comprising like minded organizations, such as **PCaSO** - *Prostate Cancer Support Organization* - based in the south and also includes research organizations.

Perhaps a little envy and even some nostalgia, brought both young and old to the stand and equally important the

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EXERCISE, DIETARY CHANGES CAN KILL PROSTATE CANCER CELLS, UCLA SCIENTISTS REPORT

AScribe Newswire - UCLA

UCLA scientists report that 11 days of daily exercise and a low-fat, high-fiber diet induce prostate cancer cells to die.

The research, published in the new issue of the journal *Cancer Causes and Control*, is the first to show that diet and exercise can kill prostate cancer cells.

"You can make changes in a short period of time that have a dramatic impact on your health - in this case, on the growth and death of prostate tumor cells," said R. James Barnard, professor of physiological science at UCLA and lead investigator on the study.

Barnard and his UCLA colleagues studied two groups of men: 14 obese men, ages 42 to 73, without prostate cancer, who participated in an 11-day diet and exercise program at the Pritikin Longevity Center; and 8 men, ages 38 to 74, who have exercised regularly and followed a low-fat, high-fiber diet for more than 14 years.

The researchers - who also include Tung Ngo and Christopher Tymchuk, UCLA graduate students working in Barnard's laboratory; Pinchas Cohen, a researcher at UCLA's Jonsson Cancer Center and professor of pediatrics at UCLA's David Geffen School of Medicine; and William Aronson, a researcher at UCLA's Jonsson Cancer Center and an associate clinical professor in the Department of Urology at UCLA's David Geffen School of Medicine -

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PROSTATE CANCER NEWS YOU CAN USE

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NOVEL APPROACH SHOWS PROMISE FOR A BLOOD TEST

In a pilot study, researchers at the University of Texas M.D. Anderson Cancer Center have designed a new type of blood test that may hold promise for evaluating disease progression in prostate cancer patients. The findings, published in the January 2003 issue of the journal Nature Biotechnology, also may offer a new insight into the biology of the disease. "The information based on this retrospective preliminary analysis may, in the future, be useful for physicians to decide among the many therapeutic options available for prostate cancer patients. As of today, these options are largely dependent on the stage of the disease," said Wadih Arap, MD, PhD, the lead author of the study from the department of genitourinary medical oncology at M.D. Anderson. By looking at the patterns of antibodies from cancer patients, the researchers found that reactivity against a protein that is present at high levels in prostate tumors correlated with poor prognosis and advanced disease. "Future studies based on these findings are likely to help us understand the mechanisms of disease progression," said coauthor Renata Pasqualini, PhD. In this report, the group led by Arap searched for small protein fragments (peptides) that can be recognized by antibodies found in the serum of prostate cancer patients. These small protein fragments turned out to be part of a tumor antigen called GRP78. "This study validates the hypothesis that humoral response can serve as a 'labeling system' of human cancer. The observations may be clinically meaningful because the presence of antibodies against this particular antigen correlated with disease progression and patient survival. The findings will stimulate investigation as to how the humoral immune response to cancer can be used as a method to monitor and understand cancer progression clinically," said coauthor Christopher Logothetis, MD, chairman of the department of genitourinary medical oncology. According to Logothetis, if the disease is detected at early stages, prostate cancer can be managed by local treatments such as surgery or radiation. At later stages of progression, prostate cancer commonly spreads into specific sites such as the skeleton. When this happens, treatment options are more limited. Novel tools for biochemically staging disease would help physicians

and patients evaluate and select the most appropriate therapeutic approach, said Logothetis. According to researchers, the long-term purpose of this project is to identify circulating antibodies that can serve as an early warning system based on individual patients' immune response against tumors. These antibodies can be used to discover what protein fragments they are recognizing, and correlate their presence with patterns and speed of disease progression. The researchers at M.D. Anderson have demonstrated that phage display technology is effective in identifying such antibodies. Before this novel blood test can be used clinically, it needs extensive validation, cautioned Arap. Pasqualini added that this particular "biological read-out" of prostate cancer progression based on the pattern of circulating antibodies in the serum of patients is just one in a series that the investigators are working to develop. "This may be one preliminary step towards the development of better tools to evaluate cancer progression."

PATIENTS UNDERGOING RADIATION THERAPY SETTING OFF SECURITY SCANNERS

State Journal-Charleston WV
Dr. Gregory Merrick was surprised to hear about a patient of his who was suspected of carrying radioactive material earlier this year while he was returning to America from Russia. Merrick, a radiation oncologist in Wheeling, said Russian security agents stopped the patient because their scanners detected radioactive material that could be part of an incendiary device. The guards soon discovered the radiation had nothing to do with a bomb - it was residual emanation from a medical treatment the patient received two months before his trip. "Once (the patient) explained everything, they were fine with it. But that shows you how sensitive those detectors are now because they need to detect plutonium," Merrick said. The Wheeling physician had treated the patient for prostate cancer using a procedure called brachytherapy, in which tiny radioactive seeds are implanted into the prostate for targeted radiation therapy. The seeds contain a Palladium isotope that becomes inactive after 60 days. Merrick's patient had brachytherapy 55 days before he set off a radiation detector at a Russian airport - just five days before the seeds "died." "We're in a new age of security," Merrick said. Since

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radiation treatments do not leave scars, "patients may want to keep their discharge sheets with them in case they are stopped," he said.

**SEXUAL DYSFUNCTION WIDESPREAD
AND
FEW TREATMENTS HELP**

A much smaller percentage of men regain "normal" sexual function after treatment for prostate surgery than has been commonly believed, a survey has found. Investigators at the University of Texas M.D. Anderson Cancer Center, working with researchers at the Cleveland Clinic, found that 85% of 1236 prostate cancer patients surveyed reported having erectile dysfunction (ED) in the past 6 months. Only 13% of the men said they had firm and reliable erections spontaneously, and while many patients tried such ED treatments as Viagra, penile injections, vacuum devices and penile prostheses, only 8% regained near-normal erections with their use. Some prostate cancer treatments such as nerve-sparing surgery and radioactive seed implants offer a somewhat better chance that a man can achieve an erection most of the time, but the overall picture is "generally dismal," said lead researcher Leslie Schover, PhD, a clinical psychologist in the department of behavioral sciences at M.D. Anderson. The investigation, funded by the American Cancer Society, was published in two parts. The first report, in the October 15, 2002 issue of the journal Cancer, examined the degree of sexual dysfunction in patients, and the second paper, published in the online edition of the December 1 Cancer, looked at the treatments patients used, mostly in vain. "Too often, prostate cancer patients are led by physicians and the popular media to believe they have a 50-50 chance, or better, to regain their erectile function, but, in fact, the great majority of survivors experience severe and lasting sexual problems and dissatisfaction in the years after treatment," said Schover, who has spent decades counseling men with ED. "Many men have been sold a bill of goods, and that's sobering." To instill "more realistic expectations," patients, and their sexual partners, should receive counseling as a routine part of their oncology care, the researchers suggested. "Men were as distressed about loss of desire and trouble having satisfying orgasms as about ED," the study reported. The survey also showed that younger age was strongly associated with better sexual outcome,

as was the influence of following medical factors: not having neoadjuvant or current antiandrogen therapy, having bilateral nerve-sparing prostatectomy surgery or brachytherapy, and having better mental and physical health. Sexual factors associated with better outcome included: having normal erections before cancer treatment; choosing a cancer treatment based on the hope that it would preserve sexual function, having more sexual partners in the past year, and having a partner who is free of sexual problems herself. The second study looked at how effective the cornucopia of therapies designed to help ED were to patients surveyed. That report found that while 59% of patients tried at least one ED treatment to improve their sex lives, only 38% found a therapy that was at least somewhat helpful, and even fewer continued to use it. The survey also found that the treatments easiest to use, such as Viagra, are the least effective in these patients, although many men continue to use them, hoping they will work. For example, more than half of patients surveyed (549 men or 52%) tried Viagra, but only 16% said it "greatly improved" sexually functioning. Yet 39% of these patients continue to use it. By contrast, patients who use the most invasive ED therapy, a penile prosthesis, reported a 44% "greatly improved" functioning - the highest rating obtained in the survey - and 81% of these patients still use this method. But only 16 patients (2%) chose this option. "Men wish Viagra would work, but we found that all current treatments except implantation of a penile prosthesis have a drop-out rate exceeding 50%," Schover said. The second-most-popular ED treatment was a vacuum device, used by 197 patients (19%). But only 19% reported "greatly improved" functioning although 41% reported that they still use the device. Penile injections, used by 179 men (18%), resulted in the second highest satisfaction result; 29% of patients who used it said it greatly improved sex, but just 34% of those patients still use the therapy. Among other findings were that 79% of men who had bilateral nerve-sparing prostatectomy tried a therapy for ED, compared to only 50% of men who had brachytherapy, despite the fact that both of these treatments appeal to men who want to preserve their sex lives. Viagra also works best in men who have both nerves spared in prostatectomy, or in men who have radiation therapy, the

researchers found. The negative impact of hormonal therapy on successful treatment for ED is also clear, said Schover. Few men with suppressed testosterone production found a successful treatment for their ED. Finally, the researchers pointed out that a patient's relationship to a sexual partner is important in explaining successful use of a medical treatment for ED, especially if that partner has good sexual function. Yet most ED clinics make little effort to include the partner in treatment planning, said Schover. "Many men regard ED as their individual problem, but sex takes place in a relationship, and couples can be helped to make a mutual decision to pursue a treatment," she said.

**NEW GENE THERAPY
BOOSTS IMMUNE SYSTEM
TO CURE CANCER**

Using a novel gene therapy approach that boosts the body's immune system, a Northwestern University researcher has cured cancer in laboratory mice. In experiments reported in the December 15, 2002, issue of Cancer Research, Chung Lee and colleagues at the Feinberg School of Medicine at Northwestern University applied the gene therapy technique to render immune cells insensitive to transforming growth factor beta (TGF-beta), a powerful, naturally occurring substance in the body called an immunosuppressor that enables cancer cells to evade surveillance by the immune system. The approach boosted the mice's immune system, which virtually eliminated cancerous tumors in the animals' lungs and prostate gland. "We hypothesized that an immunotherapy strategy that specifically blocks TGF-beta signaling in immune cells, regardless of tumor location or tumor microenvironment, could be highly successful in mediating an antitumor response," said Lee. Mice with the mutated TGF-beta gene that were later injected with prostate cancer cells, the gene-targeted approach resulted in 80% survival. All of the control mice in the melanoma and prostate cancer arms of the study that had not received the gene therapy died of metastatic cancer.

**COX-2 PROMOTES
DISEASE PROGRESSION**

"Cyclooxygenase (COX)-2, an inducible isoform of COX, has been observed to be expressed in prostate cancer. Several studies have reported

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MEN SEEK "THE TRUTH"

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Doctors agree that there is a broad gap between the more optimistic potency rates widely quoted in surgeons' books and Web sites - especially those of celebrity specialists like Johns Hopkins Hospital's Dr. Patrick C. Walsh - and the more typical experience. Published studies report post-surgical rates of impotence ranging from less than 15 percent to more than 80 percent, depending on the patients' ages and conditions and the experience of the surgeon.

Radiation treatment offers a somewhat lower risk of impotence, but, because long-term survival is not so good, doctors usually recommend surgery for younger patients, the ones most likely to be sexually active.

However, doctors say they tell patients up front about the risks and trade-offs. They also say that support groups overstate the degree of dissatisfaction because they tend to attract more men who are having problems.

But some doctors, as well as many patients, believe the prostate cancer survivors have a point: Surgeons sometimes downplay the chances of impotence as they focus on curing cancer. They sometimes quote potency rates for celebrity surgeons who do nothing but remove prostates, rather than their own rates, said Dr. Jeffrey Steinberg, acting chief of surgery at Cambridge Health Alliance, who advises the support group. Or they don't emphasize that the best numbers come from groups of younger, healthier patients.

The result, said group leader Stan Klein, is that with 180,000 men diagnosed and 55,000 undergoing prostate-removal surgery each year, thousands of survivors are glad to be alive, but painfully disappointed with their sexual function.

"It's devastating," he said. "We've had them coming in with tears in their eyes."

"I understand the frustration and anger on the part of many of those patients," Steinberg said, adding that doctors have to be extra rigorous in

preparing patients for side effects, since men sometimes hear only what they want to hear when doctors predict their sexual future.

"It's important for surgeons to tell patients what their experience is in their own practice, how many they've done, what age range they've done," he said. About 50 percent of his own patients are potent a year after surgery, he said, with better results in younger patients.

Klein, cancer-free nine years after surgery, is on a mission to paint what he calls a more realistic picture. His goal is not to discourage treatment: "With almost 32,000 men dying each year, we don't want men to say, 'I'll take my chances.'"

Rather, he said, realizing that impotence is more likely than not will prepare men better to cope with the problem and seek treatment - Viagra, injections, vaccum pumps and penile implants - that usually brings "an almost normal sex life."

Dr. Irwin Goldstein, director of the Institute of Sexual Medicine at Boston University School of Medicine, had this advice for prostate patients, whether they opt for surgery or radiation: Doctors exaggerate their ability to save your erections. Expect to be impotent. But worry only about surviving. Then, call the sexual dysfunction specialists.

"If a man owns a penis," he said, "we can make them have an erection."

Prostate cancer victims face a particularly difficult choice since the treatment options force them to decide between a greater risk of death or a greater risk of impotence. Unlike most cancers, their disease can be treated effectively with two very different techniques, surgery and radiation. While radiation causes less impotence and incontinence, surgery has better survival rates beyond 10 years. And radiation patients sometimes develop sexual side effects well after the treatment.

And for doctors, measuring safety and effectiveness of surgery is always contentious, since so much depends on individual skill and patient selection. There is some mistrust between surgeons and the

epidemiologists and others who measure their outcomes. The debate over prostate surgery has even tapped into the rivalry between Boston's hospitals and Johns Hopkins of Baltimore - home of Walsh, the surgeon who helped raise expectations so high.

In 1981, Walsh published a paper describing the nerves that run close to the prostate and help control erections. He developed the technique of removing the walnut-sized gland without cutting either of the nerves, called bilateral nerve-sparing.

His most famous study, quoted frequently on his Web site, was published in 2000. Of 62 relatively young, healthy patients he operated on, 86 percent could have sex spontaneously after a year and 93 percent were completely continent. He and five other top surgeons also reported 90 percent potency on 50 patients under age 60.

Those numbers, touted in Walsh's best-selling book, raised the bar for prostate surgeons - unrealistically, say other surgeons.

"He's a very good surgeon and he's honest, but he's very selective" in choosing patients, said Dr. Jerome Richie, chief of urology at Brigham and Women's Hospital, who says his own potency rate is 85 percent for patients in their 40s, 60 percent for those in their 60s.

In a larger study of 1,291 patients, about half over 65, University of Washington epidemiologist Janet Stanford found that 18 months after surgery, 60 percent of men reported having no erections or erections that were not adequate for sex. Even among those under 60, just 40 percent had erections adequate for intercourse.

Since not everyone can go to a top specialist, it's important for all surgeons to measure and report their own outcomes, said Dr. James Talcott, of Massachusetts General Hospital's Center for Outcomes Research. But he believes most don't - partly because the expectations are so high that real numbers would be damaging.

Talcott studied 49 patients who had

surgeries at Boston teaching hospitals. He found that most were impotent, including 15 of 19 patients who had bilateral nerve-sparing surgery. He said his results were more realistic because the patients had a wider mix of ages and were asked about their conditions by independent researchers, not doctors.

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EXERCISE, DIETARY CHANGES CAN KILL PROSTATE CANCER

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collected blood serum samples from the 14 men before they began the 11-day Pritikin program. At UCLA, the researchers mixed these serum samples in dishes with prostate cancer cells. At the end of the 11-day program, the researchers collected a second set of blood serum samples from the same 14 men, and placed these samples in laboratory dishes with prostate cancer cells.

Prostate cancer cell death

Among the 14 men at the beginning of their diet and exercise program, fewer than three percent of the LNCaP cells - prostate cancer cells - in the cell culture showed apoptosis (programmed cell death). At the conclusion of the 11-day program, more than 40 percent of these cells were on their way to death, and in the 14-year group of eight men, more than 50 percent of these cells were on their way to apoptosis, or death.

"That was the finding that made our jaws drop," Barnard said. "We don't know yet whether these dramatic changes that occurred to prostate cancer cells cultured in a laboratory will also occur in patients; we have hope that these changes will occur."

In an attempt to understand what might be inducing the apoptosis of the tumor cells, the scientists measured blood serum levels of a hormone called IGF-I, which stimulates tumor cells to grow; a high level of IGF-I is a risk factor for prostate cancer, Barnard said.

At the end of the 11 days, IGF-I levels for the 14 men had decreased by 20 percent. The eight men who had followed the diet and exercise program for 14 years had IGF-I levels 55 percent lower than the 14 men had at the start of their diet and exercise program.

"Insulin is the primary factor that stimulates the liver to produce IGF-I," Barnard said. "In previous research, we have shown that diet and exercise lower the serum insulin level; we suspected that diet and exercise should lower the IGF-I level as well, and we have found that to be true."

While IGF-I floats in the bloodstream, it binds to a protein, IGFBP-I, which limits the amount of IGF-I that is available to interact with tissue. Higher levels of this binding protein are desirable, causing a drop in free IGF-I levels, Barnard said.

Over the 11-day program, IGFBP-I levels increased by 53 percent, while in the long-term group of eight men, IGFBP-I levels were 150 percent higher than the short-term group had at the outset of the program.

"We didn't expect the results would be this dramatic," Barnard said. "We found dramatic changes in both IGF-I and IGFBP-I levels with diet and exercise. The important message is you can change your levels of both IGF-I and IGFBP-I in a very short period of time, and that may have an important impact on your prostate health."

Implications of the research

"I've been telling people for years if they want to avoid most of the health problems we have in this country, they should go on a low-fat, high-fiber diet and do about an hour of aerobic exercise every day," Barnard said. "You make up your mind: Do you want to be healthy? It's not a tough choice."

Barnard, 65, has worked with the Pritikin Longevity Center since 1978, and serves as a consultant. He weighs five pounds less than when he graduated from college, and his cholesterol dropped from 235 when he was in his early 40s to 180 when he changed his diet; he has maintained his cholesterol around

180-190 for more than 20 years.

The Pritikin program focuses on a diet of whole grains, fruits and vegetables, and small portions of meat (no more than 3-and-a-half ounces a day), and 60 minutes of exercise a day.

Prostate cancer is the most common type of cancer in American men, other than skin cancer, and the second leading cause of cancer death in men, exceeded only by lung cancer. Some 30,000 men in the United States die of prostate cancer each year.

Barnard noted that some people buy growth hormone supplements, which stimulate the production of IGF-I. He "seriously questions" older people taking such supplements.

"Where you need IGF-I is in your muscle; the way to get it is to exercise," Barnard said. "People want the easy way out; they want to take a pill."

SOY PRODUCT GENISTEIN QUELLS CANCER GROWTH MECHANISMS AT GENETIC LEVEL

by **Sonia Nichols**
AP Senior Medical Writer

The soybean product genistein is purported to influence the course of a number of diseases, including cancer. Researchers in the U.S. have confirmed that genistein targets genes responsible for controlling signals associated with prostate cancer dissemination.

Health care professionals believe that by sensitizing prostate cancer cells to chemotherapy, some individuals might avoid cancer cell metastasis. Several studies have shown that isoflavones such as genistein alter the course of prostate cancer in animals. The coauthors of a Wayne State University School of Medicine study say genistein controls prostate cancer control processes such as angiogenesis at the transcription level.

"To better understand the precise molecular mechanism(s) by which

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**GENISTEIN QUELLS
CANCER GROWTH**

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genistein exerts its effects on PC3 (prostate cancer) cells, we utilized cDNA microarray to interrogate 12,558 known genes to determine the gene expression profiles altered by genistein treatment," said Yiwei Li and colleagues, who work at the Detroit, Michigan medical school.

Genistein more than doubled the response of over 800 genes. Thirteen of those genes have been linked in some way to angiogenesis and the spread of cancer. Eleven of the 13 genes were down-regulated after genistein treatment, whereas the 2 remaining genes, associated with connective tissue signaling, were up-regulated.

Several more laboratory tests confirmed the results of the microarray analysis (Down-regulation of invasion and angiogenesis-related genes identified by cDNA microarray analysis of PC3 prostate cancer cells treated with genistein. *Cancer Letters*, 2002;186(2):157-164).

"We concluded that genistein down-regulates the transcription and translation of genes critically involved in the control of angiogenesis, tumor cell invasion, and metastasis, suggesting the possible therapeutic role of genistein for metastatic prostate cancer," said Li and coauthors.

The investigators proposed that genistein might be particularly suited for making prostate cancer cells more receptive to control by chemotherapies already on the market.

Key points reported in this study include:

- * Genistein is an isoflavone that is believed to have anticancer properties
- * Genistein down-regulates or up-regulates a number of genes linked with angiogenesis, tumor invasion, and metastasis in prostate cancer
- * The soy product may be valuable as an adjuvant for chemotherapies that treat or prevent metastatic prostate cancer.

**REPORT SHOWS
BENEFITS OF COMBINING
VITAMIN D WITH
TAXOTERE**

The addition of high-dose calcitriol to weekly treatment with the chemotherapy agent docetaxel (Taxotere) appears to improve the therapeutic response in men with androgen-independent prostate cancer without compromising safety.

Data from a phase II clinical trial suggest the combination of docetaxel/calcitriol is as much as twice as effective as the use of docetaxel alone, as measured by prostate-specific antigen (PSA) response rate. The results were so promising that a phase III trial has been launched at 15 sites throughout the United States. Results were published January 1, 2003, in the *Journal of Clinical Oncology*. Calcitriol is the active form of vitamin D

"We're excited by these promising results, especially since there is no acceptable standard treatment for this type of prostate cancer," said Tomasz Beer, MD, an oncologist at the Oregon Health & Science University (OHSU) Cancer Institute in Portland, and lead investigator of the study.

In the study, 31 of 37 patients, or 81%, who were treated with the combination regimen cut their PSA levels by more than half. In fact, 59% of patients achieved a confirmed PSA reduction of greater than 75%. Studies of docetaxel alone have reported a 42% PSA response rate. PSA is a substance produced within the prostate gland, and a high PSA level may indicate the presence of cancer. In patients with advanced prostate cancer, PSA correlates with the amount of cancer in the body.

In addition to PSA response, 8 of 15 men in the study with measurable disease responded with significant reductions of their tumors.

"Based on this data we've opened a much larger study nationwide that should tell us whether these preliminary findings continue to hold true in larger patient populations," said Beer.

Patients in the study received oral

calcitriol on the first day of the treatment cycle, followed by an infusion of docetaxel the next day. The treatment was repeated weekly for 6 weeks of an 8-week cycle until there was evidence of disease progression or unacceptable toxicity, or until the patient requested to be withdrawn from the study. Calcitriol is not the same as over-the-counter vitamin D, which could be harmful if taken in large doses.

NEWS YOU CAN USE

(continued from page 3)

that COX-2 overexpression is associated with carcinogenesis, cell growth, angiogenesis, apoptosis, and invasiveness in a variety of tumor types," researchers in Japan report. The researchers concluded: "These data demonstrate that COX-2 contributes to prostate cancer progression and suggest that it mediates this effect, in part, through increased VEGF."

Fujita and coauthors published their study in the journal *Prostate* (Cyclooxygenase-2 promotes prostate cancer progression. *Prostate*, 2002;53(3):232-240).

**ZYFLAMEND
HERBAL COX-2 INHIBITOR
EXHIBITS ANTICANCER ACTIVITY**

A new study from the Department of Urology at Columbia University suggests that Zyflamend, an herbal COX-2 inhibiting formulation, strongly suppresses the proliferation of human LNCaP prostate cancer cells and induces apoptosis. The study, entitled "Zyflamend, an Herbal COX-2 Inhibitor with In Vitro Anti-Prostate Cancer Activity," was presented at the December 13 meeting of the Society of Urologic Oncology in Bethesda, Maryland. This meeting was cosponsored by the National Cancer Institute. According to researchers, Zyflamend's effects were found to be significantly more potent than a compound in the spice turmeric called curcumin, which is believed by many researchers to be one of the most promising molecules for the prevention and treatment of cancer. Compared with Zyflamend, curcumin exhibited no COX-2 inhibiting effect on its own, suggesting that there is something in

the complexity of the whole-plant formulation that is responsible for its pronounced anti-inflammatory effect. Zyflamend was found to be almost equivalent in its COX-2 inhibiting activity to the pharmaceutical selective COX-2 inhibitor NS-398. "This study on Zyflamend is exceptionally promising. This is the first known natural blend of botanicals that is showing COX-2 inhibitory activity," said Aaron Katz, MD, director of the Center for Holistic Urology at Columbia-Presbyterian Medical Center. Dr. Katz is the lead researcher on the Zyflamend study to be presented at the NCI Urologic Oncology conference. "Our research is on-going and will proceed to clinical trials on Zyflamend's efficacy for prevention and treatment of prostate cancer. By the age 70, over 70% of men in the U.S. will develop prostate cancer, and men today face treatment options which may have potential side-effects. The need for effective natural therapy has never been greater."

**LYCOPENE SUPPLEMENTATION
 BENEFITS PATIENTS WITH
 LOCALIZED DISEASE**

Results of a small study in men newly diagnosed with localized prostate cancer show adding or increasing the amount of lycopene in their diet improved several disease factors. The "inverse association between dietary intake of lycopene and prostate cancer risk" demonstrated in previous studies prompted O. Kucuk and colleagues at Wayne State University in Michigan to conduct "a clinical trial to investigate the biological and clinical effects of lycopene supplementation in patients with localized prostate cancer." They found that "after intervention, subjects in the intervention group had smaller tumors (80% vs. 45%, less than 4 ml), less involvement of surgical margins and/or extra-prostatic tissues with cancer (73% vs 18%, organ-confined disease), and less diffuse involvement of the prostate by high-grade prostatic intraepithelial neoplasia (33% vs. 0%, focal involvement) compared with subjects in the control group." The researchers said that the results of their "pilot study [suggest] that lycopene may have beneficial effects in prostate cancer. Larger clinical trials are warranted to investigate the potential preventive and/or therapeutic role of lycopene in prostate cancer." Kucuk

and coauthors published the results of their study in Experimental Biology and Medicine (Effects of lycopene supplementation in patients with localized prostate cancer. *Exp Biol Med*, 2002;227(10):881-885).

**COMBIDEX CAN DETECT
 LYMPH NODE DISEASE
 IN PROSTATE CANCER**

Advanced Magnetics, Inc. and CytoGen Corp. announced the presentation of data showing that Combidex, an investigational magnetic resonance imaging (MRI) contrast agent, is able to distinguish malignant from normal lymph nodes in a variety of cancers, including prostate and renal cancers. The studies were presented by radiologists at the Radiological Society of North America, Inc.'s 88th scientific assembly and annual meeting in Chicago, Illinois. In one presentation, Mukesh Harisinghani, MD, assistant radiologist with Massachusetts General Hospital and instructor of radiology at Harvard Medical School, reported data from 50 patients with proven primary prostate cancer who were scheduled for radical prostatectomy. In the study, 141 lymph node groups were evaluated using MRI before and after the administration of Combidex. When imaging evaluation results were compared with histopathologic analysis, which represents the current gold standard, radiologists using the Combidex-enhanced images were able to detect malignant lymph nodes with 93% specificity and 92% sensitivity, indicating a high level of correlation.

**DIABETES DECREASES
 PROSTATE CANCER RISK**

Results from a large cohort study done in Sweden indicate that men with diabetes have a reduced risk of prostate cancer, especially if they have been hospitalized for treatment of diabetic complications. "Although diabetes mellitus is associated with an increased risk of several malignancies, a negative association with prostate cancer is biologically most plausible," said Elisabete Weiderpass and colleagues at International Agency for Research on Cancer in Lyon, France and the Karolinska Institutet in Stockholm. "The epidemiologic evidence is, however, inconsistent, limited, and

based mostly on small studies." "We did find a small, but significantly decreased risk of prostate cancer among men who had been hospitalized for diabetes mellitus," concluded Weiderpass and her coauthors (Reduced risk of prostate cancer among patients with diabetes mellitus. *International Journal of Cancer*, 2002;102(3):258-261).

**AWARENESS OF PATIENTS'
 "SELF-TREATING"
 WITH SUPPLEMENTS**

A survey of more than 45,000 men and women suggests vitamin and mineral supplements are especially popular among certain groups of Americans, some of whom may be using them to self-treat health conditions. "These findings suggest physicians, pharmacists and other healthcare providers need to be aware of the conditions their patients may be self-treating," says study author Jessie Satia-Abouta, Ph.D., of the Department of Nutrition at the University of North Carolina at Chapel Hill and formerly at the Fred Hutchinson Cancer Research Center in Seattle, Wash. The researchers found that more than 75 percent of participants regularly took a supplement. More than half of the participants were taking a multivitamin and the most popular single supplements were vitamins E and C, calcium, folate and selenium. Supplement use was most popular among participants who were older, female, highly educated, Caucasian or Native American, and who had a normal body weight. In general these findings, along with previous findings, "suggest that the public may be using dietary supplements to treat illnesses," Satia-Abouta says. The study results are published in the January issue of the *American Journal of Preventive Medicine*.

**CANCER TREATMENT EFFECT
 MAY BE PREDICTABLE**

Guardian Unlimited - 01/14/03

Scientists at the Institute of Cancer Research and the University of Surrey say it may be possible to predict how a tumour might respond to treatment before it has taken place. In a study funded by Cancer Research UK, the scientists found that tumours with higher cell densities were more likely to show a reduction in size following chemotherapy and radiotherapy.

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DRIVING HOME THE AWARENESS MESSAGE

(continued from page 1)

ladies got the message for their men. **“Take Care of Your Prostate Health”!**

The underlying theme of regular servicing and tests, to keep cars in good running, prompted the question to men: **“Do you know what’s under YOUR bonnet (hood)?”**

“Owners Manuals” were available to all, giving an insight into the need for regular PSA check-ups.

In 2002, the road show visited eight major cities in the U.K., from Glasgow to Southampton. Located in the biggest shopping malls, the attendance figures and media coverage are regarded as very successful.

More than 7,500 people have visited the stands so far. Southampton attracted the largest crowds - nearly 1,900 people in a single day! Major Ronald Ferguson, patron of PCaSO (and also a prostate cancer survivor and father of Sarah/“Fergie” - the Dutchess of York) also helped out on the day.

So far the Road Show has attracted coverage from more than 60 regional and 5 national newspapers, with an estimated readership of more than 15 million.

Other notable successes of cPc have been a petition to Downing Street (home of the British Prime Minister) delivered in 2000 by Major Ronald Ferguson, assisted by Dr. Charles “Snuffy” Myers .

This resulted in the launch of the first comprehensive “Prostate Cancer Programme” by the National Health Service, on behalf of the UK Government. However, like all governments, there is always the need to ensure that “actions speak louder than words”. Maintaining a constructive influence on their endeavours is most important, for as we all know, **“A Promise Has No Value, Until It Is Delivered”**.

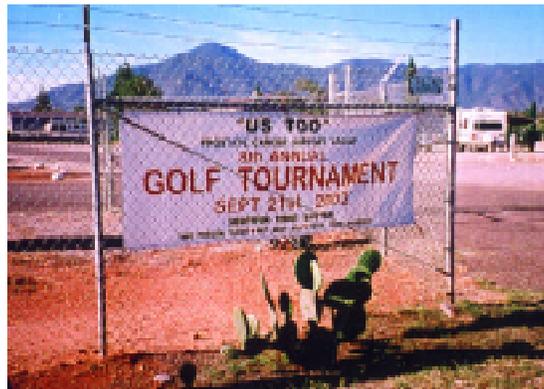
Unfortunately there are still too many

issues of ongoing neglect and failed commitments. So we are planning an even more ambitious, longer term campaign in the UK, by taking the cause right into the seat of government.

The Coalition along with all the leading prostate cancer organizations and eminent people in the field, have come together in a “Prostate Cancer Charter for Action”. We’ll let you know more about this exciting development as it progresses.

A LITTLE GOLF “DOWN MEXICO WAY” SIERRA VISTA Us Too! ONCE AGAIN HOSTS SUCCESSFUL GOLF TOURNAMENT

The Turquoise Valley Golf Club is located about three hundred yards from the US/Mexico Border. The Arizona course is wonderful but has a few “hazards” not typically found on the links. There are more than a



Cactus and Rattlesnakes and the nearby Mexico Border help to make the Sierra Vista Us Too! Golf Tournament unique.

few signs warning against extended trips into the rough where you are likely to meet some local residents - namely rattlesnakes!

But for the last few years the Sierra Vista *Us Too!* groups, one of the smaller but most active in Arizona, has hosted a Golf Tournament to raise awareness of Prostate Cancer in their corner of the world as well as funds for Prostate Cancer. The group once again made a donation to *Us Too!* from proceeds of the event. This year Sierra Vista contributed \$1,500.

Chapter Leader Willie Cotton indicates that the success of this annual event is a result of outstanding and widespread support from his community and the dedication of the men in his group.

Arizona *Us Too!* State Coordinator Rex Zeiger agrees - but also gives kudos to Willie and his leadership team. “This group is probably one of the smaller support groups in Arizona, but by far the most outstanding and energetic when it comes to supporting our *Us Too!* mission and delivering our message.” says Zeiger. “If we can continue to nourish this type of leadership and devotion, *Us Too!* can do nothing but succeed”.

CONGRATULATIONS Willie - and THANKS for your continued support to meeting the needs of men with prostate cancer, their families and men at risk!

NEWS YOU CAN USE

(continued from page 6)

RED CLOVER FLOWER MAY FIGHT PROSTATE CANCER
Daily Mail, London
Jan 11, 2003

Pills made from red clover flowers could be an effective weapon against prostate cancer, scientists say. The study appearing in the December issue of *Cancer Epidemiology Biomarkers and Prevention* (a peer reviewed journal published by the American Association for Cancer Research) found that Trinovin, a red clover supplement, causes early-stage prostate cancer cells to die in numbers five times greater than in an untreated control group.

The research, conducted at Monash University, Victoria, Australia, could explain why Asian men are far less likely to develop prostate tumours than Western men, despite having similar rates of pre-cancerous prostate cells. The Asian diet is rich in isoflavones, which are found in red clover blossoms. One previously reported study, for example, finds that 1.8 percent of men in China develop prostate cancer versus 53.4 percent of U.S. males. These findings led researchers to consider dietary differences between the cultures, particularly isoflavones.