CALIFORNIA Prostate Cancer COALITION

"Fighting Prostate Cancer in California!"

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NEWS

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PRESIDENT'S MESSAGE

There have been some new developments in the field of prostate cancer. It was announced recently that the Social Security Administration has added "Prostate Cancer – Hormone Refractory Disease – or with visceral metastases" as a category for its Compassionate Allowance list entitling a speedier review for disability benefits. Clarification is still being sought on how SSA defines this category.

The California Prostate Cancer Coalition's one-page Laminate is completed and ready for production and distribution. With one side of the Laminate for as-yet-untested and undiagnosed men, listing 10 questions and answers for an informed discussion with their physicians; and the other side for primary care physicians, we are hopeful that men will opt for at least baseline assessment of risk at age 40 (or earlier if they have a family history of prostate cancer or are African-American). We hope to definitely save lives. Knowledge is power; and the PSA test simply gives information to the patient and his physician. It's what you do with the information that is important.

At the end of January the National Alliance of State Prostate Cancer Coalitions (NASPCC) held a Legislative Advocacy Workshop Weekend in Chicago that was attended by representatives of 24 states. I attended this first-of-its-kind workshop in prostate cancer. Now Board Members Stan Rosenfeld, Sam Wells and I will be meeting with Pubic Health officials and State Department of Health Services leaders and staffers in Sacramento in February to help add definition and breadth to the State Cancer Plan's activities in early detection and treatment of prostate cancer.

CPCC held its Face to Face Board Meeting in San Francisco in late January and there was much discussion on the new HUB program for support groups and their interactions with CPCC. For more information on this exciting project, please contact Board Members Stan Mikkelsen at swmikkelsen@suddenlink.net or Larry Barman at llb1@cox.net.

Respectfully submitted,
MEREL GREY NISSENBERG

MELATONIN MAY LOWER PROSTATE CANCER RISK

Higher levels of melatonin, a hormone involved in the sleep-wake cycle, may suggest decreased risk for developing advanced prostate cancer, according to results presented at the AACR-Prostate Cancer Foundation Conference on Advances in Prostate Cancer Research, held Jan. 18-21.

Melatonin is a hormone that is produced exclusively at night in the dark and is an important output of the circadian rhythm, or the body's inherent 24-hour clock. Many biological processes are regulated by the circadian rhythm, including the sleep-wake cycle. Melatonin may play a role in regulating a range of other hormones that influence certain cancers, including breast and prostate cancers.

"Sleep loss and other factors can influence the amount of melatonin secretion or block it altogether, and health problems associated with low melatonin, disrupted sleep, and/or disruption of the circadian rhythm are broad, including a potential risk factor for cancer," said Sarah C. Markt, M.P.H., doctoral candidate in the Department of Epidemiology at Harvard School of Public Health in Boston. "We found that men who had higher levels of melatonin had a 75 percent reduced risk for developing advanced prostate cancer compared with men who had lower levels of melatonin.

"Our results require replication, but support the public health implication of the importance of maintaining a stable light-dark and sleep-wake cycle," added Markt. "Because melatonin levels are potentially modifiable, further studies of melatonin and prostate cancer risk and progression are warranted."

To investigate the association between urine levels of the main breakdown product of melatonin, 6-sulfatoxymelatonin, and risk of prostate cancer, Markt and colleagues conducted a case-cohort study of 928 Icelandic men from the AGES-Reykjavik cohort between 2002 and 2009. They collected first morning void urine samples at recruitment, and asked the participants to answer a questionnaire about sleep patterns.

The researchers found that one in seven men reported problems falling asleep, one in five men reported problems staying asleep, and almost one in three reported taking sleeping medications.

The median value of 6-sulfatoxymelatonin in the study participants was 17.14 nanograms per milliliter of urine. Men who reported taking medications for sleep, problems falling asleep, and problems staying asleep had significantly lower 6-sulfatoxymelatonin levels compared

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ONLY 11 SURGEONS RESPOND TO FDA SURVEY ON DA VINCI SURGERY

During the past several years, a harsh spotlight has shone on the da Vinci robotic surgical system in the form of adverse events (AEs) reports filed with the government, academic studies, news stories, and dozens of lawsuits. Questions swirl around the technology's safety and cost-effectiveness.

The US Food and Drug Administration (FDA) released the results on November 8, 2013 of a survey of da Vinci surgeons earlier last year, undertaken to better understand the system's strengths and weaknesses. The responses were mostly positive and few in number – only 11 surgeons turned in answers. The FDA acknowledged that a "small convenience sample of respondents" was a limitation. The manufacturer of the robotic surgery system, Intuitive Surgical, agreed.

"While we are pleased with the surveyed surgeons' very positive observations about the benefits of robotic surgery, this small informal survey cannot serve as the basis for any scientifically valid conclusions," the company said in a statement issued to Medscape Medical News. It noted that "large clinical studies have documented the comparative benefits of robotic surgery."

The number of procedures performed with the da Vinci Surgical System suggests a sizable cadre of da Vinci surgeons. First approved by the FDA in 2000, the da Vinci Surgical System was used to perform some 367,000 procedures in the US last year, most of them gynecologic or urologic in nature, according to the company. There were 2042 da Vinci systems installed in US healthcare facilities as of September 30, 2013.

Six of the 11 surgeons who responded to the FDA survey practiced at healthcare institutions participating in the agency's Medical Product Safety Network (MedSun); the remaining surgeons were selected on the basis of referrals. FDA spokesperson Erica Jefferson told Medscape Medical News that the agency does not conduct MedSun surveys "with the intention of them being large in scale."

"They are surveys that we can employ as part of routine surveillance and are one of several postmarket tools FDA uses to help evaluate device use and performance and to further understand the risk–benefit profile for devices," said Jefferson. "So we'd never rely solely on the findings of the survey itself. The number isn't as important as the feedback we're able to glean from those that do respond."

Burns, Cuts, and Punctures

The FDA initiated the survey in January, after it saw a 34% spike in Adverse Event reports – including some involving injuries and death – filed with the FDA's Manufacturer and User Facility Device Experience database from 2011 to 2012. The number of da Vinci procedures during that period increased 26%. Mishaps on file include accidental electrical burns, severed nerves and blood vessels, and punctured bladders. Critics of the da Vinci Surgical System say such mistakes are happening in part because surgeons operating the robotic arms lack haptic feedback (sensory cues generated by the sense of touch).

The FDA noted that the submission of an Adverse Event report does not necessarily mean that the device is faulty or defective. In addition, an increase in Adverse Event reports may simply reflect an increase in the number of procedures, publicity from product recalls, media coverage, and litigation.

The company came out on top in a well-publicized case in Washington State. A jury there found that Intuitive Surgical was not liable for the death of a man who underwent da Vinci–style prostate surgery. Lawyers for the man's estate failed to convince the jury that the company had not properly trained the surgeon to correctly and safely use its technology.

Obesity May Be an Issue

Overall, the results of the FDA survey shed a benign light on da Vinci surgery. All 11 responding surgeons reported "fewer patient complications and shorter hospital stays as a benefit of surgery." The FDA qualified that finding by noting that when surgeons discussed patient outcomes, it was not always apparent whether they were comparing da Vinci surgery with laparoscopic surgery or open surgery.

Sometimes surgeons performing a da Vinci procedure will switch to open surgery when a problem arises. However, surgeons in the FDA survey who have had to make this switch generally cited the patient's anatomy or comorbidities, rather than an equipment issue, as the reason why.

The surgeons mentioned some of the same product failings described in the Adverse Event reports submitted to the FDA. These included electrical arcing of monopolar shears, drift in a robotic arm during a procedure, and excessive collision of robotic arms.

The FDA asked the surgeons about the selection of appropriate candidates for da Vinci surgery. Two urologists expressed worries about performing prostatectomies in obese men. For the lone cardiothoracic surgeon interviewed by the FDA, obesity was a common reason for turning patients down for coronary artery bypass surgery with this method.

The FDA received numerous suggestions from the surgeons on how to improve da Vinci surgery. Some centered on the technology itself: smaller robotic arms, smaller surgical instruments, and the addition of haptic or tactile feedback. The surgeons also recommended that da Vinci users receive more dry-lab training and log a mandated number of hours for simulation training.

Medscape Medical News, 11 November 2013

NO OVERALL SURVIVAL BENEFIT BY ADDING SUNITINIB TO PREDNISONE IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER

In a phase III trial reported in the *Journal of Clinical Oncology*, Michaelson et al assessed the addition of the antiangiogenesis agent sunitinib (Sutent®) to prednisone in patients with progressive metastatic castration-resistant prostate cancer after docetaxel-based chemotherapy. No significant improvement in overall survival was observed with the addition of sunitinib.

In this double-blind, placebo-controlled trial, 873 men were randomly assigned 2:1 to receive prednisone at 5 mg twice daily and either sunitinib at 37.5 mg/day continuously (n = 581) or placebo (n = 285). The primary endpoint was overall survival. There were two interim analyses planned.

The sunitinib and placebo groups were balanced for age (median, 69 and 68 years), Eastern Cooperative Oncology Group performance status (0 and 1 in 50% and 50% in both), Gleason score (8–10 in 51% and 45%, ≤ 6 in 13% and 15%), disease progression (prostate-specific antigen progression only in 54% and 50%, radiographic progression in 46% and 50%), prior VEGF inhibitor therapy (2% in both), number of prior systemic therapies (one in 86% in both, two in 10% and 11%), and reason for stopping docetaxel (progression in 91% and 92%, intolerance in 9% and 8%).

The study was stopped early after a second interim analysis indicated that an overall survival difference between groups was statistically improbable. After median follow-up of 8.7 months, median overall survival was 13.1 months in the sunitinib group vs 11.8 months in the placebo group (hazard ratio [HR] = 0.914, P = 0.168). Progression-free survival was significantly longer in the sunitinib group (median, 5.6 vs 4.1 months, HR = 0.725, P <0.001). The objective response rate (no complete responses) was 6% vs 2% (odds ratio [OR] = 3.56, P = 0.040) and the stable disease rate was 26% vs 30%.

Treatment-related adverse events of any grade were more common in the sunitinib group (94% vs 62%), with the most common nonhematologic adverse events being diarrhea (41% vs 9%), decreased appetite (35% vs 12%), nausea (35% vs 12%), fatigue (30% vs 15%), hand-foot syndrome (29% vs 3%), disturbances in taste (28% vs 8%), and vomiting (25% vs 7%). The most common grade 3 or 4 adverse events were fatigue (9% vs 1%), asthenia (8% vs 2%), and hand-foot syndrome (7% vs 0%).

Bone pain (12% vs 16%) and back pain (15% vs 21%) of any cause were less common with sunitinib. Grade 1 or 2 hematologic abnormalities were much more common with sunitinib, and rates of grade 3 or 4 hematologic abnormalities were 9% vs 8% for anemia, 3% vs <1% for leukopenia, 6% vs <1% for neutropenia, 20% vs 11% for lymphopenia, and 4% vs 1% for thrombocytopenia.

Sunitinib dose reduction was required in 32% of patients, with the most common adverse events leading to dose reduction or delay being hand-foot syndrome (11%) and diarrhea, fatigue, and asthenia (9% each). Adverse events led to study drug discontinuation in 27% of the sunitinib group (most commonly due to fatigue and asthenia) and 7% of the placebo group.

A total of 57 patients (10%) in the sunitinib group and 30 patients (11%) in the placebo group died during the study, with most deaths (72% and 80%) due to prostate cancer. Death occurred due to pneumonia in one patient in each group, sepsis in two sunitinib patients, and cardiopulmonary arrest in one patient in each group. Death due to unknown causes occurred in 11% of the sunitinib group vs 0% in the placebo group.

As related by the authors, the findings are similar to those in another recently reported study (Cancer and Leukemia Group B 90401), which showed that the addition of the antiangiogenic agent bevacizumab (Avastin) to docetaxel and prednisone improved progression-free survival without improving overall survival in metastatic castration-resistant prostate cancer. They noted, “The reason that improved [progression-free survival] does not appear to translate to [overall survival] benefit with antiangiogenic agents is not clear. The magnitude of [progression-free survival] may be too small to affect [overall survival], or other factors may be involved.”

The investigators concluded: “The addition of sunitinib to prednisone did not improve [overall survival] compared with placebo in docetaxel-refractory [metastatic castration-resistant prostate cancer]…. Antiangiogenic agents may yet have a role to play in treating patients with [metastatic castration-resistant prostate cancer], but their future development in this area will require enhanced patient selection by using predictive biomarkers of response to guide therapy in a rational manner.”

The ASCO Post, 18 December 2013

MELATONIN

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with men without sleep problems, according to Markt.

Of the study participants, 111 men were diagnosed with prostate cancer, including 24 with advanced disease. The researchers found that men whose 6-sulfatoxymelatonin levels were higher than the median value had a 75 percent decreased risk for advanced prostate cancer. A 31 percent decreased risk for prostate cancer overall was observed as well, but this finding was not statistically significant.

“Further prospective studies to investigate the interplay between sleep duration, sleep disturbance, and melatonin levels on risk for prostate cancer are needed,” added Markt.

Science Daily, 20 January 2014

RESEARCHERS REVEAL POTENTIAL BIOLOGICAL FACTOR CONTRIBUTING TO RACIAL DISPARITIES IN PROSTATE CANCER

Researchers have uncovered a potential biological factor that may contribute to disparities in prostate cancer incidence and mortality between African-American and non-Hispanic white men in the United States, according to results presented at the Sixth American Association of Cancer Research (AACR) Conference on the Science of Cancer Health Disparities in Racial/Ethnic Minorities and the Medically Underserved.

In the United States, African-American men are 1.5 times more likely to develop prostate cancer and more than twice as likely to die from the disease compared with non-Hispanic white men.

"The causes of prostate cancer disparities are numerous, complex, often interrelated, and only partially understood," said David P. Turner, Ph.D., assistant professor in the Department of Pathology and Laboratory Medicine at the Medical University of South Carolina in Charleston.

"We have identified a potential relationship between sugar-derived metabolites and cancer that may provide a biological link with socioeconomic and environmental factors known to contribute to prostate cancer disparities.

"As our bodies use the sugars that we consume for energy they generate waste products, or metabolites, including molecules called advanced glycation end products, or AGEs," Turner explained. "AGEs naturally accumulate in our tissue as we grow older, and they have been implicated in diseases associated with aging such as diabetes, heart disease, and Alzheimer's disease. They can also cause increased inflammation and the generation of potentially harmful chemicals known as reaction oxygen species, which both promote cancer.

"Critically, a common source of the AGEs that accumulate in our bodies is the foods we eat, which has significant implications for cancer health disparities and our overall health.

"We found that AGE levels were highest in African-American men with prostate cancer," said Turner. "Because obesity, poor eating habits, and an inactive lifestyle all promote AGE accumulation, and these factors are often more evident in African-Americans, we hypothesize that there is a link between these factors that could help explain why African-American men are more likely to develop prostate cancer and die from the disease."

Turner and colleagues examined circulating and intratumoral AGE levels in 16 African-American and 16 non-Hispanic white men with prostate cancer. They found that AGE levels were higher in serum from cancer patients compared with individuals without cancer. When analyzing AGE levels in prostate tumor samples, levels were highest in tumor samples from African-American patients. In addition, AGE levels in prostate tumors correlated with levels of a molecule to which AGEs bind to mediate their effects, called receptor for AGE (RAGE).

"We think that the AGE-RAGE signaling pathway promotes prostate cancer and that increased AGE accumulation may represent a biological mechanism promoting prostate cancer disparity," said Turner.

Presented at the 6th AACR Conference on the Science of Cancer Health Disparities in Racial/Ethnic Minorities and the Medically Underserved, abstract PR10.

Medical News Today, 11 December 2013

CPCC PHONE NUMBER & E-MAIL ADDRESS

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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