Us TOO® PROSTATE CANCER EDUCATION & SUPPORT

HOT SHEET

JANUARY 2004

BLACK MEN SHOULD BE SCREENED FOR PROSTATE CANCER AT YOUNGER AGE

The American Cancer Society guideline to begin screening African-American men at an earlier age than other races is appropriate, according to a new study in the December 2003 issue of the International Journal of Radiation Oncology*Biology*Physics, the official journal of ASTRO, the American Society for Therapeutic Radiology and Oncology.

In 2002, adenocarcinoma of the prostate was the most common cancer diagnosed in men. As the incidence of prostate cancer has increased, so has the difference in diagnosis rates between Caucasians and African-Americans. Additionally, the mortality rate of African-Americans is double that of Caucasians.

In 1997, ACS updated screening guidelines for the early detection of prostate cancer to include the following: "Men in high-risk groups, such as those with strong familial predisposition, or African-Americans, may begin screening at a younger age (i.e. 45) (*NOTE: Us TOO International recommends that men at high risk consider establishing a 'baseline PSA' by age 40 and monitor that level annually thereafter – consult the Us TOO Website – www.ustoo.org - or the Sept 2003 HotSheet for more information*)." This study aimed to determine whether African-American men diagnosed with prostate cancer in the prostate-specific

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OLDER PROSTATE CANCER PATIENTS MAY FACE AGE BIAS-NEW STUDY IS STRONGEST PROOF THAT AGE, NOT LIFE EXPECTANCY, IS MAIN FACTOR IN DECIDING TREATMENT

Canada NewsWire

When it comes to deciding what kind of treatment a man with prostate cancer receives, the person's age trumps life expectancy, according to a new study from the University Health Network.

The findings, to be published in the January edition of the journal Cancer, run counter to the accepted medical practice of deciding treatment options based on the length of remaining time a patient is expected to live, rather than his age. The study showed that older men who are healthier and expected to live for at least another 10 years are more likely to receive inadequate cancer treatment than a younger prostate cancer patients who will probably die sooner.

"These are worrisome findings that suggests older prostate cancer patients may face a bias because of age," said Dr. Shabbir Alibhai, lead author of the study, a physician with University Health Network, and Assistant Professor with the University of Toronto's Departments of Medicine & Health Policy, Management, and Evaluation. "Even though an older

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RACIAL DIFFERENCES IN MORTALITY AMONG MEDICARE RECIPIENTS AFTER TREATMENT FOR LOCALIZED PROSTATE CANCER.

Godley PA, Schenck AP, Amamoo MA, et al.

Black men tend to have poorer overall survival rates than white men after being treated for localized prostate cancer, a new study shows.

The findings, published in the Journal of the National Cancer Institute, also show the greatest disparity to be among men who undergo surgery.

The study's lead author is Dr. Paul Godley, associate professor of medicine and epidemiology at the University of North Carolina at Chapel Hill, member of the UNC Lineberger Comprehensive Cancer Center and leader of the UNC Program on Ethnicity, Culture and Health Outcomes. He was joined by researchers from UNC's schools of medicine and public health, the Medical Review of North Carolina and Massachusetts General Hospital.

The study involved 5747 black men and 38,242 white men with clinically localized prostate cancer. Researchers found that among those who had surgery, the median survival time for black patients was 1.8 years less than for white patients (10.8

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US TOO PUBLICATIONS

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MANAGEMENT OF BONE LOSS IN MEN WITH PCA

Celestia S. Higano

Purpose: Bone loss is increasingly recognized as a common occurrence in men receiving androgen deprivation therapy (ADT) for prostate cancer. Skeletal metabolism and osteoporosis in men, assessment of bone mineral density (BMD), effects of ADT on BMD, management strategies and potential therapies for osteopenia or osteoporosis in men with prostate cancer are reviewed.

Materials and Methods: Relevant literature is reviewed concerning bone loss and osteoporosis in men with and without prostate cancer, techniques of assessing BMD, data on bone loss and fracture risk and management strategies.

Results: The incidence of osteoporotic fractures usually increases a decade later in men than in women. ADT causes significant loss of BMD, which may hasten the development of osteoporosis. Men who are treated with hormonal therapy for an increasing prostate specific antigen and who may live for many years should have baseline BMD assessments. Osteopenia or osteoporosis should be treated to minimize the risk of osteoporotic fracture. Treatment with zoledronic acid seems appropriate since it has been shown to increase BMD in men treated with ADT and to reduce the rate of skeletal related events in men with early hormone refractory prostate cancer with metastatic disease.

Conclusions: Monitoring BMD is warranted in men contemplating or receiving ADT but prophylactic therapy to prevent bone loss currently is not recommended. Men with evidence of significant bone loss who are receiving ADT should be treated. Zoledronic acid is a logical choice based on available data.

SOURCE: The Journal of Urology
2003; 170(6):S59-S64

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BISPHOSPHONATES TO PREVENT SKELETAL COMPLICATIONS IN MEN WITH METASTATIC PCA

Matthew R. Smith

Purpose: The literature on clinical trials of bisphosphonates in men with metastatic prostate cancer is reviewed to familiarize the reader with biology of bone metastases and rationale for use of bisphosphonates.

Materials and Methods: A MEDLINE review of the literature on prostate cancer and bisphosphonates was performed.

Results: In uncontrolled clinical trials bisphosphonates improved pain and analgesic scores in men with symptomatic bone metastases. In a randomized controlled trial of men with bone metastases and progressive disease after first line hormonal therapy zoledronic acid decreased the skeletal related events, a composite end point defined as fracture, surgery or radiation therapy to bone, or change in antineoplastic therapy for bone pain. Randomized controlled trials with other bisphosphonates reported no significant benefit in men with bone metastases. Problems with the study populations, drug bioavailability and potency, statistical power and end point definition may have contributed to the negative results of these other studies.

Conclusions: Zoledronic acid decreases the risk of skeletal related events in men with bone metastases and disease progression after first line hormonal therapy. Additional clinical research is needed to evaluate the optimal timing, schedule and duration of bisphosphonate treatment in men with metastatic prostate cancer. Additional research is also necessary to determine whether bisphosphonates can prevent bone metastases in men with high risk nonmetastatic prostate cancer.

SOURCE: The Journal of Urology
2003; 170(6):S55-S58

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EFFECT OF BICALUTAMIDE 150 MG, AFTER 3 YEARS OF MEDIAN FOLLOW-UP, IN NON-METASTATIC PROSTATIC CANCER

[ORIGINAL ARTICLE IN FRENCH]

Fourcade RO, et al

Purpose: To determine the efficacy and safety of bicalutamide, at the dose of 150 mg per day, as first-line monotherapy or as curative adjuvant therapy in patients with non-metastatic prostate cancer, and to investigate the

possibility of a greater benefit for certain patient subgroups.

Materials and Methods: This article recalls the preliminary results of an international endocrine therapy programme comprising three double-blind placebo-controlled clinical trials in patients with non-metastatic prostate cancer (T1-T4. Nx/N0/N1, M0). Patients were randomized to receive either 150 mg/day of bicalutamide, or placebo, as an adjuvant to radical prostatectomy, external beam radiotherapy or in the context of watchful waiting. The main endpoints were the time to objective clinical progression and overall survival. The combined data of the three trials were submitted to intent-to-treat analysis. The authors also report the results of exploratory studies performed as a function of the type of treatment and prognostic factors.

Results: After a median follow-up of 3 years of a sample size of 8,113 patients, objective clinical progression was observed in 9% of patients of the bicalutamide group (4,052 patients) and in 13.8% of patients of the placebo group (4,061 patients), corresponding to a 42% relative risk reduction (RR: 0.58; $p << 0.0001$). Reduction of the risk of disease progression was observed for the entire study population regardless of primary treatment, stage of disease or usual prognostic factors. This reduction was more marked for patients presenting poor prognostic factors. Data concerning overall survival are not available due to insufficient follow-up. Treatment was well tolerated. The adverse effects most frequently reported in the bicalutamide group were gynaecomastia and breast pain.

Conclusions: After a median follow-up of three years, bicalutamide, as first-line monotherapy or as curative adjuvant therapy, significantly reduced the risk of objective clinical disease progression in patients with non-metastatic prostate cancer. Exploratory analyses demonstrate that the benefit of bicalutamide appeared to be greater for patient with poor prognostic factors. Survival data are not yet available.

SOURCE: Prog Urol. 2003 Jun;13(3):430-9.

RADIOTHERAPY FOR MEN WITH ISOLATED INCREASE IN SERUM PSA AFTER RADICAL PROSTATECTOMY

Macdonald OK, et al

Purpose: In this retrospective study we determined the results of salvage external beam radiation therapy (RT) to the prostate bed for isolated increase of serum prostate specific antigen (PSA) after radical prostatectomy.

Materials and Methods: A total of 60 patients underwent RT for PSA failure after radical prostatectomy from 1993 to 1999. Median followup was 51 months. Biochemical disease-free survival (bDFS) with a serum PSA of 0.3 ng/ml or less was estimated using the Kaplan-Meier method. Potential prognostic factors were evaluated for significant associations with bDFS.

RESULTS: Median PSA before RT was 0.69 ng/ml. Median radiation dose was 64.8 Gy. The 5-year actuarial bDFS was 45%. There were 32 patients with a minimum followup of 4 years (median 73 months) who experienced a 5-year bDFS rate of 43%. PSA before RT ($p = 0.016$), RT dose ($p = 0.026$), surgical margin involvement ($p = 0.017$) and Gleason score ($p = 0.018$) were identified as prognostic factors for bDFS. A significant association with bDFS was present at 5 years of 65%, 34% and 0% for PSA before RT less than 0.6, 0.6 to 1.2, and greater than 1.2 ng/ml, respectively ($p = 0.036$). Patients with PSA before RT less than 0.6 ng/ml and total RT dose greater than 64.8 Gy had improved bDFS at 5 years compared to all others (77% vs 32%, $p = 0.04$). Of 60 patients 3 (5%) experienced chronic grade 3 toxicity.

Conclusions: Optimal benefit from salvage RT was achieved in patients with a PSA less than 0.6 ng/ml and doses of RT greater than 64.8 Gy. Early treatment with a sufficiently high dose of RT maximizes the potential for salvage.

SOURCE: J Urol. 2003 Nov;170(5):1833-7.

PROSTATIC ZINC AND PSA: AN EXPERIMENTAL EVALUATION OF THEIR COMBINED DIAGNOSTIC VALUE

D. Vartsky, et al

Purpose: In cancer affected prostate cells lose the ability to concentrate zinc, resulting in a substantial decrease in Zn in the prostate. We investigated the possibility of using prostatic zinc combined with prostate specific antigen (PSA) as a novel tool for the reliable diagnosis of prostate cancer.

Materials and Methods Using the x-ray fluorescence method the Zn concentration was determined in vitro in prostate samples extracted by surgery from 28 patients. Clinical records included age, serum PSA, sextant prostate needle biopsy, previous medical therapy, surgical procedure and histological findings.

Results: A new relationship was found between Zn in prostate tissue and PSA in blood, which allows improved separation between PCa and benign prostate hyperplasia, and might have a significant impact on the reliable diagnosis of PCa.

Conclusions: Zn concentration is not uniform even in the same anatomical region of the prostate, so that a number of measurements at various locations are required for a diagnostic procedure. The most interesting finding in this study is the relationship between Zn concentration and PSA. A combination of these parameters represents a significant improvement on the diagnostic value of each of them separately and provides a powerful tool for more accurate diagnosis. Although the method may be applied in vitro on biopsy samples, our study underlines the importance of developing a facility for in vivo Zn determination in the prostate.

SOURCE: The Journal of Urology 2003; 170(6):2258-2262

IMPORTANCE OF IMPLANT DOSIMETRY FOR PATIENTS UNDERGOING PROSTATE BRACHYTHERAPY

Potters L, et al

OBJECTIVES: To evaluate the disease

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IMPORTANCE OF DOSIMETRY

(continued from page 3)

and treatment-related factors for predicting biochemical freedom from recurrence (BFR) in patients with clinically localized prostate cancer undergoing permanent prostate brachytherapy.

Methods: Between November 1992 and June 1998, 883 consecutive patients with T1-T2 prostate cancer underwent permanent prostate brachytherapy. Computed tomography-based dosimetry was performed, and the minimal dose to 90% of the prostate volume relative to the prescribed dose (D(90)) was calculated. BFR was defined as three prostate-specific antigen (PSA) rises from nadir, with patients having one or two PSA rises censored early. Follow-up was calculated by censored events. Kaplan-Meier actuarial outcome was determined, and multivariate Cox regression analysis was performed to assess the significance of the D(90), initial PSA value, Gleason score, addition of external beam radiotherapy, addition of hormonal therapy, and isotope selection.

Results: The mean follow-up was 55 months (range 3 to 125). The 10-year BFR rate was 79.1%. Cox proportional analysis identified D(90) as a predictor of BFR ($P < 0.0001$), along with Gleason score, initial PSA level, and clinical stage ($P = 0.001$, $P = 0.001$, and $P = 0.011$, respectively). The addition of external beam radiotherapy, hormonal therapy, and isotope selection did not have an impact on BFR ($P = 0.128$, $P = 0.399$, and $P = 0.224$, respectively).

Conclusions: The quality of permanent prostate brachytherapy as measured by the D(90) was the most significant predictor for BFR in this study cohort at 10 years. Furthermore, adding external beam radiotherapy and/or hormonal therapy as adjuvant therapies did not independently predict for BFR. Overall, the reported 10-year BFR rates in this study were favorable. Strategies for ensuring the best quality implant should be used and, when reporting brachytherapy outcomes, the implant quality should be noted.

SOURCE: Urology. 2003 Dec;62(6):1073-7.

SERUM PRO PSA IMPROVES CANCER DETECTION COMPARED TO FREE AND COMPLEXED PSA IN MEN WITH PSA 2 TO 4 NG/ML

W. J. Catalona et al

Purpose: Pro prostate specific antigen (pPSA) is a precursor form of PSA enriched in tumor compared to benign prostate tissues that may be a more specific serum marker for prostate cancer. Serum pPSA was measured in the clinically relevant early detection PSA range of 2 to 10 ng/ml.

Materials and Methods: Research use immunoassays were used to measure native and truncated forms of pPSA. The subject cohort contained 1,091 serum specimens from men enrolled in prostate cancer screening studies at 2 sites who had undergone prostate biopsy and were divided into PSA ranges of 2 to 4 ng/ml (benign 320, cancer 235) and 4 to 10 ng/ml (benign 315, cancer 221).

Results: In PSA ranges 2 to 4, 2 to 6, 4 to 10 and 2 to 10 ng/ml, pPSA in a ratio with free PSA (%pPSA) gave the highest cancer specificity. At 2 to 4 ng/ml and 90% sensitivity, %pPSA spared 19% of unnecessary biopsies compared to 10% for free PSA and 11% for complexed PSA($p < 0.001$). Similar results were obtained at PSA 2 to 6 ng/ml. At 90% sensitivity in the PSA 4 to 10 ng/ml range, %pPSA spared 31% of unnecessary biopsies compared to 20% for % free PSA and 19% for complexed PSA ($p < 0.0001$). In the combined 2 to 10 ng/ml range, %pPSA spared 21% of unnecessary biopsies compared to 13% for % free PSA and 9% for complexed PSA ($p < 0.0001$).

Conclusions: The %pPSA significantly improved specificity for cancer detection and decreased the number of unnecessary biopsies in the PSA 2 to 4 ng/ml range. This relative improvement of %pPSA compared to % free PSA and complexed PSA was maintained throughout the PSA range of 2 to 10 ng/ml.

SOURCE: The Journal of Urology 2003; 170(6):2181-2185

PRETREATMENT NOMOGRAM THAT PREDICTS 5-YEAR PROBABILITY OF METASTASIS FOLLOWING THREE-DIMENSIONAL CONFORMAL RADIATION THERAPY FOR LOCALIZED PCA

Michael W. Kattan, et al

Purpose: There are several nomograms for the patient considering radiation therapy for clinically localized prostate cancer. Because of the questionable clinical implications of prostate-specific antigen (PSA) recurrence, its use as an end point has been criticized in several of these nomograms. The goal of this study was to create and to externally validate a nomogram for predicting the probability that a patient will develop metastasis within 5 years after three-dimensional conformal radiation therapy (CRT).

Patients and Methods: We conducted a retrospective, nonrandomized analysis of 1,677 patients treated with 3D CRT at Memorial Sloan-Kettering Cancer Center (MSKCC) from 1988 to 2000. Clinical parameters examined were pretreatment PSA level, clinical stage, and biopsy Gleason sum. Patients were followed until their deaths, and the time at which they developed metastasis was noted. A nomogram for predicting the 5-year probability of developing metastasis was constructed from the MSKCC cohort and validated using the Cleveland Clinic series of 1,626 patients.

Results: After three-dimensional CRT, 159 patients developed metastasis. At 5 years, 11% of patients experienced metastasis by cumulative incidence analysis (95% CI, 9% to 13%). A nomogram constructed from the data gathered from these men showed an excellent ability to discriminate among patients in an external validation data set, as shown by a concordance index of 0.81.

Conclusion: A nomogram with reasonable accuracy and discrimination has been constructed and validated using an external data set to predict the probability that a patient will experience metastasis within 5 years after 3D CRT.

SOURCE: Journal of Clinical Oncology, Vol 21, Issue 24 (December), 2003: 4568-4571

THE ROLE OF THE FDA IN THE NATIONAL CANCER PROGRAM: FRIEND OR FOE?

Philip S. Schein, et al

Approximately 1.3 million new cases of invasive cancer will be diagnosed in the United States in the year 2003 resulting in over 550,000 deaths. As a disease group, cancer is responsible for 25 percent of all deaths in the country and overall it ranks as the second leading cause of mortality. Cancer is a serious international problem with even higher rates of incidence and death projected for developing countries in the future.

The cooperative role between the FDA and the National Cancer Institute is described in a commentary co-authored by Dr. Philip Schein, Ms. Barbara Scheffler, and Dr. Stephen Carter. Dr. Schein, a leading international authority in cancer therapy, is a past Chairman of the FDA's Oncologic Drugs Advisory Committee (ODAC) and has served as President of the American Society of Clinical Oncology (ASCO). He is also the former Chairman and CEO of U.S. Bioscience.

In order to meet the aggressive goals of the National Cancer Institute to eradicate death and suffering from this disease by the year 2015, new FDA-approved therapies must be available to the public. According to data released by the FDA's Division of Oncology in April of this year, 38 new chemical entities (NCEs) were approved over the past 13 years to treat a variety of tumors. This translates to an average of 3 NCE approvals per year for the management of cancer including measures to reduce adverse reactions associated with the use of chemotherapy; there were only 2.5 new agents per year that could be classified as therapies that destroy cancer cells. These data must be considered in the context that the term "cancer" serves to describe over 100 different diseases, each requiring the development of specific therapies. There were no new approved drugs that directly treat important tumors such as those of the head and neck, gastric, and cervix, and only one for pancreatic cancer during the 13-year period of analysis. Moreover, as treatments become more specific, and targeted to newly defined molecular targets found in smaller subsets of patients, the required number of NCEs to effectively deal with this disease group will predictably increase. According to Dr. Schein, is it safe to say that at the current rate at which new therapies for cancer are reaching the public, the goals of the NCI, to the extent that they require advances in therapeutics, will not be achieved in the timeframes that have been defined.

"The limited progress in the delivery of new therapies for the broad range of diseases we call 'cancer' has not received sufficient attention despite the substantial investment and resource commitment being made by both the private and public sectors. There are an estimated 400 new anticancer drugs in development, but with so few reaching the public in the form of newly approved therapies one has to question whether the current level of commitment will be sustained, especially by large pharmaceutical companies. These concerns come at a time when significant scientific progress — a vastly improved understanding of cancer biology — has created important new opportunities for the rationale design of effective and safer treatments," said Dr. Schein.

"However, the FDA cannot assume the entire responsibility for the current dilemma," said Dr. Schein. The quality of the drug sponsor's development programs, including decisions on study designs and the degree to which they have engaged the FDA, are important issues. In addition, there are practical issues such as the ability or willingness of a drug sponsor to make the investment necessary to define new treatments for each form of cancer, recognizing that many of the diseases qualify for "orphan status" which connotes limited commercial potential. However, with new leadership appointments at both the FDA and NCI, there is now evidence of a possible change in policy and direction as witnessed by a series of new anti-cancer drug approvals since May of this year. As this paper explains, the mandate of the NCI to reduce the morbidity and mortality inflicted by cancer will require a bold commitment and a spirit of cooperation between the FDA and the NCI.

"There are encouraging signs of increasing coordination between the FDA and the NCI, a process that is largely being driven by the leadership of these two governmental agencies. This is a very welcome development. What is also required, however, is a comprehensive review and redefinition of the policies and procedures by which we currently discover, develop, and approve new therapies for cancer. The field can no longer remain complacent with the current level of productivity and limited return on investment, especially when one recognizes that this disease group accounts for approximately 25 percent of all deaths in the United States, not to mention an inestimable degree of patient suffering," stated Dr. Schein.

SOURCE: The Oncologist, 2003;8:501-506

FDA APPROVES NEW DRUG FOR ADVANCED PCA

BioTech Week

The U.S. Food and Drug Administration (FDA) has approved Plenaxis (abarelix), a drug for advanced prostate cancer for patients who have no alternative therapy.

The drug, indicated for the treatment of the symptoms of men with advanced prostate cancer who cannot take other hormone therapies and who have refused surgical castration, will be marketed under a voluntary risk management program (RMP) agreed to and administered by the sponsor that will restrict the use of Plenaxis to patients with advanced prostate cancer, who have no alternative therapy, because of an increased risk of serious, and potentially life-threatening, allergic reactions associated with its use. About 5-10% of men with prostate cancer have the type of advanced, symptomatic disease that would make them candidates for Plenaxis.

Plenaxis is a type of medicine (called a gonadotropin-releasing hormone (GnRH) antagonist) that lowers the male hormone testosterone, which is a key factor involved in most prostate cancer growth. The effectiveness of Plenaxis in lowering testosterone production in men with advanced, symptomatic prostate cancer was demonstrated in a study of 81 men.

The study showed that such patients could avoid surgical castration by undergoing at least 12 weeks of treatment. Some of the men also experienced other benefits

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AGE BIAS

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prostate cancer patient's prognosis may be better than a younger patient's, they likely won't receive important treatment that could significantly extend their life."

Even after adjusting for the remaining life expectancy of a patient, researchers found that a prostate cancer patient younger than 60 years old was 25 times more likely to be treated with curative surgery than a man 70 years or older even if both were expected to have the same number of years left to live.

A study published earlier this year by Dr. Alibhai showed that healthy older men, particular those in their 70s, who have aggressive prostate cancer benefit significantly from surgery or radiation therapy. With appropriate treatment these patients can receive an extra year of life or more, with most having an improved quality of life as well, the earlier study showed.

"This new study is important because it is the strongest data so far to show that many treating doctors are not sensitive to the issue of age," said Dr. Neil Fleshner, a urologist and head of Princess Margaret Hospital's Genitourinary site group. "Life expectancy, not age, should be the main factor in determining which prostate cancer patients receive appropriate treatment."

The research was supported in part by the Department of Medicine, University of Toronto; the Physicians Services Incorporated Foundation; the Toronto Rehab Foundation; the Canadian Institutes for Health Research; and the Mary Trimmer Chair in Geriatric Medicine Research, University of Toronto.

University Health Network is a major landmark in Canada's healthcare system, and a teaching hospital of the University of Toronto. Building on the strengths and reputation of each of the three hospitals, Toronto General Hospital, Toronto Western Hospital and Princess Margaret Hospital, UHN brings together the talent and resources needed to achieve global impact and provide exemplary patient care, research and education.

FDA APPROVES NEW DRUG

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from the use of this product, including decreased pain and relief from urinary problems. However, 3 of the 81 patients in the clinical trial experienced serious allergic reactions, one of which included loss of consciousness.

The FDA and the manufacturer have agreed that marketing of Plenaxis should be restricted to those patients with advanced, symptomatic prostate cancer and who do not have other treatment options because of this increased risk of serious, and potentially life-threatening, allergic reactions. Because of the risk of low blood pressure and fainting as part of the allergic reaction to Plenaxis, patients who receive the drug are to be monitored for at least 30 minutes after receiving a dose of the drug in their health care provider's office setting.

Moreover, the manufacturer will not be distributing the drug through retail pharmacies; rather, the drug will be distributed directly to physicians and hospital pharmacies enrolled in the Plenaxis RMP which will be designed to help ensure that patients and physicians are fully informed of the risks and benefits of Plenaxis before using it.

Plenaxis is administered as an injection into the muscles of the buttocks every 2 weeks for the first month of therapy, followed by once every 4 weeks thereafter. Because the drug may stop working in certain patients, doctors should perform blood tests about every 2 months to make sure Plenaxis is working by keeping the level of testosterone low.

The most common side effects seen in the clinical trial were hot flashes, sleep disturbances, pain, including back pain, breast enlargement or pain, and constipation.

TESTOSTERONE BLOCKADE MAY ALTER MEMORY

In men with prostate cancer, treatment with drugs designed to suppress testosterone appears to have mixed, but minor, effects on mental function, researchers report. Spatial ability may be impaired but verbal memory seems to be improved. Anti-hormone therapy, also known as androgen suppression therapy, blocks the body's production of the male hormone testosterone, which fuels prostate cancer growth.

As lead investigator Dr. Monique M. Cherrier told Reuters Health, overall "although some men may experience subjective sense of difficulties with cognitive functioning during periods of androgen suppression, our findings suggest a lack of evidence for significant changes using objective (measures) of cognitive function."

Cherrier and colleagues at the University of Washington in Seattle came to these conclusions after studying 19 men with prostate cancer and increasing levels of prostate specific antigen (PSA). PSA is a protein produced by prostate cells and over-produced by prostate tumor cells. High PSA levels can indicate cancer.

All of the men had localized prostate cancer, meaning it had not spread outside the prostate gland. None of them had been treated with anti-hormone therapy prior to entering the study. In the study, the men were treated intermittently with testosterone-suppressing leuprolide and flutamide over a 9-month period.

Treatment reduced PSA and testosterone in all patients. Furthermore, the researchers report in the November issue of the Journal of Urology, testing showed no significant changes in measures of verbal and spatial memory, executive function or language.

"The only exception to this," Cherrier said, "was our finding of a decrease in the ability to mentally rotate complex three-dimensional figures." However, "this ability returned to normal when treatment stopped and (hormone) levels returned to normal."

Another finding was that there was of an improvement in a measure of verbal memory during treatment, which continued in the off-treatment period.

SOURCE: Journal of Urology
November, 2003

FROM THE GENE TO THE CLINIC: PCA DEATH CAN NOW BE AN EXCEPTION?

F. Labrie, et al

Advances in genetics and cancer treatments means a diagnosis of prostate cancer is no longer a death sentence, researchers report. "The most significant discovery of the second half of the 20th century in the field of PCa therapy is probably the observation that the human prostate, as well as many other peripheral human tissues, synthesize locally an important amount of androgens from the inactive steroid precursors dehydroepiandrosterone (DHEA) and its sulfate DHEA-S," scientists report.

"In parallel with these observations, two important discoveries also made by our group are applied in the clinic worldwide, namely the use of LHRH (luteininizing hormone-releasing hormone) agonists to completely block testicular androgens, while, simultaneously, the androgens made locally in the prostate from DHEA are blocked in their access to the androgen receptor by a pure antiandrogen of the class of flutomide," wrote F. Labrie and colleagues, University of Laval, Center Hospital.

"This treatment, called combined androgen blockade, has been the first treatment demonstrated to prolong life in patients with prostate cancer. While the first studies were performed in patients with advanced and metastatic disease, our recent data indicate a remarkable level of efficacy of the same treatment applied to localized prostate cancer, namely a 90% possibility of cure," the researchers wrote. "However, in order to be able to treat localized PCa, early diagnosis must be achieved," .

The researchers concluded: "In the first large-scale randomized study of prostate cancer screening, we have demonstrated that 99% of prostate cancers can be diagnosed at the localized or potentially curable stage, using simple annual measurement of PSA (prostatic specific antigen). Today's data show that with the simple application of the available diagnostic and therapeutic tools, death from PCa should be an exception."

SOURCE: Med Sci, 2003;19(10):910-919).

SUPPORT & PSYCHOLOGICAL CARE NEEDS

Kathleen Lintz , et al

While there are numerous uncertainties surrounding prostate cancer's detection and treatment, more research focusing on the psychological needs of prostate patients is required. This study investigated the support and psychological care needs of men with PCa. Patients were approached during urological oncology clinics and asked to complete several surveys. Of the 249 patients meeting study entry criteria, there was an 89% response rate resulting in a cohort of 210 patients. The data showed that significant unmet need exists across a number of domains in the areas of psychological and health system/information. The more commonly reported needs were fears about cancer spreading (44%), concerns about the worries of those close to you (43%), and changes in sexual feelings (41%). Half of all patients reported some need in the domain of sexuality, especially men younger than 65 years. Needs were being well met in the domain of patient care and support. A significant number of patients reported having used or desiring support services, such as information about their illness, brochures about services and benefits for patients with cancer (55%), a series of talks by staff members about aspects of PCa (44%), and one-on-one counselling (48%). Quality of life (QoL) was most negatively impacted in those who: were 65 years old, had been diagnosed within one year, or had metastatic disease. Men 65 had decreased social functioning, greater pain, increased sleep disturbance, and were more likely to be uncomfortable about being sexually intimate. Patients recently diagnosed had increased fatigue, more frequent urination, greater disturbance of sleep, and were more likely to have hot flushes. Those with advanced disease scored lower on 12 out of 15 QoL categories. PSA level had no effect on QoL or anxiety/depression scores. Men with advanced disease had greater levels of depression and those 65 years old were more likely to be anxious. Although most men with prostate cancer seem to function quite well, a substantial minority report areas of unmet need that may be targets for improving care.

SOURCE: Psycho-Oncology, Volume 12, Issue 8 , Pages 769 - 783

RACIAL DIFFERENCES IN MORTALITY

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years vs. 12.6 years, respectively).

The differences in median survival times between black and white patients were smaller among patients treated with radiation therapy (.7 years) and among patients who had nonaggressive therapy, also called "watchful waiting" (1.0 years). About 75% of the estimated 189,100 prostate cancers diagnosed nationwide in 2002 were clinically localized at the time of diagnosis, so any disparities in outcomes among such patients are of great interest, Godley said. Clinically localized cancer is disease confined to the prostate. Scientists merged the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) data with Medicare file information to compile their findings.

"Previous research into prostate cancer outcome disparities assumed that patients receiving similar treatment would have similar medical outcomes," said Godley. "We felt it was important to examine whether black and white patients treated with surgery or other treatments actually had similar survival. The disparities in survival persisted even after adjusting for geographic region where the patient was treated, tumor grade, other medical conditions and socio-economic factors. Figuring out why survival among blacks is worse and why surgical patients have the largest disparity will take more research."

Several reasons could account for these disparities, researchers said. One is that black patients had reduced access to specialized radiation therapy, which is preferred over surgery for patients in whom locally advanced cancer is suspected. Another possible explanation is genetic differences between races in response to prostate cancer treatment.

Their report concluded that, "Researchers should continue to investigate racial disparities in treatment outcomes as well as the specific social, biologic or environmental conditions that may be responsible for these disparities"

SOURCE: J Natl Cancer Inst, 2003;95:1702-1710)

BLACK MEN & PSA

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antigen (PSA) era differed in initial presenting serum PSA levels (iPSA) compared to Caucasian men and to determine any trends in iPSA in African-American and Caucasian men between the time periods before the guideline change (1990-1996) and after (1997 to 2001).

Of the 4,519 patients with prostate cancer initially seen, 2,332 patients qualified for this analysis. Among these patients, there were 1,968 Caucasian and 364 African-American participants. Between 1990 and 2001, mean iPSA has slowly changed. There was a significantly higher iPSA level among African- American men compared to Caucasian men for both time periods of the study. Analysis revealed that African-American men presented with about 36 percent higher PSA level at presentation than Caucasian men for the first time period and 13 percent higher PSA level at presentation than Caucasian men for the second time period. Taken as a whole, this analysis suggests that the difference in iPSA between African-American men and Caucasian men diminished in 1997 to 2001 compared to the earlier time period.

Age at diagnosis was significantly younger for African-American men compared to Caucasian men. This effect was seen in both time periods. Between 1990 and 1996, African American men were 2.5 years younger than Caucasian men at the time of diagnosis. After 1996, the age gap increased to 3.1 years.

"The overall decline in initial PSA levels in both racial groups is good news as it shows that patients have become more aware of the disease and are coming to us when their cancer is most treatable," said Charlie Pan, M.D., the lead author of the study and a member of the Department of Radiation Oncology at the University of Michigan in Ann Arbor, Mich. "The racial differences in initial PSA levels observed in the study prove that African-American men are more susceptible at an earlier age to this disease and should continue to be screened at a younger age than Caucasians, as recommended by the American Cancer Society in its screening guidelines."

ELDERLY PROSTATE CANCER PATIENTS CAN TOLERATE RADIATION THERAPY

Elderly men with prostate cancer can tolerate external beam radiation treatment, University of Pittsburgh Medical Center researchers found after a 10-year study.

They presented the results Dec. 3 at the Radiological Society of North America's annual meeting in Chicago.

The study included 33 men, aged 80 and older. Most had advanced and aggressive forms of prostate cancer. They were all treated with external beam radiation therapy at the same radiation levels used to treat patients in their 50s and 60s.

The men in the study had a five-year survival rate of 61.6 percent and had no unusual or prolonged treatment interruption due to illness from the radiation therapy.

"The 61 percent survival rate is better than the five-year survival rate for lung cancer patients. So why not give elderly patients the benefit of the doubt? There's a good chance they'll live another five years," study author Dr. Melvin Deutsch says in a prepared statement.

But he notes that some elderly prostate cancer patients — those who are severely ill or incapacitated, for example — are not good candidates for radiation therapy.

Deutsch says some doctors believe the effort and cost of radiation therapy isn't beneficial to elderly prostate cancer patients. But this study shows that they can endure the treatment.

"When an 80-year-old patient comes to me with prostate cancer, assuming he's otherwise healthy, I'm going to treat him with radiation. If it can keep the cancer from coming back, then I say do it," Deutsch says.

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