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Us TOO® PROSTATE CANCER EDUCATION & SUPPORT

HOTSHEET

July 2007

HIGHLIGHTS FROM THE 2007 ANNUAL MEETINGS OF THE AMERICAN UROLOGICAL ASSOCIATION (AUA) AND AMERICAN SOCIETY OF CLINICAL ONCOLOGY (ASCO)

AUA UPDATES PROSTATE CANCER TREATMENT GUIDELINES

New guidelines for treating localized prostate cancer emphasize honest communication with the patient regarding his risk, treatment options and potential outcomes, experts stressed at the American Urological Association (AUA) 2007 Annual Meeting.

The focus on risk stratification is one of the most important ways in which these guidelines differ from the first ones released in 1995, said Ian Thompson, MD, chair of the AUA Prostate Cancer Guideline Panel. "Categorization by risk helps determine the patient's risk of cancer recurrence and how effective treatment will be."

Other new recommendations include that patients are encouraged to enroll in clinical trials and that hormone therapy be avoided unless the patient has symptoms or a short life expectancy or if the tumor is extensive or poorly differentiated.

Much has changed in the 12 years since the initial guidelines were devel-

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DENDREON ANNOUNCES FDA CONFIRMS DATA REQUIRED FOR PROVENGE® LICENSURE

Dendreon Corporation announced that the Company received confirmation that the U.S. Food and Drug Administration (FDA) will accept either a positive interim or final analysis of survival from its ongoing IMPACT study to supplement the Biologics License Application (BLA) for Provenge (sipuleucel-T). This information was obtained in a recent follow up meeting with the FDA to discuss the additional clinical data required to support the licensure of Preovenge requested by the FDA in the Complete Response Letter the Company received on May 8, 2007.

"The FDA indicated that either a positive interim or final analysis of survival, as described in the IMPACT Special Protocol Assessment Agreement, would address their request for the submission of additional clinical data in support of our efficacy claim," said Mitchell H. Gold, MD, president and chief executive officer of Dendreon. "We anticipate completing enrollment in the IMPACT study this year and anticipate interim survival results in 2008. We are committed to making Provenge available as rapidly as possible to help the many men with late-stage prostate cancer who currently have few appealing treatment options."

Management presented an operational update and financial guidance at the Bank of America 2007 Health Care Conference at The Four Seasons, Las Vegas on May 31st. The presentation was audio webcast live and is available for replay from Dendreon's website, <www.dendreon.com>. The replay of the presentation will be available for 90 days.

The Company anticipates net cash utilized for operating and capital expenditures for 2007 of approximately $95 million. The Company anticipates spending levels to decrease substantially in 2008 to approximately $55 million because it has already incurred many of the third-party costs neces-

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CONSIDER SOURCE OF LOCALIZED PROSTATE CANCER RECOMMENDATIONS

Localized prostate cancer needs a balanced view of treatment options from both urologists and radiologists, researchers said here.

The majority of younger Medicare-age patients who saw only a urologist before deciding on treatment opted for radical prostatectomy, said urologist Thomas L. Jang, MD, of Memorial Sloan-Kettering Cancer Center in New York, and radiation oncology colleagues, at the American Society of Clinical Oncology meeting.

Older men overwhelmingly chose primary androgen therapy or watchful waiting, the investigators found in a review of data on 85,000 men in the National Cancer Institute's Medicare-linked Surveillance, Epidemiology and End Results (SEER) database. In contrast, patients of all ages favored radiation therapy if they had pretreatment visits with a urologist and a radiation oncologist.

Although many men have a radical prostatectomy without seeing a radiation oncologist, "urologists exercise discretion," said Dr. Jang. "They rarely perform radical prostatectomy on men who have a limited life expectancy based on advanced age." Noting that most patients opt for radiation therapy if they have a radiation oncology consult, he emphasized that "it is essential that men have access to balanced information."

None of the principal treatment options for prostate cancer has clearly demonstrated superiority over the others, Dr. Jang noted. As a result, most patients decide on treatment on the basis of physician recommendations and perceived tolerance for different types of adverse effects. Within that decision-making environment, prostate cancer patients should get an unbiased, balanced perspective on treatment options.

The SEER data included men who had been diagnosed from 1994 through 2002, and all were 65 years or older when diagnosed. Half the men consulted only a urologist before making a treatment decision. Another 44% saw a urologist and a radiation oncologist, 3% consulted a urologist and medical oncologist, and 3% received input from all three specialties.

Treatment choices varied by patient age. Most men ages 65 to 69 opted for prostatectomy (44%) or radiation therapy (39%). The preference shifted toward radiation oncology (52%) for men ages 70 to 74, and only 6% that age had prostatectomies. Most ages 80 and older opted for primary androgen deprivation therapy or watchful waiting, and only 1% had surgery.

Of 42,309 men who consulted only a urologist, 34% had a prostatectomy, 27% chose androgen deprivation, and 34% opted for watchful waiting, leaving only 6% who chose radiation therapy. Choices varied distinctly by age. Dr. Jang reported than 70% of men ages 65 to 69 had radical prostatectomy if the consulted only a urologist. The proportion opting for surgery decreased to 45% of those ages 70 to 74, 10% of those 75 to 79, and 1% of those 80 and older. The number opting for androgen deprivation or watchful waiting increased with age. No more than 8% of any age group chose radiation therapy.

The picture changed dramatically when patients consulted both a urologist and a radiation therapist. Of the 37,540 who saw physicians in both specialties, 83% chose radiation. Among all age groups, the proportion of patients choosing radiation therapy ranged from 79% to 87%. Prostatectomy was favored by 15% of men ages 65 to 69 years but by no more than 7% of men in the older age groups. Echoing Dr. Jang's conclusions, Bend, Ore., oncologist Archie Bleyer, MD, who moderated the presentation, said "the results are of concern and affect more men than not."

Dr. Jang had no relevant disclosures. Dr. Bleyer disclosed that he has received honoraria from Enzon Pharmaceuticals. The study was funded, in part, by grants from the National Institutes of Health and the National Cancer Institute.

MedPage Today, 4 June 2007

PROVENGE UPDATE

(Continued from page 1)

sary to prepare for the commercialization of Provenge. These costs include items such as third party clinical trial costs, inventory purchases, capital expenditures related to New Jersey manufacturing and other outside infrastructure costs.

Dendreon's BLA was submitted under a Fast Track designation and was accepted for filing by FDA in January 2007. The BLA was based primarily on a multi-center, randomized, double-blind, placebo-controlled Phase 3 study (D9901) that showed that the group of men with asymptomatic, metastatic, androgen-independent prostate cancer (AIPC) who received Provenge had a median survival time 4.5 months longer than the median survival seen in the group that had been assigned to receive placebo. For the men receiving Provenge, there was a 41 percent overall reduction in the risk of death (p-value = 0.010; HR = 1.7). In addition, 34 percent of those receiving Provenge were alive 36 months after treatment compared to 11 percent of patients that were randomized to receive placebo.

Treatment with Provenge in these trials was generally well tolerated. The majority of side effects were mild, including infusion-related fever and chills that were usually of low grade and typically lasted for one to two days following infusion.

IMPACT (**IM**munotherapy for **P**rostate **A**deno**C**arcinoma **T**reatment), also known as D9902B, is an ongoing Phase 3 clinical trial measuring overall survival in men with AIPC receiving Provenge vs. those receiving placebo.

In order to be eligible to participate in the IMPACT study, a person must meet certain criteria, such as having cancer that has spread outside the prostate (metastatic) or cancer that has worsened while on hormone therapy among other additional criteria. Interested patients should contact the Dendreon Prostate Cancer Information line at 866-4PROSTATE (866-477-6782).

Dendreon Corporation
31 May 31 2007

DENDREON SUED AFTER PROVENGE'S OK PUT OFF

A shareholder lawsuit has been filed against Seattle-based Dendreon, alleging the company misrepresented its clinical trial results and didn't provide clear information about when the U.S. Food and Drug Administration (FDA) would rule on its prostate cancer drug.

The suit claims shareholders "suffered substantial losses" when the FDA on May 8 decided to delay consideration of the drug, Provenge, until further studies are completed. Dendreon "failed to disclose" that the FDA could make a ruling on Provenge before May 15, according to the suit, which seeks class-action status. A Dendreon spokeswoman declined comment Friday on the suit, which was filed in federal court in Seattle by Oklahoma-based law firm Federman & Sherwood.

The suit also claims that Dendreon misrepresented its late-stage clinical studies of Provenge, specifically regarding their statistical significance and whether they proved the drug's effectiveness. In addition, the suit alleges that Dendreon CEO Mitchell Gold's sale of 202,000 shares on April 2 shows that he was aware the FDA might not approve Provenge. The sale netted Gold about $2.7 million. It was Gold's first sale of Dendreon stock during his six years at the company, and represented about 20 percent of his stock and option holdings.

The suit could be one of many filed as a result of Dendreon's stock nose-dive, said David Miller, president of Seattle-based Biotech Stock Research. Shares of the company were trading as high as $23.53 in early April after an advisory panel to the FDA endorsed the drug on April 29. But they plunged 65 percent — wiping out almost $1 billion in market value — after the FDA decided to delay the drug. Dendreon's stock closed at $6.53 on May 25th.

Over the last 90 days, the company's trading volume reached as high as 132 million shares a day. The company has an average daily trading volume of about 29 million shares, with about 81 million shares outstanding.

<http://seattletimes.nwsource.com/html/businesstechnology/2003722793_ dendreon26.html>

31 May 2007

^{223}RADIUM HELPS IN HORMONE-REFRACTORY PROSTATE CANCER

^{223}Radium, an investigational bone-seeking radioisotope, appeared to slow progression of skeletal metastases in hormone-refractory prostate cancer, researchers reported here.

In a phase II study of 64 men, bone-alkaline phosphatase -- a marker for progression of hormone-refractory prostate cancer -- decreased by a median of 65.6% after four radium-223 treatments, said Øyvind S. Bruland, MD, PhD, of the Norwegian Radium Hospital Trust in Oslo, Norway. This compared with a 9.3% increase in a placebo group (P<0.0001). Dr. Bruland reported the findings during a poster discussion at the American Society of Clinical Oncology meeting and the results were published simultaneously online by *The Lancet Oncology*.

Dr. Bruland and colleagues enrolled 64 men at 11 centers in Sweden, Norway, and England from February 11, 2004 through May 3, 2005. Thirty-three men were randomized to external beam radiation plus four radium-223 injections and 31 to external beam radiation and saline injections. Treatment lasted 12 weeks with injections at baseline and again at four-week intervals for a total of four injections. From baseline to four weeks after the final radium-223 injection there was a median decrease of 23.8% in PSA versus a 44.9% increase in PSA in the placebo arm (P = 0.003), they said.

Moreover, the median time to PSA progression was 26 weeks in the radium arm vs. eight weeks for placebo (P = 0.048, log rank). Median overall survival was 65.3 weeks in the radium group versus 46.4 weeks in the placebo arm (P = 0.066, log rank). After 18 months of follow-up, 15 of the radium patients survived compared with eight assigned placebo, they wrote.

Dr. Bruland said the four injections of ^{223}radium were so well tolerated that his group is considering a study using a six-injection protocol. Unlike other radioisotopes, ^{223}radium had little to no

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UPDATED AUA TREATMENT GUIDELINES

(continued from page 1)

oped, Dr. Thompson explained. More than 28,000 scientific articles have been published in peer-reviewed medical journals between October 1995 and October 2005.

Thanks to this research and to the advent of widespread prostate-specific antigen (PSA) screening in the late 1980s, prostate cancer mortality dropped from 34,475 in 1995 to an estimated 30,350 in 2005. Clinicians are more likely today to diagnose the disease in its early stages and to offer patients a wider range of therapies than in years past or to not offer therapy at all if that is what the patient chooses. Today's patients are better informed and more likely to participate in their treatment decisions than in earlier times. Mortality, however, from prostate cancer, while lower than it was a decade ago, is still high, and will probably remain high as the population ages. The panel tried to take all of this into account when they formulated the new guidelines.

The guidelines, which appear in the June issue of the *Journal of Urology* (Vol. 177, pp. 2106-31, 2007), state that patients at every risk level should be informed of the findings of recent, high-quality clinical trials. They define low-risk patients as men with a prostate-specific antigen level of 10 ng/mL or less, a Gleason score of 6 or less, and a clinical stage of T1c or T2a, with no regional lymph node or distant metastases.

According to the guidelines, low-risk patients considering external beam radiation should be told that the evidence to date shows that higher doses of radiation may reduce the risk for PSA recurrence and that radical prostatectomy may lower the risk for cancer recurrence and improve survival compared with watchful waiting.

Ultimately, however, the choice belongs to the patient. "There is probably no one best treatment at this tumor stage — two patients with similar tumors may make very different decisions," warned Dr. Thompson, who is professor of Urology at the University of Texas Health Sciences Center in San Antonio, TX.

In part, this is because there is still no consensus on the optimal treatment for patients with localized prostate cancer, despite the enormous strides in diagnosis and treatment modalities. Solid evidence does support some recommendations — for example, that surgery prolongs survival, Dr. Thompson said. But good data have been hard to develop on other aspects of treatment, largely over problems finding enough patients to participate in clinical trials. "Some studies have been closed due to lack of randomization. In the absence of randomized clinical trials, some questions simply cannot be answered."

Several panel members affirmed the value of PSA testing. "Most of us believe there has been a difference made" since clinicians began measuring PSA, said panel co-chair Brantley Thrasher, MD, professor and chair of Urology at the University of Kansas Medical Center, Kansas City. PSA screening has allowed a staged migration to occur, added panel member Anthony V. D'Amico, MD, chief of Genitourinary Radiation Oncology, Dana-Farber Cancer Center in Boston, Massachusetts. "Men are presenting at a younger age and lower stage. We are seeing fewer and fewer biochemical recurrences, and when they do occur, they are less lethal. Thousands of papers support this."

Although they concentrate on low-risk patients, the guidelines offer some clues to treating higher-risk patients as well. Chemotherapy added to radiation therapy improves survival, Dr. D'Amico noted. He also cited a study by Dr. Thompson showing an unequivocal survival advantage in patients receiving adjunctive radiation following surgery, although it is the only study so far to show that effect.

The guidelines also suggest that "combination therapy is best," said Dr. Thrasher. "It looks like high-risk patients don't do well on monotherapy."

Presented May 21, 2007 at the AUA 2007 Annual Meeting, Media Advisory session.

Medscape Daily News, 22 May 2007

HIGH CALCIUM LEVELS MAY RAISE PROSTATE CANCER RISK

The results of a study published in the *International Journal of Cancer* (Vol. 120, pp. 2466-72, 2007) indicate there is an association between dietary calcium and the risk of prostate cancer.

It has been suggested that increased consumption of calcium and dairy products raises the risk of prostate cancer, report Dr. Panagiota N. Mitrou, of the National Cancer Institute, Rockville, Maryland, and colleagues.

To further investigate, the researchers used data from the Alpha-Tocopherol, Beta-Carotene (ATBC) Cancer Prevention Study to examine dietary levels of calcium and dairy products and their relationship with prostate cancer risk. The ATBC study included 29,133 Finnish male smokers between age 50 and 69 years old at study enrollment who completed a 276-item food questionnaire to assess the content of their diet.

During 17 years of follow-up, the team identified 1,267 cases of prostate cancer. A total of 27,028 participants had complete data available and were included in the final analysis.

"We found a strong, graded, positive association between calcium intake and total prostate cancer risk," the researchers report. After adjusting for potentially influential variables, the risk of prostate cancer was 63 percent greater for subjects who consumed 2,000 milligrams per day or more of calcium compared with those consuming less than 1,000 milligrams per day, a statistically significant difference.

A positive association was also observed between total dairy intake and prostate cancer risk, but this disappeared after eliminating the influence of calcium. In other words, the positive association between dairy fat and prostate cancer disappeared after calcium was eliminated, the authors note.

They point out that PSA screening has not been widely adopted in Finland. “Therefore, a large proportion of cases in our study were detected as a result of clinical symptoms,” Mitrou's team explains. “This lessens the possibility that our results are influenced by detection bias.”

Reuters Health, 5 June 2007

PRIMARY THERAPY FOR INTERMEDIATE RISK PROSTATE CANCER: ANY DIFFERENCES IN OUTCOMES, QOL, OR SALVAGE OPTIONS WITH SURGERY VS. RADIOTHERAPY

Dr. Peter Carroll, from UCSF, moderated a session on "Primary Therapy for Intermediate Risk Prostate Cancer: Any Differences in Outcomes, QOL, or Salvage Options with Surgery vs. Radiotherapy" at the annual SUO meeting at the AUA. Dr. Eric Klein, Cleveland Clinic presented the lecture, which was followed by panel discussion.

Dr. Carroll began with presenting the definition and data on intermediate risk CaP and the treatment trends in the US. Regarding intermediate risk prostate cancer he posed the questions; how do we define intermediate risk disease, is this a spectrum of risk, which such patients require combination treatment and are there patients better suited for one form of treatment vs. another?

Dr. Klein presented data from the Cleveland clinic that showed that there is no difference in biochemical recurrent between external-beam radiation therapy and radical prostatectomy. Local recurrence rates favor surgery patients, but this may be artifactual. A slight advantage to radical prostatectomy was found in surgical patients compared to external-beam radiation therapy or brachytherapy. He cited a study with 24 month follow-up that accrued over 1,000 patients. Forty-nine percent of men one year after surgery had complaint of sexual dysfunction and 21 percent had urinary complaints after brachytherapy and 1 percent had bowel complaints after either form of external-beam radiation.

Over time, side effects of radical prostatectomy improved with time, but obstructive symptoms from brachytherapy could persist. At 24 months the sexual QoL domains are similar, although patients who received radiotherapies had lower starting points. Obesity resulted in worse urinary and vitality outcomes for all forms of treatment. He summarized that cancer control at 53 months were similar among treatment groups but all therapies had detriments.

The panel consisted of Drs. Eric Klein, Anthony D'Amico, Harvard University, Derek Raghavan, Cleveland Clinic, and Gerald Andriole, Washington University. Discussion surrounding treatment monotherapy for intermediate risk disease yielded the point that recurrences after 10-15 years may pose some risk. The heterogeneity of this group of patients makes stratification of treatment complex, they agreed. The risks of monotherapy with potential recurrence was weighed against the toxicity and unproven outcomes of combination up front.

Reported by UroToday.com; contributing Editor Christopher P. Evans, MD, FACS. UroToday claims that it is the only urology website with original content written by global urology key opinion leaders actively engaged in clinical practice.

UroToday.com, 26 May 2007

US TOO SEEKS BOARD MEMBER APPLICATIONS

Us TOO is pleased to announce the annual public call for nominations to the Us TOO International Board of Directors. The Board Membership Committee, chaired by Don Lynam, will review and evaluate nominees and submit recommendations to the full Board for approval at its December Board meeting.

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

Letters of nomination with a vita or resume should be sent by August 15, 2007 to Thomas Kirk, President/CEO, Us TOO International, 5003 Fairview Avenue, Downers Grove, IL 60515 or e-mail tom@ustoo.org.

STATINS MAY OFFER PROTECTION AGAINST PROSTATE CANCER

An analysis of data on lipid use for coronary prevention and prostate cancer occurrence revealed a dose-dependent reduction in prostate cancer risk among statin users compared with non-users, Teemu Murtola, MD, of the University of Tampere School of Public Health in Finland.

The cancer-risk reduction was not seen in men with a history of treatment with other types of cholesterol-lowering drugs, suggesting a possible non-lipid effect of statins on prostate cancer biology and etiology, said Dr. Murtola at the American Urological Association meeting in Anaheim, CA. Physicians should make men on statin therapy for treatment and prevention of cardiovascular disease aware of the possible association between statin use and decreased prostate cancer, Dr. Murtola said.

He presented results from the Finnish Prostate Cancer Screening Trial, conducted from 1996 through 2004. The trial involved more than 23,000 men, and data collected included information on cholesterol drug usage during 1995 through 2004. A total of 6,755 men had a history of statin use, and 934 had used other types of lipid-modifying drugs, primarily fibrates and resins. The overall occurrence rate of prostate cancer was 4% in statin users, a 50% reduction compared with the 8% among non-users. After stratifying statin users into dosage quartiles, Dr. Murtola found a dose-dependent reduction in prostate cancer risk.

Patients in the lowest statin-dose quartile had a 6.2% occurrence rate of prostate cancer, which translated into a relative risk of 0.76 compared with non-users. Patients in the highest statin quartile had a prostate cancer rate of 1.8, or a relative risk of 0.21 compared with non-users ($P < 0.001$ for trend across quartiles). Statins' apparent prostate cancer benefit extended to all Gleason grades, and compared with non-users the relative risk ranged from 0.47 for Gleason grade 2 to 6 to 0.55

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FROM THE DOCTOR: PHYSICIAN COMMENTARY ON SELECTED ARTICLES IN THIS MONTH'S *HOTSHEET*

By Gerald W. Chodak, MD

This issue starts with updated guidelines for managing men with localized prostate cancer. Among the changes is the need for better communication to patients about their risk from their disease, the treatment options and the potential outcomes. As previously encouraged in this column, patients should actively ask questions about the specific complication rates associated with their treatment that has occurred with their treating doctor. Only then can patients decide which treatment is most appropriate for themselves among the options available.

Another important change was to encourage patients to participate in clinical trials, which are vital for further improvements to occur. Patients may need to be more pro-active on this front, however, because most urologists do not participate in those trials and seldom are aware of their design or enrollment criteria. Some members of the committee again reiterated their belief that PSA screening is beneficial, and once again I must write that their opinion has yet to be confirmed scientifically. Until studies are completed, that issue will remain unresolved.

No doubt, many patients were disappointed to learn that Provenge approval was delayed until more information is available. While this delay is unfortunate, it was intended to allow

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BOOTS ON THE GROUND IN DC

Us TOO volunteers and staff have been actively working with the Raise A Voice coalition to increase access for people with advanced prostate cancer to new treatments. This effort led to support for and attendance at two rallies (one in the Chicago area during ASCO and one in Washington, DC), a new webpage "ProvengeNow," a meeting with Dr. Andy von Eschenbach and staff members of FDA and a Congressional staff briefing. *For more information and links, visit the Us TOO webpage, click on Advocacy.*

LYCOPENE DOESN'T PREVENT PROSTATE CANCER, AND BETA-CAROTENE MAKES IT WORSE

Lycopene, abundant in tomatoes and popularly thought to be particularly useful in preventing prostate cancer, has no effect on disease risk, a large prospective study showed. What's more, high serum levels of β-carotene, in the same family of carotenoid antioxidants as lycopene, appears to be associated with a three-fold increased risk for aggressive prostate cancer, found Ulrike Peters, PhD., MPH, of the Fred Hutchinson Cancer Research Center and colleagues. Among more than then 28,000 men studied, those who had the highest serum levels of lycopene did not have a lower occurrence of prostate cancer or less aggressive tumors than men in the lowest tier, the investigators reported in the May 2007 issue of Cancer Epidemiology, Biomarkers & Prevention.

"It is disappointing, since lycopene might have offered a simple and inexpensive way to lower prostate cancer risk," Dr. Peters said. "Unfortunately, this easy answer just does not work." The β-carotene finding was unexpected, but not surprising, the researchers noted, given that β-carotene is known to increase risk for lung cancer and cardiovascular disease among smokers. "While it would be counterproductive to advise people against eating carrots and leafy vegetables, I would say to be cautious about taking β-carotene supplements, particularly at high doses," Dr. Peters said.

The study was one of the largest, but not the only one, to find that lycopene was more hype than hope when it comes to prostate cancer prevention. In 2005, Peter Clark, MD, of Wake Forest University, and colleagues, reported results of a trial intended to see if 36 men with recurrent prostate cancer could be protected by lycopene, as measured by PSA doubling time. They found no statistically significant changes in either PSA doubling time or PSA slope compared to baseline .

In the current study, Dr. Peters and colleagues conducted a nested case-control study involving men enrolled in the longitudinal NIH-funded Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, a multicenter study designed to examine methods of early cancer detection and cancer risk factors. The investigators focused on 692 non-Hispanic white men with incident prostate cancer who were diagnosed one to eight years after study entry. They also looked at 844 randomly selected, matched controls. Among the

(Continued on page 8)

Prostate cancer patients and advocates rally in Washington, DC, June 4, 2007

NO DISADVANTAGE SEEN WITH INTERMITTENT ANDROGEN SUPPRESSION FOR ADVANCED PROSTATE CANCER

Intermittent androgen suppression (IAS) therapy for prostate cancer does not diminish survival nor hasten tumor progression compared with continuous therapy, and it may confer a small advantage in quality of life, Kurt Miller, MD, reported here at the 2007 annual meeting of the American Urological Association.

Many urologists already use intermittent therapy in the hopes of sparing patients the adverse effects and quality-of-life reductions associated with continuous androgen suppression (CAS), said Christopher Amling, MD, professor and director of the Division of Urology at the University of Alabama School of Medicine in Birmingham. "These findings will help practicing urologists feel more comfortable with using IAS," said Dr. Amling, who was not involved in the study.

The patients were 335 men with stage D1 or D2 prostate cancer randomized to receive continuous (n = 170) or intermittent (n = 165) treatment with goserelin and bicalutamide. The primary end point was time to disease progression, defined as a 3-fold increase over the baseline PSA level, despite hormone suppression. Men treated intermittently were taken off therapy when their PSA levels decreased by 90%, or to less than 4 mg/dL. Therapy was resumed when PSA rose by 10 mg/dL or more. Of those patients, 88% were off therapy more than 50% of the time. Ultimately, 65% of the patients receiving intermittent therapy and 66% of those receiving continuous treatment experienced disease progression for any reason.

There was a trend toward a longer median time to disease progression for patients in the intermittent-therapy group, 17 months, compared to 12 months for men on continuous therapy, but the difference was not statistically significant (P = 0.1758). Median survival times were 51.4 months and 53.8 months with intermittent and continuous therapy, respectively (P = 0.658).

On quality-of-life measures such as pain, vitality, emotional well-being, and social functioning, there were no differences between the groups. Starting at about 1 year, measures of general well-being were slightly higher among men receiving intermittent treatment, but the difference was not significant. Men in this group also experienced a higher rate of adverse events, but here too the difference was not significant.

These findings suggest that intermittent therapy is a safe and viable option for patients with stage D1 or D2 prostate cancer, said Dr. Miller, professor and chairman of urology at Benjamin Franklin Medical Center, in Berlin, Germany. "Is intermittent blockade now the standard of care? No, but we can offer it safely to patients with advanced prostate cancer," he concluded.

The study was funded by AstraZeneca.

This abstract (LBA 1723) was submitted to and accepted by the 2007 AUA Annual Meeting held in Anaheim, CA, which was held from May 19-25, 2007. The abstract appeared in the *Journal of Urology*, Vol. 117 (4 Suppl), p. 573.

Medscape Medical News
25 May 2007

STATINS MAY REDUCE RISK

(Continued from page 5)

for Gleason grade 8 to 10.

PSA levels were reduced by all types of cholesterol-modifying drugs, but only statins were associated with a reduced risk of prostate cancer. In fact, the use of fibrates and resins was associated with greater reductions in PSA values compared to untreated patients than statin use was. However total quantity of drug use did not correlate with the impact on PSA levels for any of the lipid-modifying agents.

"The association of decreased PSA among men with hypercholesterolemia should be studied further," said Dr. Murtola. "This association could have implication recommendations regarding the interpretation of serum PSA values."

MedPage Today, 22 May 2007

FROM THE DOCTOR

(Continued from page 6)

the company to provide clear proof that the treatment is truly beneficial. Hopefully that information will be available next year. Patients should realize that without clear evidence of benefit from new treatments, a new therapy should not be approved.

For those of you who were investing in the company's stock, I hope you were smart enough to sell at least some of it when it increased so rapidly without being too greedy.

An interesting article about therapies for localized prostate cancer revealed a disconcerting finding; patients who were seen only by a urologist were far more likely to undergo radical prostatectomy, whereas the reverse was true when patients were seen by a radiation therapist. The study does not prove cause and effect, meaning that it is not possible to conclude that patients are not being informed adequately about radiation. No one will ever know what transpired during the consultation between each of those patients and their physician. Nevertheless, patients should be aware that surgeons more often recommend surgery than radiation without any scientific proof that it is better. Before making your decision, make sure you have good unbiased information about all the treatments available.

Dietary supplements and statins again made the news with studies suggesting that β-carotene made cancer worse, another concluding that lycopene does not protect against the disease and one other study suggesting statin intake may reduce the risk of prostate cancer. The conclusions from these types of studies, which are not randomized or controlled, MAY or MAY NOT be correct. Certainly, they are interesting and provocative and suggest that a proper study is warranted. But they do not prove or disprove the value or harm from taking any of these agents.

Interesting preliminary information was also provided from a study of intermittent hormone therapy. This

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LYCOPENE NOT BENEFICIAL

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692 cases, there were 270 aggressive cancers, (90 with regional invasion or distant metastasis and 235 having a Gleason score of 7 or greater). The researchers found no association between serum lycopene and total prostate cancer (odds ratio, 1.14) and no association with a lower risk for aggressive cancer (odds ratio 0.99).

They did find, however, that β-carotene levels were associated with an increased risk of aggressive prostate cancer (odds ratio, 1.67) and that β-carotene was associated with a three-fold risk for regional or distant-stage disease (odds ratio 3.16). None of the other carotenoids they examined were associated with prostate cancer risk.

"Consistent with other recent publications," the investigators said, "these results suggest that lycopene or tomato-based regimens will not be effective for prostate cancer prevention."

They acknowledged that their study was limited by using only a single serum sample, by the relatively short 8-year follow-up and by the potential for residual confounding factors.

MedPage Today, 17 May 2007

^{223}RADIUM

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myelotoxic effect. He said this was not surprising since ^{223}radium was specifically chosen because it emits alpha radiation, which has a higher energy level and penetrates less into tissue than does beta radiation.

"So it doesn't get into the bone marrow but has a significant effect on bone metastases," he said. There was no significant difference in time to first skeletal-related event -- 14 weeks in the radium group and 11 weeks in the placebo group. Dr. Bruland said, however, that the study has a number of limitations including its small sample size and the fact that all patients also received external-beam radiation. Moreover, he noted that when the study was started docetaxel (Taxotere) was not really the standard of care in Scandinavia so ^{223}radium has not been evaluated in the setting of current standard treatment.

The study was funded by Algeta, ASA, Norway, which is developing ^{223}radium, and Dr. Bruland disclosed that he is a consultant to the company.

MedPage Today, 4 June 2007

FROM THE DOCTOR

(Continued from page 7)

treatment has demonstrated reduced side effects over time but to date there is no long term data assessing the impact on survival. This study still does not provide that information, but at least in the short term, no harm was seen by men using intermittent therapy. Longer follow-up is needed to make firmer conclusions.

Lastly, a new therapy with interesting early findings is ^{223}Radium combined with radiation for patients with bone metastases and progressive disease. The combination resulted in delayed progression and even better survival compared to patients receiving radiation alone. Larger studies will be needed to confirm its efficacy.

From the Editorial team: With every issue of the Us TOO HotSheet, we try to provide readers with a physician's perspective on information and news releases published each month. Our goal is to provide patients and their families with a different, critical look at the latest information appearing about this disease, helping the reader understand the strengths and limitations of the information provided. Feel free to provide us with your feedback.

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