CALIFORNIA Prostate Cancer COALITION

"Fighting Prostate Cancer in California!"

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NEWS

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PRESIDENT'S MESSAGE

Starting with the December 2013 issue, our CPCC Newsletters will no longer be mailed to all readers and support groups. However, the Newsletter will continue to be available on our web site <www.prostatecalif.org> and can be downloaded. All of the Newsletters will be archived so readers are always able to get back issues as well. Newsletters also will be distributed by email to all readers and support groups that subscribe on the web site.

Our work continues on the two-sided Laminate with questions and answers for both patients and primary care physicians. The questions and answers are directed to the as-yet-undiagnosed prostate cancer patient (as well as to the primary care physicians who tend to follow the USPSTF Guidelines which recommend against PSA testing). Our own CPCC Board Member Dr. Joseph Scherger, an esteemed Family Practice physician in Southern California, had an editorial published in the Journal for the American Academy of Family Physicians in which he stressed the importance of PSA testing and the dangers of waiting until a patient is symptomatic. Additionally, in a Prostate Cancer SPORE group conference call held recently, others in those SPORES expressed interest in being able to distribute this Laminate.

There have been so many new treatment alternatives for advanced prostate cancer that have been approved in the last few years but we need to see that a standard of care is developed that will determine the sequencing of these therapies. At the present time it is different for each patient. At least these new treatment choices are available which could not have been said 10 years ago.

On January 11 and 12, 2014 the National Alliance of State Prostate Cancer Coalitions will hold a State Legislative Advocacy Training Workshop in Chicago. If anyone would like to attend the Workshop, please let me know. We can extend the discounted hotel rate to all who would like to participate.

Respectfully submitted,
MEREL GREY NISSENBERG

TESTOSTERONE TREATMENTS LINKED WITH HEART RISKS

Testosterone therapy may increase risks for heart attacks, strokes and death in older men with low hormone levels and other health problems, a big Veterans Affairs study suggests. Results raise concerns about the widely used testosterone gels, patches or injections that are heavily marketed for low sex drive, fatigue and purported anti-aging benefits, the authors and other doctors said. The new study was published in the Journal of the American Medical Association.

Men who used testosterone were 30% more likely to have a heart attack or stroke or to die during a three-year period than men with low hormone levels who didn't take the supplements. Hormone users and nonusers were in their early 60s on average, and most had other health problems including high blood pressure, unhealthy cholesterol and diabetes.

The nationwide study analyzed health data on 8,700 veterans with low testosterone levels, the main male sex hormone. All had a heart imaging test done and many had risk factors for heart problems, including blocked heart arteries. Risks linked with testosterone were similar in men with and without existing heart problems.

Nearly 26% of men using testosterone had one of the bad outcomes within three years of the heart test, compared with 20% of nonusers. It's unclear how the hormone might increase heart risks but possibilities include evidence that testosterone might make platelets in the blood stick together, which could lead to blood clots, the study authors said.

The research doesn't prove that testosterone caused the heart attacks, strokes or death, but echoes a previous study in older men and should prompt doctors and patients to discuss potential risks and benefits of using the products, said study lead author Dr. Michael Ho, a cardiologist with the VA's Eastern Colorado Health System in Denver, CO.

Previous studies on the supplements' health effects have had mixed results, with some research suggesting potential heart benefits but none has been conclusive.

An editorial in the journal said it is uncertain if the study results apply to other groups of men, including younger men using the hormone for supposed anti-aging benefits. "There is only anecdotal evidence that testosterone is safe for these men," said editorial author Dr. Anne Cappola, a hormone expert at University of Pennsylvania and an associate journal editor.

"In light of the high volume of prescriptions and aggressive marketing by testosterone manufacturers, pre-

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EXPERTS PROPOSE WAYS TO BOOST ENROLLMENT IN CANCER TRIALS

The National Cancer Institute (NCI) and the American Society of Clinical Oncology (ASCO) have joined forces to develop recommendations aimed at increasing the participation of cancer patients in clinical trials.

"Participation in clinical trials is the best option for care in many instances, and should be available for all cancer patients," said Neal J. Meropol, MD, chief of the division of hematology and oncology at University Hospitals Case Medical Center and Case Western Reserve University School of Medicine in Cleveland, OH.

"Clinical trials need to be offered to patients everywhere, including rural areas, not only to patients at major cancer centers." Clinical trials are the foundation for advancing cancer care, yet so few cancer patients are able to participate, he added. "This is a big problem for society."

Dr. Meropol cochaired a recent symposium sponsored by NCI and ASCO which aimed to develop recommendations for overcoming issues related to the accrual of cancer patients in clinical trials. The symposium, "Cancer Trial Accrual Symposium: Science and Solutions" brought together more than 350 cancer research experts, including clinical investigators, researchers of accrual strategies, research administrators, nurses, research coordinators, patient advocates, and educators. The recommendations were published online October 15 in the *Journal of Oncology Practice*.

Reports have shown that less than 5% of cancer patients actually get to participate in clinical trials and the barriers preventing enrollment are well known. One important barrier is at the patient level. "Patients fear randomization or getting a placebo. Or they simply are unaware that clinical trials exist," Dr. Meropol said.

Barriers to accrual at patient, community physician and provider levels, and at the site level (where clinical trials are organized) were addressed at the symposium.

Recommendations at the patient and community level include involving patient advocates, community leaders, representatives of target minority groups, peer mentors, and patient navigators in recruitment and retention. Simplifying patient consent forms and enhancing communication during the informed-consent process, and having multilingual staff and medical interpreters on the recruitment team were also recommended.

At the physician and provider levels, more can be done to promote access to clinical trials, Dr. Meropol said. The recommendations for physicians and providers include developing evidence-based training initiatives to improve communication and disseminating the availability of local trials to primary care providers. One way to do this is with information technology, such as registries and electronic health records.

At the organizational level, creating a culture acknowledging the importance of clinical trials and gives incentives for accrual is critical, Dr. Meropol said. Promoting accrual via leadership best practices, e.g., establishing a culture of commitment to clinical trials and adopting formal quality-improvement processes to increase the efficiency of opening and conducting trials were recommended.

"Clinical trials should be considered as an option in the care for all patients with cancer, regardless of their socioeconomic status or where they choose to receive their care. If all sites participating in cancer clinical trials identify ways in which to improve their own accrual, we will be able to advance cancer research more rapidly and ultimately improve the lives of people at risk for or diagnosed with cancer," the recommendations conclude.

Medscape Medical News, 25 October 2013

RISK STRATIFICATION OF PATIENTS WITH EXTRAPROSTATIC EXTENSION AND NEGATIVE LYMPH NODES AT RADICAL PROSTATECTOMY: IDENTIFYING OPTIMAL CANDIDATES FOR ADJUVANT THERAPY

Eisenberg MS, Karnes RJ, Kaushik D, Rangel L, Bergstralh EJ, SA Boorjian SA

J Urol 190:1735–1741, 2013

Purpose: Randomized trials demonstrate a benefit to adjuvant radiation therapy (RT) after radical prostatectomy (RP) in patients with pathologically locally advanced tumors. However, limited data exist on natural history, specifically in men with extraprostatic extension (EPE), and wide variability in outcomes has been reported. We evaluated long-term outcomes in patients with pT3aN0 disease and determined predictors of recurrence in these men.

Materials and Methods: We evaluated 20,744 patients who underwent RP at our clinic between 1987 and 2011. Of these men 1,073 with pT3aN0 disease were identified who did not receive neoadjuvant or adjuvant therapy. Biochemical recurrence-free survival (bPFS) was estimated using the Kaplan-Meier method. Multivariate stepwise selection was used to develop a prognostic model for biochemical recurrence (BCR).

Results: Median followup after RP was 10.9 years, during which 449 patients experienced BCR. On stepwise selection PSA (HR 1.3, p = 0.0003), clinical tumor stage (HR 1.2, p = 0.001), pathological Gleason score (HR 1.9, p <0.0001), surgical margin status (HR 1.6, p <0.0001) and detectable first postoperative PSA (HR 2.2, p <0.0001) were significantly associated with BCR. Cumulative weighted scores of these variables were used to stratify patients into quintiles according to BCR risk. The 15-year bPFS rate in the lowest to the highest risk group was 70%, 56%, 44%, 34% and 25%, respectively (p <0.0001). The c-index for this model was 0.69.

Conclusions: We present a model to individualize the estimation of BCR in men with pT3aN0 disease at RP. These data may be used for patient counseling, specifically in regard to risk stratification when discussing secondary therapy.

NEW DRUG BOOSTS SURVIVAL IN PROSTATE CANCER

Men with advanced prostate cancer gained an extra 3 months of life with an investigational immunomodulator, including a 7-month survival improvement in patients with bone metastases, a randomized trial showed.

Treatment with tasquinimod was associated with a median overall survival (OS) of 33 months compared with 30 months in placebo-treated patients. The rate of disease progression slowed by almost 50% in men treated with tasquinimod. The difference in OS achieved statistical significance only in an adjusted analysis.

The immunomodulator was generally well-tolerated, and a biomarker analysis provided a few clues to tasquinimod's activity and antitumor response, Andrew J. Armstrong, MD, of Duke University, and co-authors concluded in an article published online in Clinical Cancer Research.

"The current data suggest an overall favorable efficacy and safety profile for tasquinimod and not only justify its evaluation as a single agent in the pre-docetaxel phase III trial ... but also justify further combination studies with other active systemic therapies in men with castration-resistant prostate cancer," they concluded. "Tasquinimod's mechanism of action is not necessarily prostate cancer-specific and further evaluation in other tumor types is also warranted."

Tasquinimod has anti-angiogenic, immunomodulatory, and anti-metastasis properties. Among other molecules, the agent targets S100A9, an immunomodulatory protein expressed by myeloid-derived suppressor cells (MDSC). MDSCs are present in the tumor microenvironment and stimulate angiogenesis and immune tolerance. Studies demonstrated impaired tumor growth in S100A9 knockout models, suggesting S100A9 as a reasonable therapeutic target.

An international, phase II, randomized clinical trial showed that patients treated with tasquinimod had significantly better 6-month progression-free survival (PFS, primary endpoint) compared with placebo (69% vs 37%, P=0.0001). In addition, the median PFS was two times longer in the tasquinimod group (7.6 vs 3.3 months, P=0.0042).The findings reported are from long-term follow-up and correlative biomarker studies, the latter being an exploratory analysis.

The final analysis of the trial included 201 men with metastatic castration-resistant prostate cancer (CRPC) that was minimally symptomatic or asymptomatic. They were randomized 2:1 to tasquinimod or placebo, and the results also showed significant improvement in 6-month and overall PFS in the tasquinimod group.

The authors also reported data for OS, which was a secondary endpoint. An adjusted analysis of OS yielded a hazard ratio (HR) of 0.64, i.e., a 36% reduction in the hazard among men treated with tasquinimod (95% CI 0.42-0.97, P=0.034). Men with bone metastases appeared to derive greater benefit from tasquinimod, reflected in a median OS of 34.2 months v 27.1 months in the placebo group, although the difference did not achieve statistical significance (HR 0.73, 95% CI 0.46-1.17).

During the open-label phase of the study, patients in either treatment group could cross over to the opposite therapy. Subsequently, 41 (61%) of patients in the placebo group crossed over to tasquinimod. Patients who crossed over lived 22 months longer than did those who opted not to be treated with tasquinimod, although the authors acknowledged that patients who crossed over had more favorable prognostic characteristics.

MedPage Today, 21 November 2013

NO IMPROVEMENT NOTED IN OVERALL OR CAUSE-SPECIFIC SURVIVAL FOR MEN PRESENTING WITH METASTATIC PROSTATE CANCER OVER A 20-YEAR PERIOD

Wu JN, Fish KM, Evans CP, Devere White RW, Dall'era MA

Cancer 20 November 2013; Epub ahead of print

Background: Prostate cancer mortality in the United States has declined by nearly 40% over the last 25 years. However, to the authors' knowledge, the contribution of prostate-specific antigen (PSA) screening for the early detection of prostate cancer remains unclear and controversial. In the current study, the authors attempted to determine whether improvements in survival over time among patients with metastatic prostate cancer (mPCa) have contributed to the decline in mortality.

Methods: Men aged ≥ 45 years who presented with de novo mPCa from 1988 to 2009 were identified within the California Cancer Registry. Overall survival (OS) and disease-specific survival (DSS) were estimated using the Kaplan-Meier method. A multivariate analysis with Cox proportional hazards modeling was performed to adjust for different distributions of variables between groups.

Results: A total of 19,336 men presented with de novo mPCa during the study period. On multivariate analysis, OS was found to be better for men diagnosed from 1988 through 1992 and 1993 through 1998 than for men diagnosed in the most recent era (hazards ratio [HR], 0.78; 95% confidence interval [CI], 0.72-0.85 [P < .001] and HR, 0.79; 95% CI, 0.74-0.86 [P < .001]). There was no improvement in DSS observed when comparing the most contemporary men (those diagnosed between 2004 and 2009) with those diagnosed between 1988 and 1997.

Conclusions: In this analysis of men presenting with de novo mPCa, no consistent improvement in OS or DSS could be demonstrated over time. These data suggest that improvements in survival for patients with advanced disease have not contributed substantially to the observed drop in prostate cancer mortality over the PSA era and that stage migration secondary to PSA screening plays a more prominent role.

RE-IRRADIATION FOR SALVAGE OF PROSTATE CANCER FAILURES AFTER PRIMARY RADIOTHERAPY

Ramey SJ, Marshall DT

World J Urol 31:1339-45, 2013

Purpose: To review the literature on use of radiation as a salvage option after local-only failure following initial treatment with radiation.

Methods: PubMed was searched from inception to June 2012 using terms designed to include relevant articles on salvage radiation as a treatment for local-only failures after radiation.

Results: Eighteen separate studies were found which demonstrated widely different patient populations, treatment methods, follow-up periods, and reporting. Only one phase II prospective study was found with no randomized controlled trials. Biochemical disease-free survival (bDFS) at four to 5 years ranged from 20 to 75 percent.

Patient selection may have influenced these varying rates since some studies with lower bDFS had higher risk populations. Factors associated with improved bDFS included post-treatment prostate-specific antigen (PSA) nadir of <0.5 ng/mL, pre-salvage PSA <6, Gleason score ≤7, and PSA doubling time (PSADT) >10 months. Overall survival ranged from 54 to 94 percent, and disease-specific survival ranged from 74 to 100 percent. The crude rate of grade 3-4 genitourinary toxicities among all studies was 13 percent (range 0-47 percent), and the crude rate of grade 3-4 gastrointestinal toxicities was 5 percent (range 0-20 percent). Incontinence rates were low among reviewed studies at 4 percent (range 0-29 percent).

Conclusions: Brachytherapy represents a reasonable salvage option for patients with local recurrence after initial radiotherapy for prostate cancer. However, rates of toxicities, as in other salvage treatments, can be fairly high, and the likelihood of death from prostate recurrence variable. Prospective studies are needed to better define the efficacy and toxicity of this treatment modality.

HEART RISKS OF TESTOSTERONE SUPPLEMENTS

(Continued from page 1)

scribers and patients should be wary" and more research is needed, she wrote. Annual prescriptions for testosterone supplements have increased more than five-fold in recent years, climbing to more than 5 million and $1.6 billion in U.S. sales in 2011, the study noted.

Dr. Nathaniel Polnaszek, a urologist with Scott & White Healthcare in Round Rock, TX, who prescribes testosterone for men in their 40s and 50s, with low levels and erectile dysfunction, called the study "concerning."

Testosterone levels gradually decline as men age, and guidelines from doctors who specialize in hormone-related problems say hormone supplements should only be considered in men with symptoms such as sexual dysfunction. They're not advised for men with prostate cancer because of concerns it could help the disease spread.

AbbVie, Inc. the manufacturer of AndroGel® issued a statement in response to the study. They noted that the approval by FDA required the package insert to include any potential risks. "We encourage discussion between physicians and patients that leads to proper diagnosis based on symptoms, lab tests and a patient's other health needs," AbbVie said.

Associated Press, 5 November 2013

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For more information concerning CPCC or its programs and services, you can call us at (707) 786-7009 or send us an E-mail at cpcc@prostatecalif.org.

CPCC HELPLINE

This service is available for families and significant others of men with newly diagnosed prostate cancer, are undergoing treatment or have suffered recurrent disease. Members of CPCC provide this service and are available to respond to your inquiries 7 days a week between 10:00 AM and 10:00 PM Pacific time. You may call:

Stan Rosenfeld	(415) 459-4668
Erlinda Patterson (Spanish)	(909) 754-8392

CPCC WEBSITE

Go to our website <www.prostatecalif.org> for our calendar of events, legislative page, support group meetings and lending library. You can also access copies of past issues of CPCC News in PDF or Word format. There are direct links to other websites including current NCI trials.

CPCC publishes all major events in bi-monthly newsletter (February, April, June, August, October and December). We need your notice by the 9th of the month before printing. E-mail Stan Mikkelsen at cpcc@prostatecalif.org.

"YOUR CONTRIBUTIONS MAKE OUR WORK POSSIBLE"

Enclosed is my gift of $_____. **Mail to:** CPCC, 6709 La Tijera Blvd, Suite 473 Los Angeles, CA 90045

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