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Us TOO[®]
PROSTATE CANCER
EDUCATION & SUPPORT

HOT SHEET

DECEMBER 2003

Us TOO 2003 HOLIDAY GREETINGS

This is the time of year we reflect on our lives and remember those we are thankful for. The Us TOO Board of Directors and staff are thankful for YOU, the prostate cancer survivors, family members, caregivers, chapter support group leaders and other volunteers, friends who are no longer with us and their families, physicians and other medical professionals, collaborators and all the others who have supported Us TOO during this last year.

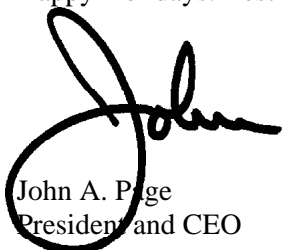
Because of your support and the donations and grants we have received, we were able to provide prostate cancer educational information and support to tens of thousands of patients – all without cost or consideration to ability to pay.

We are proud to report that during 2003, Us TOO has grown by more than two dozen new chapters this year alone. We have also made great strides at increasing our reach overseas through our prostate cancer awareness and early detection efforts worldwide – especially throughout Europe through our participation in the Europa Uomo prostate cancer coalition.

If Us TOO has helped you in any way or you approve of our accomplishments and ongoing efforts to improve the lives of those with prostate cancer, their families and men at risk, we ask that you consider making a simple end-of-year, tax-deductible gift to Us TOO. Your support is vital to the ongoing operation and mission of Us TOO. Your contributions will help us continue to touch the lives of so many men and their families who might not have otherwise received the information and support they need to deal with this disease. Although we have received a number of new grants this year, such funds are typically earmarked for specific program expenses and cannot be used for basic programs and operations. Your financial support is greatly appreciated and definitely makes a difference. A contribution form is included on the last page of this issue – but you can also contribute electronically through the links on the Us TOO website – www.ustoo.org. And remember, your contributions to Us TOO are tax deductible!

Thank you for your continued dedication and support.

Happy Holidays. Best regards to you and your family,



John A. Page
President and CEO



Us TOO PUBLICATIONS

In addition to the Hot Sheet, *Us TOO* also publishes a FREE e-mail based news service which provides updates on the latest prostate cancer related news. To subscribe or link to the archives simply visit the *Us TOO* Website: www.ustoo.org

News items contained in all *Us TOO* publications are obtained from various news sources and edited for inclusion. Where available, a point-of-contact is provided.

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PREVENTION AND TREATMENT OF PROSTATE CANCER

From the new book:
Updated Guidelines for Surviving Prostate Cancer
By Dr. E. Roy Berger
and James Lewis, Jr., PhD

Prevention

- Low Fat Diet - Diets low in both saturated and polyunsaturated fats are associated with a reduced risk of many forms of cancer, including prostate cancer. Food with monounsaturated fats are recommended including olive oil, almonds, filberts, macadamia nuts, pistachios, and cashews.
- Studies have also shown reduced risk of prostate cancer in men who have several servings of fish rich in the omega-3 fats per week including wild-caught salmon, tuna, sardines, herring, haddock, cod, halibut, and arctic char.
- Exercise one-half to one hour daily
- Antioxidants: There is a strong case for the role of antioxidants in the prevention of prostate cancer. In addition, antioxidants may slow the progression of existing prostate cancer.
 - o Selenium: 200 mcg per day. In a trial of 1,000 subjects that received selenium, prostate cancer deaths were decreased by 64 percent. If the men had a normal PSA when they entered the trial, prostate cancer deaths were reduced by 75 percent. Selenium at this dose causes no side effects.
 - o Vitamin E: In studies, men receiving vitamin E experienced a 40 percent drop in deaths due to prostate cancer.
 - o Lycopene: This is the red pigment in tomatoes. Men receiving lycopene before surgery had less extensive cancer than those receiving no treatment.
 - o Other sources of antioxidants: Green tea, chocolate, olives, red beet, many of the red to purple berries such as elderberries and blueberries, broccoli, kale, mustard greens and turnips.

A Sample Antioxidant Program

- Selenium-yeast 200 mcg a day
- Vitamin E (mixed tocopherols or gamma- and delta-enriched) 200 IU
- Lycopene (cooked tomatoes) 30 mg a day
- Vitamin C 500 mg (time-release form) twice a day
- Green tea 4-10 cups a day
- Cabbage family one or more servings each day
- Sulfur (in the form of taurine, N-acetylcysteine, or glutathione)
- Redpurple fruits and vegetables daily

Treatments:

- Radical prostatectomy: surgery to remove the entire prostate; types of radical prostatectomy are retropubic, perineal and laparoscopic.
- External beam radiation therapy: treatment with high-energy radiation given from a source located outside the body. The newest form is Intensity Modulated Radiation Therapy (IMRT), a sophisticated computer program that pinpoints the cancer for radiation treatment so that the surrounding healthy tissue of the bladder and rectum is spared.
- Seed implantation: treatment for prostate cancer in which radioactive seeds are inserted in the prostate gland to kill malignant cells.
- Combination of external beam radiation therapy and seed implantation.
- Cryosurgery: use of liquid nitrogen probes to freeze a particular portion of an organ to extremely low temperatures to kill the tissue prior to surgery used to destroy cancerous tissue; when used to treat prostate cancer, the cryoprobes are guided by transrectal ultrasound.
- Hormone therapy (HT): use of hormones, hormone analogs, and certain surgical techniques to treat disease (e.g., advanced prostate cancer), either on their own or in combination with other hormones, or in combination with other methods of treatment. Because prostate cancer is usually dependent on male hormones to grow, hormonal therapy can be an effective

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means of alleviating symptoms and retarding the development of the disease.

Where are we in the fight against prostate cancer:

- Randomized control trials will offer more information regarding prevention and treatment over the next 5-10 years.
- PIVOT Study: This study involves prostate cancer patients who undergo radical prostatectomy versus those who choose observation and ongoing treatment.

A CLUE TO RACIAL DIFFERENCES IN PROSTATE CANCER?
ACS NEWS TODAY

Doctors have long known that prostate cancer is more deadly in African American men and strikes them at younger ages than men of other races. What they don't know is why that's so.

A small pilot study published in *The Journal of Urology* (Vol. 170, No. 3: 990-993) may offer up a clue.

Researchers at the University of North Carolina, Chapel Hill, found higher levels of androgen receptor protein, a protein that helps stimulate prostate cancer, in tissue samples taken from black men compared to tissue samples taken from white men.

"To my knowledge, this is the first biological difference found between the two races that could explain the difference in aggressiveness of prostate cancer in African American men," said study co-author James Mohler, MD, who left North Carolina in May to become chair of the department of urologic oncology at Roswell Park Cancer Institute in Buffalo, New York.

But, he cautions, it's too early to say for sure that the mystery has been solved.

"This is a very, very preliminary finding — that needs to be confirmed before anybody attaches any significance to it," he said.

Just 50 Men Studied

Mohler and his colleagues examined prostate tissue samples from 25 African American men and 25 white men whose prostate had been removed after they were diagnosed with localized prostate cancer. The men were similar in age, and had similar cancer stages and degrees of spread.

The cancerous tissue taken from the black men had 81% more androgen receptor protein than cancerous tissue from the white men. Even the prostate tissue that didn't have cancer had 22% more androgen receptor protein in the African American men.

That means that the normal prostate tissue in this group of African American men was more stimulated to develop cancer, and the cancer that had already developed was more stimulated to grow, Mohler said.

He had not expected to find such a difference. "I was very surprised by these findings, so we're trying to confirm them in a very large study."

Until More is Known, Screening Important

Additional study is crucial, agreed Durado Brooks, MD, director of prostate and colorectal cancer at the American Cancer Society. "We certainly need to view this in a much larger group of men," he said.

Future studies must take into account other factors that could influence the development of prostate cancer, like obesity, he said.

Researchers should also compare men of different races who have the same levels of prostate specific antigen (PSA), he added. PSA is a marker of prostate cancer, and African American men with the disease tend to have higher levels of it than white men with prostate cancer. That trend held true in this pilot study, too. Could androgen receptor protein be linked to PSA levels, independent of race?

Until additional studies are completed, Mohler said, there is no way to translate his findings into practical advice for men concerned about prostate cancer.

"I am unsure what the clinical repercussions are of this finding," he said, "and it's certainly premature to even

speculate until they're confirmed."

What African American men can do is follow ACS recommendations for the early detection of prostate cancer, Mohler said. African American men are advised to talk with their doctor about prostate cancer screening at age 45, or even younger if they have a strong family history of the disease.

Brooks agreed. "At this point, this study doesn't give us enough information to alter current recommendations, but it does give interesting food for thought and a very interesting direction for future investigators."

THE BUFFALO NIAGARA PROSTATE CANCER CONSORTIUM

Continuing medical education initiatives can improve patient care, change physician practice behavior, and reduce costs. But to achieve these goals, CME providers need to look outside the traditional models. A case in point is the Buffalo Niagara Prostate Cancer Consortium in New York.

For men who have prostate cancer, there are multiple treatment options available. The problem is that the treatment recommendations patients receive vary considerably, often depending on the type of specialist they consult. So what can be done to address that problem?

When Michael R. Kuettel, MD, PhD, arrived at Roswell Park Cancer Institute, Buffalo, N.Y., as chief of radiation medicine, he developed the idea of a consortium/peer review concept that would incorporate community physicians, academic centers, and patient advocates. He sent out invitations to all physicians involved in the treatment of prostate cancer in the western New York area to attend a retreat to discuss prostate cancer detection, work-up, treatment, and follow-up. The result was the creation of the BNPCC, which brings together community urologists; radiation oncologists; patient advocates from Us TOO, an international patient support and advocacy group; and representatives from academic institutions, healthcare organizations, and insurance carriers. Patients can have their cases go through a peer-review process by these members.

(continued on page 4)

BUFFALO NIAGARA PCA CONSORTIUM

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By bringing together the various disciplines at one table, the general biases associated with each of the disciplines are overcome.

How It Works

After a patient sees his own urologist, he usually sees Kuettel for an additional consultation. The patient's information is then presented anonymously to the group during multidisciplinary consortium meetings that take place twice a month. Each session is certified for one hour of AMA Category 1 credit.

The consortium reviews the patient's case, then informs the patient of the proposed treatment recommendations by phone within 24 hours, and also notifies the patient's urologist and primary care physician. The patient, urologist, and primary care physician then discuss the treatment recommendations and decide which one to implement.

All consortium members receive minutes of the peer-review meetings. In addition, the consortium has developed relationships with experts around the country. The M.D. Anderson Cancer Center in Houston does peer reviews of medical physics and radiation oncology. Washington University Medical Center (Medical Physics) in St. Louis performs a post-plan digital data peer review (a process whereby treatment plans are sent electronically to other institutions for review), and the Radiation Therapy Oncology Group in Philadelphia reviews both clinical and physics data and serves as the operations and statistical center.

All pathology is re-reviewed by pathologists who are proficient in evaluating prostate morphology. If they make any changes to the original pathology report after examining a patient's biopsy, the pathology is reviewed again by a panel of three pathologists from Roswell Park Cancer Institute. The BNPCC sends a percentage of pathology specimens to be reviewed by other experts in the United States.

It Gets Results

As experts in outcome measurements advise, CME providers need to decide the

results they want before designing activities. The specialists who spearheaded the prostate cancer initiative did just that. Before developing their program, they decided there was a need to create a consortium to

- enhance prostate cancer screening and diagnosis;
- standardize prostate cancer treatment and recommendations;
- follow National Comprehensive Cancer Network (NCCN) guidelines for patient work-up, treatment recommendations, follow-up, and testing;
- offer eligible patients the choice of entering clinical trials;
- track and publish patient outcomes; and
- work with local insurance carriers to improve quality, while containing costs.

The BNPCC also developed a system for measuring the outcomes and benefits. The group tracks more than 250 variables for each patient and has reviewed more than 600 patient cases since January 2001. The consortium has noted immediate changes in physician practice, including the following:

Approximately 70 percent of all eligible patients have been entered into NIH/NCI-sponsored clinical trials.

The use of computed tomography and bone scans for low-risk patients, and the overall use of hormone therapy, were reduced as follows (figures are from the first nine months of operation):

- 73 percent reduction in the use of unnecessary CTs,
- 93 percent reduction in the use of unnecessary bone scans,
- 39 percent reduction in use of hormone therapy.

Ten percent of the reviewed pathology required reclassification of the Gleason score, used to measure the aggressiveness of the cancer, resulting in a change of treatment recommendations. Another six

patients had their prostate cancer diagnosis reversed — they were found not to have prostate cancer at all.

Favorable economics, including higher reimbursement rates and rising referrals from non-consortium sources.

Why It Works

This approach has been successful for several reasons. Patients can seek out the BNPCC on their own, or they can be referred by their urologist or primary care physician. There is no charge to the patient — insurance companies pay for the cost of the consult. This process also allows patients and their physicians the opportunity to discuss treatment recommendations together so the patient can make an informed treatment decision.

From the physician's standpoint, previously existing biases are eliminated when they agree to follow the NCCN guidelines for patient work-up, treatment recommendations, follow-up, and testing. The participating physicians did not perceive this consortium as a threat because patients were always referred back to their own physician. That "trust factor" is what has allowed this consortium to attract new members in an ever-expanding geographical region. The AMA Category 1 credit was just an added incentive to encourage participation.

Insurance companies also see the added value in a process that entails following guidelines and tracking outcomes. And in exchange, physicians receive higher reimbursement rates.

It Can Work for You, Too

This consortium model, which has worked so well for members of the BNPCC, can be applied to other areas of medicine to enhance screening and diagnosis, standardize treatment options and recommendations, and track patient outcomes. It would be most easily applied to those disciplines that have a set of national standards and guidelines for patient care in a particular clinical area or disease site. This tends to eliminate differences of opinion.

In this era of managed care, this is one way healthcare providers, patients, and payers can work collaboratively to improve the quality of care while containing costs.

US TOO ELECTS NEW DIRECTORS

The Us TOO Board Membership Committee had a difficult job on its hands in reviewing nearly two-dozen candidates to serve on the Us TOO International Board of Directors.

Three incumbent candidates were eligible and re-elected to serve another three-year term (January 1, 2004 – December 31, 2006). Those Directors are Russ Gould, Jo Ann Hardy and Joe Piper. One other Director, Dr. Ronald Fabrick, was not eligible for re-election after serving ten years as a Director. In recognition of his contributions to the organization, Ron has been elected as a Director Emeritus.

Three newly elected Directors will also be joining the Board. Robert Fidoten, PhD and Tom Hiatt will serve full three year terms (Jan 1, 2004 – Dec 31, 2006). Sharon Sequella, RN will be filling an unexpired term starting immediately through Dec. 31, 2004.

Dr. Fidoten has been a member of the Pittsburgh UPMC Us TOO chapter for nearly six years and as Vice Chair for the past two years. He became involved with Us TOO weeks after his diagnosis to seek information about treatment options, to listen to patient commentary, and hear medical experts present valuable information. That experience led him to become an active participant and try to help others facing a similar circumstance and dilemma. He retired from industry 14 years ago, and joined the faculty in the Department of Communication, at Slippery Rock University where he is an Associate Professor, teaching courses such as The Communication Age and Issues in Communication Technology. He also manages the department's internship program. Bob's specialized interests include communication as it is linked to advertising and marketing, public relations, and office technologies. Recent publications include the chapter on Office Technologies in the bi-annual work *Communication Technology Update* (Focal Press). During his business career (25 years at PPG Industries) he had responsibility for many administrative areas including Information Systems, technical writing, human resources, accounting, purchasing, public relations and other functions. He holds a Ph.D. in

Information Science from the University of Pittsburgh, and degrees from New York University and Pratt Institute.

Tom Hiatt is a PCa survivor and retired vice president of Eastman Kodak Co. with chemical engineering, legal and business education and experience. He has served over ten years on hospital boards (as chair of quality committees and vice chair of the board). In addition, he has chaired and served on numerous other not-for-profit boards and board committees. Currently, he chairs an offshore captive insurance company. Tom brings extensive business experience, understanding of public policy, lay knowledge of the healthcare world and an insight into not-for-profit organizations to the Us TOO Board.

Sharon Saquella is a Registered Nurse from Maryland who has worked with PCa patients since 1994. She started the Anne Arundel Medical Center PCa Support Group in January of 1995 which continues today. Though she no longer works for that hospital, she continues to volunteer her time coordinating the Group. In the almost 10 years since the Group was formed, she has missed only one meeting. She also resurrected the Georgetown University Hospital PCa Support Group and continued to nurture it for about 9 months after leaving employment there, until a new nurse was hired. Her expertise in the area of Prostate Cancer comes from reading journal articles, attending classes and seminars, as well as hands-on work with men from biopsy through all phases of treatment. Sharon has coordinated free PCa screenings both at Anne Arundel Medical Center and at Georgetown University Hospital. While at Georgetown, over 700 men were screened for prostate cancer during a 6 week period. For 8 of the last 10 years she has participated in the local American Cancer Society's Relay For Life along with men from her Support Group. Even though goals at the hospital have changed and PCa screenings are no longer conducted, the members of her Support Group still place PCa awareness information at many local churches and businesses in the area. She hopes to help push for greater nationwide acceptance of routine early detection PCa screening by Family Practice physician's, broader partnering with local hospitals for PCa Awareness Seminars and an increase in PCa Support Groups EVERYWHERE.

LOW-CARB DIET KEEPS PROSTATE CANCER AT BAY?

A low-carbohydrate diet may be more effective than reducing fat intake for prevention of prostate cancer, suggests a laboratory study by researchers in the US. Previous studies have suggested a link between the amount of saturated fat in the diet and the risk of progression to advanced prostate cancer.

But Ada Elgavish and colleagues from the University of Alabama at Birmingham found that carbohydrate intake may be more significant for men wishing to delay progression to advanced prostate cancer.

"In the low-fat versus low-carbohydrate debate, we're finding that under conditions in which diet is provided ad libitum, a diet with fewer carbohydrates may be more effective in preventing progression to advanced, lethal prostate cancer than a diet with low fat content," said Dr Elgavish, lead author of the study, presenting the research at this week's AACR meeting, Frontiers in Cancer Prevention Research.

"However, the results of this study are preliminary. Men should talk to their doctors before changing their diets," she added.

The investigators compared the relative risk of developing advanced prostate cancer with a low-carbohydrate or a low-fat diet provided ad libitum (as much as wished), beginning before tumours developed and continuing until middle age.

The study was carried out in TRAMP mice, biologically engineered to develop prostate cancer after puberty, developed by Dr Greenberg and associates at Baylor College of Medicine in Houston. Two groups of TRAMP mice were fed diets containing the same amount of calories, with either 10 per cent or 45 per cent fat (mostly lard). Carbohydrates, mostly corn starch and sucrose, replaced fat in the low-fat diet. Researchers measured food intake and body weight throughout the 23-week study.

After the onset of middle age, mice fed the 45 per cent fat diet had a consistently higher body weight due to higher body

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LOW CARB DIET

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fat. When the study ended, 95 per cent of the mice fed the 45 per cent fat diet had survived, compared with only 68.2 per cent of those fed with the 10 per cent fat diet.

In addition, the percentage of mice with advanced prostate cancer in the 45 per cent fat group was one-third of that in the group fed the 10 per cent fat diet, reported the researcher.

If the results are confirmed in humans, they present significant turnaround in thinking on prostate cancer. Last year researchers from the Fred Hutchinson Cancer Research Center reported finding decreased risk for late-stage prostate cancer in men on low-fat and moderate calcium diets. Numerous other studies support a low-fat, high fibre diet, advised by the Pritikin programme, to keep prostate cancer at bay. The new study suggests more research is needed to clarify advice for prostate cancer patients.

DOSE OF PTEN PROTEIN FOUND TO DETERMINE PROGRESSION OF PCA

In patients with prostate cancer, one change that can be seen at the molecular level is the loss of the PTEN tumor suppressor gene, a gene responsible for restricting cell proliferation. One or both copies of the PTEN gene are found to have been lost in 70 percent of prostate cancer patients at the time of diagnosis. It has generally been believed that one remaining copy would still protect against tumor progression to advanced metastatic cancer.

But now, for the first time, scientists at Memorial Sloan-Kettering Cancer Center have established mouse models for prostate cancer that have varying "doses" or amounts of Pten protein produced from the remaining gene. Their results show that the activity of the single Pten gene does not necessarily protect against prostate cancer. Instead, the dose determines whether the tumor will become either an aggressive cancer or take a slow path towards microscopic features of growth, but remain benign. This new understanding of the natural history of the disease could allow researchers to develop

novel clinical strategies to diagnose, treat, and possibly prevent prostate cancer. This article will appear both as HTML and in print in the December 23, 2003 issue of the new, open access journal published by the Public Library of Science. It appears in PDF form online as a pre-issue publication on October 27, 2003 at www.plosbiology.org.

"We have shown that prostate cancer development is not just affected by mutation and loss of the PTEN gene but that its progression is dose-dependent on the PTEN protein, which we have measured for the first time," said Pier Paolo Pandolfi, M.D., Ph.D., Head of the Molecular and Developmental Biology Laboratory at Memorial Sloan-Kettering and the study's senior author. "Two men, each with one PTEN gene left, could have totally different disease outcomes depending on the actual dose of PTEN protein coming from that gene."

Earlier studies by Drs. Pier Paolo Pandolfi and Antonio Di Cristofano had demonstrated that loss of the Pten tumor suppressor gene in mice is responsible for a variety of malignant tumors. In humans, these were shown to include melanoma and cancers of the breast, prostate, and brain. Although the loss of just one Pten gene is enough to affect cell signaling, the loss has only been associated with slow-growing, mild lesions in the mouse prostate, comparable to early stages of the human disease. Therefore, many scientists in the field assumed that one copy of the Pten gene was still sufficient to prevent the progression to malignant cancer, in agreement with the classic definition of tumor suppressor genes.

To test this assumption, two sets of mouse models were generated. In one, the Pten gene was engineered to be removed completely from the prostate only (whole body deletion cannot be studied since it causes a lethal defect in the embryo). In the second model, mice were engineered to have only one half-active copy of the Pten gene left (roughly 30 percent protein level). In stark contrast to mice with one gene copy, the mice with no Pten gene showed aggressive, invasive prostate cancer that developed in just a short period, perhaps suggesting that the major danger in having only one copy of the Pten gene (50 percent of the normal protein level) would be to lose it (and go to zero percent).

However, the mice with one half-active gene also developed prostate tumors while those with the fully active copy did not. This refuted the notion that only complete loss of the Pten gene can cause prostate cancer and instead suggests that prostate tumor development correlates closely with the actual Pten protein level.

"We analyzed the mice at a time when they should have been healthy but instead found massive prostate enlargement and cancer," explained Lloyd Trotman, Ph.D., a member of Dr. Pandolfi's Molecular and Developmental Biology Laboratory at Memorial Sloan-Kettering and a first author of the study along with Masaru Niki M.D., Ph.D. "Most importantly, this showed that dropping the Pten protein dose slightly below the 50 percent level has dramatic consequences for disease progression in just a short period."

"This study shows the consequences of serial reductions in a critical gene on prostate cancer development and progression," said Dr. Howard Scher, Chief of the Genitourinary Oncology Service at Memorial Sloan-Kettering. "It shifts the focus from targets of the PTEN gene to the PTEN protein itself. Restoring the function of the gene to stabilize the PTEN level may be clinically beneficial. These findings also show that to understand an individual's prognosis and to optimize the therapeutic approach to an individual patient's tumor, it will be necessary to determine the absolute level of key signaling proteins, and not simply whether the protein is present or absent. Developing these methods is an area of active investigation."

GINGER CURBS TUMOR GROWTH IN MICE

Common spices and herbs contain ingredients that may prevent the formation of major tumors, such as intestinal and prostate cancers, according to research presented at the American Association for Cancer Research's Second Annual International Conference on Frontiers in Cancer Prevention Research. In particular, a recent study is showing notable cancer prevention potential for the use of ginger extract.

"These studies are extremely important and must be continued to help us

understand better ways of preventing cancer which do not require extraordinary measures," said Raymond DuBois, MD, PhD, of Vanderbilt University, and program chairman of the meeting. "We're hoping that, armed with this information, individuals will become more proactive about their health on a daily basis, in consultation with their doctors."

The ginger family has been used for thousands of years in the treatment and prevention of various illnesses, and has been hypothesized to have anticancer and therapeutic properties. Ann M. Bode, PhD and Zigang Dong, PhD, researchers at the Hormel Institute, University of Minnesota, recently determined that ginger compounds may be effective in preventing and potentially treating colorectal cancer. The theory was tested on human colorectal carcinoma cells (HCT116) in athymic nude mice, that are incapable of rejecting implanted human tumor cells. Prior to tumor cell injection, mice were fed either 500 mcg of [6]-gingerol (the source of ginger's spiciness) or .001% ethanol in water (control) three times per week for 2 weeks. Following injection, the mice were fed the same ratios. Mice were weighed and tumors were measured by calipers twice each week.

Overall results showed that tumor development was significantly slower in those mice fed [6]-gingerol. The first measurable tumors were observed in both groups on day 15 after injection. However, the control group experienced 13 measurable tumors whereas the [6]-gingerol group reported only 4 measurable tumors. All mice in the control group developed tumors by day 28, as compared to day 38 for the [6]-gingerol group. Results showed that mice fed [6]-gingerol survived significantly longer than those receiving the control, implying that the tumors grew much slower in the first group. By day 49, all control mice contained tumors at least 1 cubic centimeter in size. By comparison, 11 mice in the [6]-gingerol group still had not developed tumors of that size.

Preliminary results also suggest that many of the tumors in the control group were invasive into the abdominal cavity, whereas the [6]-gingerol group appeared to be less invasive.

"These results strongly suggest that our hypothesis on the value of ginger is correct," said Bode, lead author of the

study. "As we continue to study the spice in other tumor areas, we hope it will translate into significant anticancer properties for humans."

COMBINATION THALOMID REGIMENS IN REFRACTORY SOLID TUMORS

Interim data from studies assessing thalidomide in combination regimens for certain solid tumors were presented at the annual Chemotherapy Foundation Symposium XXI in New York.

Dr. Paul Mathew from M.D. Anderson Cancer Center updated findings of data presented at the European Cancer Conference (ECCO) in Copenhagen, Denmark. The trial, headed by Dr. Danai Daliani, investigated THALOMID in combination with chemotherapy (paclitaxel and estramustine) in androgen-independent prostate carcinoma. Patients in this Phase I/II study had failed previous treatments and had no options remaining. The study results demonstrate that 76% of evaluable patients had a prostate-specific response in second line therapy. Eighteen of 33 patients (55%) who were evaluable for response achieved a 50-79% decline in PSA levels, and seven patients (21%) had an 80% or greater decline in their PSA levels. "These preliminary results of the clinical study on patients who had exhausted all other treatment clearly justify further clinical investigation of this combination therapy," commented Sol J. Barer, Ph.D., President and COO of Celgene Corporation. Phase II studies are now underway to evaluate this combination further.

Study Details:
THALOMID in combination with chemotherapy in androgen-independent prostate carcinoma results: 30 patients [median age 66 (range, 49-80); median Zubrod performance status 1 (range, 0-2)] were entered (10 in the phase I and 20 in the phase II study) and received a median number of 3 (range, 1-8) cycles. Patients had 1 (n=20) or 2 (n=10) prior chemotherapy regimens. Twenty-nine pts are evaluable for toxicity (1 pt developed DVT prior to Rx initiation and did not receive any therapy); 25 are evaluable for response [2 pts were taken off study before 2 cycles (1 refused Rx

after 1 week, 1 developed pneumonia after cycle 1) and 4 pts are too early]. During cycle 1 of the phase I study: at 200 mg/d THALOMID, 0 of 3 pts showed grade 3/4 toxicity; at 400 mg/d T, 1 of 4 patients experienced grade 3 neutropenia (<7 days duration) and 1 of 4 patients had grade 3 edema (relieved promptly by diuretics); at 600 mg/d T, 0 of 3 pts had grade 3/4 toxicity. Of the 22 total patients assigned to the 600mg/d dose level of THALOMID (in both phases of the study), 10 tolerated only 400 mg/day and 1 patient tolerated 200 mg/d. All dose reductions of THALOMID were due to somnolence/fatigue (grade 1-2). Peripheral neuropathy was limited to grade 1. Four of 29 pts developed grade 3/4 DVT (requiring Rx discontinuation in 2 pts), 2 additional patients discontinued Rx due to intercurrent infection, and 1 patient died from sepsis. To date, 18 of 25 (72%, 95% confidence interval 51-88%) evaluable for response patients achieved a sustained (more than 6 weeks duration) > 50% post-therapy decline in PSA and 3 of 25 (12%) patients showed sustained > 80% post-therapy PSA decline. Measurable disease response and improvement in bone pain were seen.

STATINS MAY IMPROVE RESPONSES TO RADIATION THERAPY IN LOCALIZED PCA

According to results presented at the 45th annual meeting of the American Society for Therapeutic Radiation and Oncology, statins, which are agents used to lower lipid levels, may improve responses to radiation therapy in patients with localized prostate cancer.

Prostate cancer is the second leading cause of cancer deaths in American men, with 1 out of every 6 men being diagnosed within their lifetime. Localized prostate cancer refers to cancer that has not spread from its site of origin. Patients with localized prostate cancer may be stratified into low, intermediate and high-risk groups, depending upon specific features of their cancer. The risk groups indicate the probability of cancer recurrence and/or spread and are becoming important in deciding upon treatment decisions. Surgery, radiation therapy, watchful waiting and/or hormone therapy are all

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STATINS

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accepted treatment approaches for localized prostate cancer, with no definitive approach proving clear superiority to another at present. The prostate is a walnut-sized male sex gland that is responsible for producing a component of semen. Screening for prostate cancer is typically offered to men beginning at the age of 50 years, which includes prostate specific antigen (PSA) testing! . Prostate specific antigens are proteins normally shed by the prostate; however, in the presence of cancer, or progression of cancer, levels in the blood are elevated. Therefore, PSA levels are measured during and following treatment as one way to determine response to therapy. Researchers continue in their quest to improve upon available therapeutic modalities for the treatment of prostate cancer.

Researchers from the Memorial Sloan-Kettering Cancer Center (MSKCC) recently conducted a clinical study evaluating the use of statins in men with localized prostate cancer. The study included 905 men, 153 of whom were taking statins at the time of prostate cancer diagnosis. All patients received similar radiation regimens for treatment of their cancer. Analysis included sub-grouping of patients into low, intermediate and high-risk patients, depending upon PSA levels and Gleason scores (aggressiveness of cancer). The most benefit from statins was achieved in the intermediate and high-risk patients, with an 18% reduction in cancer

recurrences based on PSA levels at approximately 5 years following therapy, compared to those not taking statins. Upon analysis of several variables among patients, those that were associated with improved PSA levels were the following: statin use, radiation dose, Gleason score, high levels of cholesterol, PSA levels prior to treatment and extent of cancer.

The researchers concluded that if these results can be reproduced in future larger trials, the use of statins may provide considerable anti-cancer benefit when combined with radiation for the treatment of localized PCa, particularly since they are associated with few side effects

KI-67 A STRONG PREDICTOR OF OUTCOME FOR PCA PATIENTS

The largest known biomarker study for prostate cancer patients treated with radiation therapy shows that the presence Ki-67 may be a significant predictor of patient outcome for men with prostate cancer treated with both radiation and hormones. The study was sponsored by the Radiation Therapy Oncology Group and was presented by Alan Pollack, M.D., Ph.D., chairman of radiation oncology at Fox Chase Cancer Center, at the 45th annual meeting of the American Society for Therapeutic Radiology and Oncology (ASTRO) in Salt Lake City.

The Ki-67 biomarker is a proliferation

antigen that is detected by a process called immunohistochemical staining. When a tumor cell tests positive for Ki-67, the tumor is actively growing.

Prostate cancers typically have very low percentages of growing cells and they grow slowly. Pollack and others have previously shown in smaller studies that the greater the proportion of prostate tumor cells with Ki-67, the more aggressive the cancer. Prior studies involved small patient numbers and did not definitively establish the usefulness of the Ki-67 biomarker.

“Our study conclusively shows that Ki-67 was the most significant determinant of distant metastasis and death in PCa patients,” explained Pollack. “The relationship of Ki-67 to patient outcome is a continuous function, wherein the higher the percent of Ki-67, the greater the risk of an adverse result. In addition, Ki-67, along with PSA, Gleason score and stage, appears to be valuable in determining whether high-risk patients may be spared long-term androgen deprivation.”

Pollack says that a consistent threshold for the application of Ki-67 on a routine basis has not been previously established. In this study, when greater than 7.1% of the tumor cells stained for Ki-67, there was a significantly increased risk of distant metastasis and death due to PCa. Furthermore, Pollack adds, Ki-67 should be very useful in stratifying patients in future clinical trials.

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