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US TOO® PROSTATE CANCER EDUCATION & SUPPORT

# HOTSHEET

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## STUDY DEMONSTRATES FRACTURE PREVENTION IN MEN WITH NON-METASTATIC PROSTATE CANCER UNDERGOING ANDROGEN DEPRIVATION THERAPY (ADT)

Results from the HALT (Hormone AbLation Therapy) study in 1,468 men undergoing ADT for non-metastatic prostate cancer show that patients treated with denosumab experienced a 62 percent reduction in the risk of suffering a new vertebral fracture with denosumab compared to placebo at 36 months, with significant reduction observed as early as 1 year. Bone loss and increased fracture risk are serious and under-recognized ADT consequences of and currently there are no approved therapies for these patients.

In this multi-center, randomized, double-blind, placebo-controlled study, men receiving 60 mg denosumab administered subcutaneously experienced a 6.7 percent increase in BMD at the lumbar spine compared to those receiving placebo (primary endpoint) at 24 months. Increases in BMD at the lumbar spine were observed as early as one month after starting treatment with denosumab and continued to increase throughout the study. In addi-

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## CORONARY ARTERY DISEASE MAY INCREASE RISK WITH HORMONES FOR PROSTATE CANCER

Neoadjuvant hormonal therapy for prostate cancer doubled the risk of death over a 12 year period in men with congestive heart failure (CHF) or myocardial infarction (MI) secondary to coronary artery disease (CAD), data from a large retrospective study reported in the 26 August 2009 issue of *JAMA* showed (Vol. 302, pp. 866-73, 2009). Men with no comorbidity or a single CAD risk factor did not have an increased mortality risk from hormones given before definitive treatment for localized prostate cancer, according to the study.

When added to radiation therapy, hormonal therapy improves survival in men with unfavorable-risk prostate cancer. However, "given our current findings, future studies assessing the effect of both the duration and extent of hormonal therapy on the risk of all-cause mortality in men with known coronary artery disease are needed," Akash Nanda, MD, PhD, of Brigham & Women's Hospital and Dana-Farber Cancer Institute in Boston, and colleagues said. "This study should heighten awareness about the potential for harm with neoadjuvant hormonal

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## FDA ISSUES FINAL RULES TO HELP PATIENTS GAIN ACCESS TO INVESTIGATIONAL DRUGS

The US Food and Drug Administration (FDA) published two rules today that seek to clarify the methods available to seriously ill patients interested in gaining access to investigational drugs and biologics when they are not eligible to participate in a clinical trial and do not have other satisfactory treatment options.

To support the effort to help these patients, the agency also is launching a new Web site where patients and their health care professionals can learn about options for investigational drugs. In general, these options include being treated with a drug that has been approved by FDA, being given an investigational drug as part of a clinical trial, or obtaining access to an investigational drug outside of a clinical trial.

The new rule, "Expanded Access to Investigational Drugs for Treatment Use," makes investigational drugs more widely available to patients by clarifying procedures and standards. The other rule, "Charging for Investigational Drugs Under an Investigational New Drug Application," clari-

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# 'WATCHFUL WAITING' IS A VIABLE OPTION FOR PROSTATE CANCER PATIENTS WITH LOW-RISK TUMORS

Appropriately selected prostate cancer patients, including older men and men with small, low-risk tumors, may safely defer treatment for many years with no adverse consequences, according to a new study in the *Journal of Clinical Oncology* (JCO). Led by researchers at Beth Israel Deaconess Medical Center (BIDMC), the study appeared online 31 August 2009.

"With the advent of PSA [prostate antigen] screening nearly 20 years ago, we started to detect prostate cancers at much earlier stages," explains corresponding author Martin Sanda, MD, Director of the Prostate Cancer Center at BIDMC and Associate Professor of Surgery at Harvard Medical School. "Consequently, while PSA testing has enabled us to successfully begin aggressive treatment of high-risk cancers at an earlier stage, it has also resulted in the diagnosis of cancers that are so small they pose no near-term danger and possibly no long-term danger," he adds.

Sanda, together with coauthors from Brigham and Women's Hospital, the Harvard School of Public Health and the University of California, San Francisco, looked at the Health Professionals Follow-Up Study, a large cohort study comprising 51,529 men who have been followed since 1986. Every two years, the participants respond to questionnaires inquiring about diseases and health-related topics, including whether they have been diagnosed with prostate cancer.

A total of 3,331 men reported receiving a diagnosis of prostate cancer between 1986 and 2007. Further analysis found that among this sub-group, 342 men – just over 10 percent – had opted to defer treatment for one year or longer. Ten to 15 years later, half of the men who had initially deferred treatment still had not undergone any treatment for prostate cancer.

"We wanted to find out how this group of men fared in the long-term," explains Sanda. "So we looked at the data they provided us at an average of eight years after their initial diagnosis, and compared it with data provided by prostate-cancer patients who had opted for aggressive treatment, such as surgery, radiotherapy or hormonal therapy.

"We found that the deaths attributed to prostate cancer were very low among the men with low-risk tumors," explains Sanda. "Our analysis showed that only two percent of the men who deferred treatment eventually died of the disease, compared with one percent of the men who began treatment immediately following their diagnosis. This is not a statistically significant difference."

There are three types of prostate cancer: High risk, which are large, faster-growing cancers; intermediate risk; and low-risk, which are small and slower growing cancers. While there is ample evidence that treating intermediate and high-risk cancers with surgery, radiation or hormone therapy can save lives, whether and how best to care for low-risk cancers remains uncertain.

"These findings showed that men diagnosed with low-risk tumors who deferred treatment were still doing fine an average of eight years – and up to 20 years – following their diagnosis. "Only half of these men wound up undergoing any treatment 10 to 15 years post-diagnosis," says Sanda. "This means that they were able to avoid the disruption in their quality of life which might have occurred had they undergone immediate treatment.

"If this approach was more broadly accepted as a standard care option for suitable low-risk prostate cancers, it might help us avoid throwing the baby out with the bathwater when it comes to the PSA test," he adds. "Instead of just abandoning the PSA test because it might be leading to an overdiagnosis of prostate cancer, we could conduct PSA screening in a way that allows more aggressive prostate cancers to be treated, while less aggressive tumors could initially be monitored. This would avoid problems due to treatment of 'overdiagnosed' low-risk cancers, while preserving the lifesaving benefits of treating aggressive cancers that have been detected through PSA testing."

*Science Blog, 31 August 2009*

## HALT TRIAL IN ADT-TREATED PATIENTS

*(Continued from page 1)*

tion, denosumab produced significant increases in BMD at non-vertebral sites (total hip 4.8 percent, femoral neck 3.9 percent, and distal 1/3 radius 5.5 percent), compared to placebo.

"Bone loss and fractures are an important but often unrecognized problem for prostate cancer survivors. Bone loss is an early adverse effect and even short-term ADT negatively impacts skeletal health. Prevention of bone loss and fractures has been a key unmet medical need for men with prostate cancer," said Matthew Smith, MD, PhD, study author, associate professor of medicine and the director of Genitourinary Medical Oncology at Massachusetts General Hospital Cancer Center. "In this large international study, denosumab markedly increased BMD and decreased the risk of fractures in many men receiving ADT for prostate cancer. The efficacy of denosumab was apparent as early as one month and was sustained for three years."

In the HALT trial, the overall incidence and type of adverse effects (AEs) with denosumab were similar to placebo. Rates of AEs were similar in both groups (87 percent). Rates of serious AEs were 35 percent for denosumab and 31 percent for placebo. The most common AEs across both treatment arms were arthralgia, back pain, constipation, pain in extremity, and hypertension. There were no reports of osteonecrosis of the jaw the among patients treated with denosumab. More patients receiving denosumab developed cataracts, though none were considered treatment-related. One patient in the denosumab arm developed hypocalcemia, vs. none in the placebo arm. New primary malignancies were reported in 5 percent of patients in each group. Serious AEs of infections were reported in 6 percent of denosumab-treated patients and in 5 percent of placebo-treated patients.

"Amgen scientists in the 1990s were the first to identify the RANK Ligand pathway, a pivotal physiologic mechanism that controls bone remodeling," said Roger Perlmutter, MD, PhD, Executive Vice President of Research and Development at Amgen. "Today's publications in the *New England Journal of Medicine* underscore the significance of this finding, and highlight Amgen's focus on using innovative research to address grievous illness."

*Amgen news release, 13 August 2009*

## PET/CT SCANS MAY HELP DETECT RECURRING PROSTATE CANCER EARLIER

A new study published in the September issue of The Journal of Nuclear Medicine shows that positron emission tomography (PET)/computer tomography (CT) scans with the imaging agent choline could detect recurring prostate cancer sooner than conventional imaging methods in some patients who have had their prostates surgically removed.

Many men diagnosed with prostate cancer choose to have a radical prostatectomy, which involves surgical removal of the entire gland and surrounding tissue. However, prostate cancer recurs within five years in as many as 30 percent of these patients. Physicians monitor patients who have undergone the procedure by checking levels of prostate-specific antigen (PSA) in the blood. If PSA is detected after radical prostatectomy – known as biochemical relapse – then imaging techniques are essential to determine whether and exactly where in the body the cancer has recurred. The study examined PET/CT scans with radioactively labeled choline – a promising molecular imaging tool which has been shown to be more accurate than conventional imaging techniques such as CT, magnetic resonance imaging (MRI) and bone scintigraphy in detecting recurrent prostate cancer.

"In most patients with biochemical relapse after radical prostatectomy, conventional imaging methods often return false-negative results, meaning that the imaging techniques fail to detect cancer that is present in the body," said Paolo Castellucci, MD, of

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## INVESTIGATIONAL DRUGS

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fies the specific circumstances and the types of costs for which a manufacturer can charge patients for an investigational drug when used as part of a clinical trial or when used outside the scope of a clinical trial.

"With these initiatives, patients will have the information they need to help them decide whether to seek investigational products," said Margaret A. Hamburg, MD, Commissioner of Food and Drugs. "For patients seeking expanded access to investigational drugs and biologics, the new rules make the process easier to understand."

Clinical trials are studies of drugs and biologics that are still in development and have not yet been approved by the FDA. Many patients enroll in clinical trials to gain access to investigational therapies and contribute to finding out how well an investigational therapy works, and how safe it is for patients. Obtaining a drug or biologic under an expanded access program may be an option for some patients who are not able to enroll in clinical trials.

FDA has allowed expanded access to experimental drugs and biologics since the 1970s. That access has allowed tens of thousands of patients with HIV/AIDS, cancer, and other conditions to receive promising therapies when no approved alternative is available.

"The final rules balance access to promising new therapies against the need to protect patient safety and seek to ensure that expanded access does not discourage participation in clinical trials or otherwise interfere with the drug development process," said Janet Woodcock, MD, director of the FDA's Center for Drug Evaluation and Research. "Clinical trials are the most important part of the drug development process in determining whether new drugs are safe and effective, and how to best use them."

For additional information on FDA's expanded access program, go to <www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/AccesstoInvestigationalDrugs/ucm176098.htm>.

*FDA news release, 12 August 2009*

## ROBOTIC SURGERY FOR PROSTATE CANCER MAY IMPROVE FUNCTIONAL OUTCOME

New research suggests that robot-assisted laparoscopic prostatectomy (RALP) provides comparable oncologic control as retropubic radical prostatectomy but is associated with better functional outcomes.

As reported in the August issue of *BJU International* (Vol. 104, pp. 534-9, 2009), men treated with RALP rather than standard prostatectomy had better recovery of urinary continence and erectile function. Positive surgical margin rates were similar with each operation.

These findings are from Dr. Vincenzo Ficarra and colleagues, who analyzed data on 103 patients treated with RALP and 105 treated with retropubic radical prostatectomy at the University of Padua, Italy.

Aside from RALP patients being slightly younger (median age 61 vs. 65 years), the groups were comparable clinically and pathologically. The group treated with RALP had a longer median operative time (185 vs. 135 minutes), however it had less blood loss (300 vs. 500 mL) and a lower red blood cell transfusion rate (1.9% vs. 14%), compared to the group treated

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## PSA TEST ADVOCATED FOR THE EARLY DETECTION OF PROSTATE CANCER - SEE CNN'S LARRY KING AND HIS GUEST PANEL (VIDEO)

CNN's Larry King and his expert guest panel – including John McEnroe, Colin Powell, Mike Milken, and Joe Torre – discuss the importance of the PSA test for the early detection and treatment of prostate cancer.

The show aired on television on 21 August 2009. To view the video, "Larry King Live: Beating Prostate Cancer," go to <www.cnn.com/video/savp/evp/?loc=dom&vid=/video/bestoftv/2009/08/21/lkl.cancer.long.cnn>.

*CNN, 21 August 2009*

## DOC MOYAD'S WHAT WORKS & WHAT IS WORTHLESS COLUMN, ALSO KNOWN AS "NO BOGUS SCIENCE" COLUMN

**"Coenzyme Q10 (CoQ10) dietary supplements have no good evidence in prostate cancer and are over-hyped (just like…well read column for answer to this joke), but they may slightly help those with Parkinson disease or with muscle/joint problems from a statin drug!"**

Mark A. Moyad, MD, MPH,
University of Michigan Medical Center, Department of Urology

**Bottom Line:**

CoQ10 dietary supplements have not been shown to impact prostate cancer or a rising PSA, but it may have some slight benefit in other areas, but overall most folks should not spend much money on this product.

Rich Rodriquez is the greatest football coach in the country! He will win his first game of the season this year, and if he does not please call my therapist ASAP. That is all I have to say about that and now on to my column…

CoQ10 (also known as "ubiquinone") supplements are not cheap, and I have seen them touted or advertised to do almost anything from reduce blood pressure, reduce PSA, help your heart, reduce wrinkles and even make breakfast for you. It seems that so many companies are advertising it for almost everything and suggesting that you take it on a regular basis regardless of your health. PLEASE!!! Let's cut through the BS and review why most individuals should NOT be taking CoQ10 supplements daily.

There are several studies in medicine that just do not get attention because of the bad timing of when they were released. In 2005, researchers put individuals with a rising PSA after surgery or radiation on a combination dietary supplement that included 200 mg of CoQ10 a day and although their blood levels of this and other nutrients increased dramatically after several weeks there was no impact on PSA compared to placebo.[1] In fact, the average PSA increased a couple of points. Does this study suggest that CoQ10 is dangerous for men with a rising PSA? Maybe or maybe not, but is it worth the risk? Another study completed a long time ago suggested a benefit with CoQ10, but no one has ever repeated those results.

Who should take CoQ10? A 2002 study from the Archives of Neurology found that 1,200 mg a day of CoQ10 may help some patients with early Parkinson disease and now a larger study is testing this earlier finding. In the meantime, I have met families of Parkinson patients that are using it now and not waiting for more evidence, and I have met families that use a lower dose because 1,200 mg/day is a lot and is expensive.

There have also been approximately 3 recent studies on taking anywhere from 100-200 mg of CoQ10 a day if you are have muscle pain from a statin or cholesterol lowering drug. However, one was positive and the other two showed no benefit. Still, it may be something to talk to your doctor about if you are having these issues only.

However, I am a bigger fan of switching statin drugs (there are 6 on the market today) or asking your doctor to take it less often (every other day or 2-3 times a week) if you are having this problem compared to taking CoQ10 supplements. Regardless, I will keep you up to date on the statin and CoQ10 ongoing research.

The bottom line is that CoQ10 supplements can help some specific conditions (maybe), but they are as over-hyped as an Ohio State Football team in a BCS Championship game!

(OUCH!!! Man, I am going to pay for that joke… please do not send hate mail Ohio State fans – I am just redirecting my anger because Michigan has not beat you in 5 freakin years! Still, Michigan has a better academic ranking and medical school – ouch!!! Sorry again! Ohio State fans, I just can't stop myself!!! )

1. Hoenjet KM, Dagnelie PC, Delaere KP, et al, Eur Urol 47: 433-9, 2005

## PET/CT SCANS

*(Continued from page 3)*

the nuclear medicine unit, hematology -oncology and laboratory medicine department, Azienda Ospedaliero-Universitaria di Bologna Policlinico S. Orsola-Malpghi, University of Bologna, Italy, and lead author of the study. "Our study found that for some patients, PET/CT with choline can improve the detection of cancer soon after PSA levels are measured. This enables physicians to tailor treatment to individual patients in the early stages of recurrence, thus increasing their chances of recovery."

The study included a total of 190 patients who had undergone radical prostatectomy and showed biochemical relapse in followup examinations. These patients were grouped according to PSA levels and studied with choline PET/CT scans. In addition, researchers also factored in PSA kinetic factors such as velocity – or the rate at which PSA levels change – and the PSA doubling time for each patient.

The study found that whole body PET/CT imaging with choline is significantly better than conventional imaging technologies in detecting prostate cancer in patients with biochemical relapse after radical prostatectomy. Researchers also found a strong association between PET/CT detection of recurrent cancer, PSA levels, and PSA kinetics. The authors suggest that based on the results, only patients with a high probability of having a positive scan based on PSA levels and kinetics should undergo choline PET/CT scans. By using these criteria, the number of inappropriate choline PET/CT scans can be reduced and early detection of prostate cancer relapse can be improved.

Martin Pomper, MD, PhD, professor in the department of radiology and radiological science, Johns Hopkins Medical Institutions, Baltimore, MD said "The article by Castellucci, et. al., in this issue illustrates nicely how connecting a serum marker – in this case PSA – with imaging can facilitate choosing the correct patients for an imaging study, as well as cut back on false negative results for that study."

*ScienceDaily, 2 September 2009*

## NEW METHOD OF SCREENING COULD LEAD TO MORE POTENT CANCER DRUGS

Many researchers believe that tumor growth is driven by cancerous stem cells that, for reasons not yet understood, are highly resistant to standard treatments. Chemotherapy agents may kill off 99 percent of the cells in a tumor, but the stem cells that remain can make the cancer recur, the theory holds. Stem cells, unlike mature cells, can constantly renew themselves.

If effective drugs against cancer stem cells can be developed, one obvious strategy would be to use them in combination with standard chemotherapeutic agents, so that all cell types in a tumor could be attacked. In that way, cancer would be attacked as AIDS now is, with a cocktail of chemicals that blocks all escape paths. That way, cells are unable to change their DNA to dodge an effective drug, and would be more likely to perish if confronted with many drugs at the same time.

A team at the Broad Institute, a Harvard-MIT collaborative for genomics research, has devised a way of screening for drugs that attack cancer stem cells but leave ordinary cells unharmed. The Broad team, lead by Piyush B. Gupta, screened some 16,000 chemicals, including all known chemotherapeutic agents approved by the FDA. The team reported in the journal *Cell* that 32 of the chemicals selectively targeted cancer stem cells.

These particular chemicals may or may not make good drugs, but the screening system proves for the first time, the researchers say, that it is possible to target cancer stem cells with drugs that leave ordinary cells alone. Only one of the 32 chemicals is approved as a drug for cancer.

Eric S. Lander, Director of the Broad Institute, said: "Given the new drug screening system and the idea of using combinations of drugs against cancer, there is a potential for a real renaissance in cancer therapeutics. We have not been able to do that yet with cancer, but if we could, it's a numbers game, and we win."

But the theory is not without critics. "The cancer stem cell hypothesis has in the past year been challenged on many fronts," said Bert Vogelstein, a leading cancer geneticist at Johns Hopkins University. "For example, a paper on melanomas last year showed that 100 percent of melanoma cancer cells were cancer stem cells." If many of a tumor's cells are stem cells, then existing chemotherapy agents are clearly killing them, Dr. Vogelstein said, and the cancer stem cell theory is not an effective guide to finding new drugs. The theory has also aroused opposition because, in its extreme version, it implies that standard chemotherapy goes after the wrong targets and is ineffective.

Some advocates of the idea believe that to dissolve tumors, it would be necessary only to target cancer stem cells, if such drugs existed. But the Broad Institute team and others take the view that a combination of drugs attacking each of the different types of cells in a tumor would be the best strategy. One reason for using a combination of drugs is the suspicion that mature cancer cells may be able to convert themselves back into stem cells, a route that is apparently prohibited to normal mature cells.

The basic insight of the cancer stem cell theory is that there is a hierarchy of cells in a tumor, with the stem cells at the top generating the mature cells that are the majority. Most researchers accept that this is good description of leukemias because Gleevec, a highly effective drug for chronic myelogenous leukemia, does not kill the stem cells, and the leukemia returns if the treatment is stopped.

But with solid tumors, "the jury is out," Dr. Vogelstein said. If stem cells are very common in solid tumors, not just a small resistant reservoir of cells, "then there's no difference between the stem cells and the bulk cancer."

Still, in Dr. Vogelstein's view, the Broad Institute's new screening method is important whether or not the cancer stem cell theory is correct. "Because most of the compounds in use now clearly aren't doing the job we'd all like," he said, "then novel methods for screening could be extremely valuable."

*New York Times, 14 August 2009*

## LOCALLY RECURRENT PROSTATE CANCER AFTER INITIAL RADIATION THERAPY: A COMPARISON OF SALVAGE RADICAL PROSTATECTOMY VERSUS CRYOTHERAPY

Pisters LL, Leibovici D, Blute M, Zincke H, Sebo TJ, et al

**J Urol 182: 517-25, 2009**

**PURPOSE:** We compared the treatment outcomes of salvage radical prostatectomy (RP) and salvage cryotherapy (CT) for patients with locally recurrent prostate cancer after initial radiation therapy (RT).

**MATERIALS AND METHODS:** We retrospectively reviewed the medical records of patients who underwent salvage RP at the Mayo Clinic between 1990 and 1999, and those who underwent salvage CT at MD Anderson Cancer Center between 1992 and 1995. Eligibility criteria were PSA <10 ng/mL, post-RT biopsy showing Gleason score ≤8 and prior RT alone without pre-salvage or post-salvage hormonal therapy. We assessed the rates of biochemical disease-free survival, disease specific survival and overall survival in each group. Biochemical failure was assessed using the 2 definitions of (1) PSA >0.4 ng/mL and (2) 2 PSA increases above the nadir PSA value.

**RESULTS:** Mean followup was 7.8 years for the salvage RP group and 5.5 years for the salvage CT group. Compared to salvage CT, salvage RP resulted in superior biochemical disease-free survival by both definitions of biochemical failure (1) PSA >0.4 ng/mL, salvage CT 21% vs salvage RP 61% at 5 years, p <0.001 and (2) 2 PSA increases above nadir value with salvage CT 42% vs salvage RP 66% at 5 years, p=0.002) and in superior overall survival (at 5 years salvage CT 85% vs salvage RP 95%, p=0.001). There was no significant difference in disease specific survival (at 5 years salvage CT 96% vs salvage RP 98%, p=0.283). After adjusting for post-RT biopsy Gleason sum and pre-salvage treatment PSA on multivariate analysis, salvage RP remained superior to salvage CT for the end points of any increase in PSA >0.4 ng/mL (HR 0.24, p <0.0001), 2 PSA increases (HR 0.47, p=0.02) and overall survival (HR 0.21, p=0.01).

**CONCLUSIONS:** Young, healthy patients with recurrent prostate cancer after radiation therapy should consider salvage radical prostatectomy as it offers superior biochemical disease-free survival and may potentially offer the best chance of cure.

## CONTEMPORARY RISK PROFILE OF PROSTATE CANCER IN THE UNITED STATES

Shao Y-H, Demissie K , Shih W, Mehta AR, Stein MN, et al

**J Natl Cancer Inst 101: 1280–3, 2009**

National-level data that characterize contemporary prostate cancer patients are limited. We used 2004-2005 data from the Surveillance, Epidemiology, and End Results Program to generate a contemporary profile of prostate cancer patients (N = 82,541) and compared patient characteristics of this 2004-2005 population with those of patients diagnosed in 1998-1989 and 1996-1997. Among newly diagnosed patients in 2004-2005, the majority (94%) had localized (i.e., stage T1 or T2) prostate cancer and a median serum prostate-specific antigen (PSA) level of 6.7 ng/mL. Between 1988-1989 and 2004-2005, the average age at prostate cancer diagnosis decreased from 72.2 to 67.2 years, and the incidence rate of T3 or T4 cancer decreased from 52.7 per 100,000 to 7.9 per 100,000 among whites and from 90.9 per 100,000 to 13.3 per 100,000 among blacks. In 2004-2005, compared with whites, blacks were more likely to be diagnosed at a younger age (mean age: 64.7 vs. 67.5 years, difference = 2.7 years, P <0.001) and to have a higher PSA level at diagnosis (median PSA level: 7.4 vs. 6.6 ng/mL, difference = 0.8 ng/mL, P <0.001). In conclusion, more men were diagnosed with prostate cancer at a younger age and earlier stage in 2004–2005 than in earlier years. The racial disparity in cancer stage at diagnosis has decreased statistically significantly over time.

## ERECTILE AID USE BY MEN TREATED FOR LOCALIZED PROSTATE CANCER

A study in the *Journal of Urology* (Vol. 182, pp. 649-54, 2009) reports on the use of erectile aid (EA) following treatment for localized prostate cancer (CaP). Participants with a diagnosis of CaP were prospectively recruited between 1999 and 2003. Clinical and pathological data was abstracted and QOL outcomes were prospectively abstracted at baseline and 1, 2, 4, 8, 12, 18, 24, 30, 36, 42 and 48 months. SF-36 physical and mental composite summary scores were used to study general health-related QOL. Disease specific QOL was assessed by analysis of urinary, sexual and bowel function and bother scores.

A total of 425 men participated in the study and at 24 and 48 months, 75% and 60% completed questionnaires. Treatments were radical prostatectomy (RP) in 275 men, external beam radiotherapy (EBRT) in 70, and brachytherapy in 80 others. Two-hundred thirty seven of 425 men (56%) used an EA in the post-treatment period. Men using an EA were younger and chose RP as opposed to a RT modality compared to patients not using an EA. The CaP tended to have lower PSA and Gleason scores in those using an EA. Regarding HRQOL scores and EA usage, men using an EA had a higher mean physical composite score at baseline than those without EA use, but mental composite scores were comparable in men using vs. not using EA. There was less urinary bother and better sexual function at baseline in men using EA.

No significant between-group difference were noted in urinary control, bowel function or sexual bother. EBRT-treated patients were less likely to use EA than those treated with RP. Patients with moderate or severe sexual bother and those with one or more co-morbid conditions were more likely to use EA. The baseline sexual function was significantly better in men with RP than either form of RT, but function at 2 and 4 years was comparable in the 3 groups. Sexual bother was comparable in the 3 groups at baseline but worsened significantly with time in men treated with RP.

*<www.UroToday.com>, 03 August 2009*

## THE DOCTORS NOTE – GERALD CHODAK, MD

Lately it seems that a number of studies have appeared questioning the overall impact of screening and aggressive treatment for localized prostate cancer. While upsetting to many, the facts appear to show that many of the men who do get diagnosed and treated probably did not need it. Hence the growing challenge to find and treat the dangerous ones while sparing the others from unnecessary treatment and the accompanying side effects. The article based on the Health Professionals Study suggests that men who deferred therapy for low-risk localized disease had about the same mortality from prostate cancer as those undergoing immediate treatment. This is consistent with another study just published in the Journal of the National Cancer Institute that showed at least 20 men must undergo therapy to prevent a single death from the disease. Perhaps, as more urologists become aware of these findings they will move away from a clear bias toward treating almost everyone, to an approach that recognizes immediate treatment can be deferred for a significant portion of the men being diagnosed by PSA testing.

For those men who do not have low risk disease and do undergo radiation, some will develop a biochemical recurrence. Although we know that the high risk group is likely to recur and perhaps die from their disease, their optimal management is still unclear because of the absence of well controlled trials. When uncontrolled studies are published such as the one cited in this *HotSheet* comparing salvage prostatectomy to salvage cryotherapy, the controversy is rarely resolved.

This study from the Mayo clinic concluded that salvage prostatectomy is superior to cryotherapy but we must ask how reliable the conclusions are. Unfortunately, there are so many problems with the comparison it is surprising the study was ever published. An incomplete list of those problems include: a higher proportion of higher grade and stage tumors in the cryotherapy group, inconsistent and inferior freezing methods in the cryotherapy group, no data given to show that comparable radiation techniques and doses were used, differences in follow-up, small numbers of patients, no information on the interval between radiation and recurrence and selection biases associated with trying to compare a group of patients accumulated at two different institutions. There is simply NO WAY to assess the validity of these findings. In essence it is 'garbage in, garbage out' and readers should not assume that these results are proof that salvage prostatectomy is a better choice for recurrent disease.

Two other studies potentially suffering from a retrospective study design are the article on hormone therapy in men undergoing brachytherapy and the comparison of open vs. robotic prostatectomy. The former study found that men with congestive heart failure or a previous MI receiving hormone therapy had a significantly higher mortality than those not getting hormones. This finding suggests that hormone therapy should be avoided in men with the high risk factors. Growing evidence has suggested that hormone therapy is being overutilized and one consequence may be an increased risk for cardiovascular mortality. Still, caution is needed to carefully assess if this is a valid conclusion.

Basing a recommendation using a retrospective analysis presents numerous biases, similar to those described in the previous study. Furthermore, data from randomized studies combining hormone therapy or placebo with radiation therapy have not found this correlation so far. It is well known that hormone therapy results in a reduction in hematocrit and some weight gain which may both be problematic in men with severe heart disease. These data at least make doctors aware that men about to receive hormone therapy should be carefully screened for underlying heart disease that may adversely affect a patient's survival.

The prostatectomy study from Europe claims that better functional results occur using the robotic method. However, patient selection, the non-random study design and a lack of describing how the information was gathered about urinary control makes the con-

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## CAD RISK WITH ADT

*(Continued from page 1)*

therapy use in select men," they added. The results did not identify specific comorbid conditions that eliminated the survival benefit.

The investigators retrospectively analyzed medical records on 5,077 men with clinical stage T1-T3 N0 M0 prostate cancer treated with brachytherapy from 1997 to 2006 at a single center. Patients with unfavorable risk characteristics (stage T2c, PSA >20 ng/mL, or Gleason score ≥8) received neoadjuvant hormonal therapy, which is generally given only to favorable-risk patients to effect cytoreduction and facilitate brachytherapy.

About half of the patients (2,653) had no history of comorbidity, and 42.7% (2,168) had a risk factor for CAD: diabetes in 179, hypercholesterolemia in 326, and hypertension in 1,663. Additionally, 136 patients had CHF secondary to CAD, and 120 had a history of MI related to CAD.

The authors reported that 1,521 (30%) patients received hormonal therapy. Among men with no comorbidity, neoadjuvant hormonal therapy did not increase the risk of mortality after a median follow-up of five years (9.6% versus 6.7%, HR 0.97, P=0.86). Men with a single CAD risk factor also did not have an increased mortality risk when treated with hormones after 4.4 years of follow-up (10.7% versus 7.0%, HR 1.04, P=0.82). In contrast, men with CAD-induced CHF or MI, followed for a median of 5.1 years, had an all-cause mortality of 26.3% with hormonal therapy and 11.2% without (HR 1.96, 95% CI 1.04 to 3.71, P=0.04).

The authors acknowledged several study limitations: its retrospective nature, inclusion of a limited number of CAD risk factors, and assumption that physicians based diagnoses on guideline-supported evidence.

*MedPage Today, 25 August 2009*

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What happened on June 8, 1990?
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## THE DOCTOR'S NOTE

*(Continued from page 7)*

clusions questionable. Studies in the United States have yet to demonstrate a superiority of any prostatectomy method in terms of cancer control or adverse events. In fact, that debate combined with the large cost difference for robotic prostatectomy has prompted me to produce a video asking if insurance should pay the least costly amount when a man has a prostatectomy unless data clearly prove that the more costly method delivers better results ((http://boards.medscape.com/forums?128@200.0SgMaqdqcsw@.29f59240!comment=1. The bottom line is valid conclusions are very difficult to support using uncontrolled studies.

Lastly, another supplement, Co-Q10 is discussed by Dr. Moyad making it clear that proof of benefit for men with prostate cancer is lacking. His advice should be heeded more than it is; namely, men should avoid taking these and other supplements until studies clearly determine they are useful and SAFE! There is simply no way to know if this or other over-the-counter therapies a man receives are worth the money spent on them.

## ROBOTIC SURGERY

*(Continued from page 4)*

with retropubic radical prostatectomy.

The rates of complications within each group were similar, being roughly 10% in each group. Likewise, positive the rates of positive surgical margins for pT2 cancers were similar in each group, at approximately 12%.

At 12 months, 97% of RALP patients had urinary continence compared with 88% of radical prostatectomy patients ($p = 0.01$). The corresponding average times for continence to return were 25 and 75 days, respectively. Among patients who had bilateral-nerve sparing procedures, 81% of RALP-treated subjects had recovered erectile function at 12 months compared with just 48% of those treated with radical prostatectomy.

"Our data justify the use of robotic surgery for treating clinically localized prostate cancer as an alternative to the traditional retropubic approach, although at present the costs of RALP are higher," the authors conclude.

*Reuters Health, 31 July 2009*

## COMPOUND TARGETS, DESTROYS CANCER STEM CELLS IN MICE

Research shows that cancer stem cells may play a role in cancer metastasis and in causing cancer to reappear even after successful treatment. Yet studying cancer stem cells in the lab has proven problematic. The cells tend to lose their stem cell-like properties when grown outside the body.

In the study, which appears online in the journal *Cell*, researchers were able to generate large numbers of cancer cells in the lab with stem cell-like qualities. They then analyzed thousands of chemical compounds to determine which ones effectively killed breast cancer stem cells. They found that a chemical called salinomycin destroyed both lab-generated cancer stem cells, as well as naturally occurring ones. Compared to Taxotere®, salinomycin reduced cancer stem cells by more than 100-fold and inhibited breast tumor regrowth in mice.

More research is needed to determine exactly how salinomycin works and if it will be as effective in humans as it was in mice, researchers said.

*HealthDay News, 13 August 2009*

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