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NEWSLETTER

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♦ A DECADE OF CHANGE IN THE TREATMENT OF PCa ♦

It is now estimated that one in seven men will be diagnosed with prostate cancer during his lifetime and approximately 220,800 new cases of prostate cancer will be diagnosed in 2015 alone. The American Cancer Society predicts in 2015 there will be approximately 27,540 deaths from prostate cancer. But help is on the way!

Major treatment strategies have been approved over the past decade, dramatically increasing survival rates and changing the treatment paradigm for prostate cancer. Greater improvements are expected within the next decade through precision medicine.

In 2005, there were only a handful of approved medications. However, today there are many more and they work by several different mechanisms, allowing them to extend life in novel ways.

In 2005, the relative 10-year survival rate for prostate cancer was 92% and the relative 15-year survival rate was 61%, according to the American Cancer Society. Today, the numbers are significantly higher: the relative 5-year survival rate for all stages of prostate cancer is almost 100%, the relative 10-year survival rate is 99%, and the 15-year relative survival rate is 94%.

“The greatest advances in the management of prostate cancer in the last decade have come directly from our understanding of the biology of what causes prostate cancer cells to become resistant to treatments we had a decade ago,” said Dr. Anthony D'Amico, Brigham and Women's Hospital and Dana-Farber Cancer Institute, in Boston, MA. He said the Prostate Cancer Foundation (PCF), which was formerly the Association for the Cure of Cancer of the Prostate (CaP CURE), helped usher in a new era in terms of research. It included leading scientific and clinical experts and it helped expedite new treatments. **(Continued on page 13)**

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♦ FROM THE EDITOR ♦

Do you know persons who would benefit from receiving this newsletter? Put them in contact with the editor as shown at the top, left, of this page. Also, we solicit your recommendations for topics for our quarterly meetings. Contact the editor with your suggestions.

♦ SPEAKER'S REMARKS - AUGUST 6, 2015 ♦

Our August program featured a presentation by Dr. Stephen Lewis, a radiation oncologist at WRNMMC. His topic was "Emerging Therapies in Radiation and Immunology." Unfortunately, we were unable to produce a copy of his presentation for inclusion in the newsletter.

♦ MEETING SCHEDULE FOR NOVEMBER 5, 2015 ♦

Our speaker for Thursday, November 5,, 2015, is Dr. Timothy J. Tausch, Department of Urology, Fort Belvoir Community Hospital and WRNMMC. His topic is "Prostate Cancer Survivorship: Urinary Incontinence After Treatment." Your family members and friends are also welcome. Come join us.

(The presentation also may be viewed via video teleconference at the Fort Belvoir Community Hospital. Go to the Oaks Pavilion, 1st floor, Room 332, to participate.)

SEE THE BACK PAGE OF THIS NEWSLETTER FOR IMPORTANT INFORMATION ABOUT THIS MEETING.

♦ PROSTATE-SPECIFIC ISSUES ♦

Complementary and Alternative Medicines Among Elderly Oncology Patients. Alternative medicines are widely thought to be harmless, at the least, and very often helpful for a wide range of discomforts and illnesses. However, although they are marketed as *natural*, they often contain active ingredients that react chemically and biologically with other therapies. Researchers performed a comprehensive review of all of the medications taken by senior oncology patients and found that as many as 26% were using complementary or alternative medicines (CAM). Nightingale, et al., College of Pharmacy at Thomas Jefferson University in Philadelphia, report that patients often fail to disclose the CAMs they take because they think they are safe, natural, nontoxic, and not relevant to their cancer care; because they think their doctor will disapprove; or because the doctor doesn't specifically ask.

A number of CAMs are known to interfere with certain cancer treatments. For example, St. John's wort can make some cancer therapies less effective, according to the National Institutes of Health. Others can interfere with anesthesia during surgery for cancer. But not all interactions have been studied. CAMs fall under the category of health supplements and are therefore not regulated by the Food and Drug Administration (FDA), which means that dose and potency—and, in turn, reaction in the body—can vary widely between products and between patients.

The use of CAM in this subpopulation warrants substantial interest and concern on behalf of medical oncologists and allied health professionals because of the potential clinical implications associated with CAM use. Patients may be combining these agents while receiving concurrent systemic chemotherapy, radiation therapy, and/or surgical interventions which have the potential to compromise the safety and efficacy of treatment interventions. The research team found that 26% of patients were taking CAMs at some point during the continuum of their cancer care, with the highest usage among women older than 80 years, a population that had not been captured by previous studies. Among those taking complementary medicines, 68% were age 80 years and older.

Commonly used alternative medications in this population included alternative therapies for macular degeneration, stomach probiotics, joint health, and mega-dose vitamins or minerals. While the current study did not examine the potential adverse events caused by these medications, the researchers say that some can have a biochemical effect on the body and other drugs. They also stress the importance of a comprehensive screen of all of the medications that older cancer patients take, including CAMs, and clear and transparent documentation of CAM use should be recorded in the patient's medical record. (Source: Journal of Geriatric Oncology, September 14, 2015)

Managing Bone Health in Prostate Cancer. Many men experience bone loss and joint pain related to their prostate cancer. Communicating with your health care team is important to maintaining healthy bones. There are also lifestyle changes you can make to help keep your bones strong. This article answers some commonly-asked questions about prostate cancer and bone health. It also discusses steps you can take to care for your bones.

What causes bone problems when you have prostate cancer? Bone loss can result from your treatment. Testosterone, the male sex hormone, fuels the growth of prostate cancer.

Hormone therapy slows cancer's growth by lowering the body's production of testosterone or blocking it from entering cancer cells. However, the lack of testosterone can weaken bones and put men with prostate cancer at increased risk for fractures. Radiation, chemotherapy, and some pain medications can decrease bone strength as well.

Men with prostate cancer are at risk for bone metastases. Sometimes, prostate cancer travels to other parts of the body. The most common place for it to spread is to the bones, and this can cause bone pain and fractures. The bones most often affected are the spine, hips and ribs. However, bone pain does not always mean that cancer has spread to the bones. Other conditions can cause it. If prostate cancer has spread to your bones, there are several treatment options that can improve your quality of life. Your doctor may prescribe medicines called bisphosphonates to prevent thinning of the bones. Oral bisphosphonates approved for treating osteoporosis include alendronate (Fosamax) and risedronate (Actonel). An intravenous, or IV, bisphosphonate called zolendronic acid (Zometa) is also available. It has been shown to reduce bone loss and increase bone strength in men receiving treatment for prostate cancer.

Bone metastases can also be treated. Treatment options include hormone therapy and radiation to treat the cancer, and surgery to repair bones that have been damaged. Zolendronic acid can also be used. Consider enrolling in a clinical trial for additional treatment options. Clinical trials are studies that test new treatments to prove that they are safe and effective. New treatments are also compared to the standard treatments to see if they are better.

What steps can you take to care for your bones?

Schedule an annual bone exam. Bone density scanning, also called DXA or bone densitometry, is the best way for doctors to measure your bone mineral density (BMD). BMD is a measure of bone strength. It is important to get this test before starting hormone therapy so it can serve as a base line of your bone health. This lets your doctor compare your results over time and see how your treatment may be affecting your bones.

Make your dentist part of your health care team. If possible, visit your dentist for a complete oral exam before starting treatment. During and after treatment, continue to see your dentist regularly. As always, practice good oral hygiene with regular brushing and light flossing, and avoid mouthwash that contains alcohol.

Strive for a healthy diet. Your bones especially need calcium and vitamin D to stay strong. Low-fat dairy products, like milk and cheese, are good sources of calcium. So are dark leafy greens and beans. Fatty fish such as salmon, tuna and sardines also are a good source of vitamin D. Ask your doctor about the benefits of vitamin D and calcium supplements.

Make exercise part of your routine. Exercise maintains bone strength and reduces the loss of calcium in your bones. Regular, weight-bearing exercise, such as walking or light weightlifting is recommended. Such activities encourage your bones to strengthen. Try doing some exercise outdoors, as sunshine is a source of vitamin D. It's important not to injure your bones, though. Talk to your doctor about the right kind of exercise for you. (Source: Cancer Therapy Advisor Fact Sheet, April 16, 2015.

The Comparative Harms of Open and Robotic Prostatectomy. Robotic assisted radical prostatectomy (RALP) has largely replaced open radical prostatectomy (RRP) for the surgical management of prostate cancer despite conflicting evidence of superiority with respect to either disease control or functional sequelae. A recent study examined sexual and urinary function between men undergoing RRP versus those undergoing RALP.

Subjects surgically treated for prostate cancer were selected from two large population-based prospective cohort studies. The combined cohort consisted of 2,438 men, 1,505 of whom underwent RRP and 933 of whom underwent RALP. Men undergoing RALP reported better urinary function at 6 months, but not at 12 months. Subjects undergoing RALP also reported superior sexual function at 6 months and 12 months. Sensitivity analyses largely supported the sexual function findings, but with inconsistent support for urinary function results.

This population-based study reveals that men undergoing RALP likely experience less decline in early urinary continence and sexual function compared to those undergoing RRP. The clinical meaning of these differences is uncertain and longer follow-up will be required to establish whether these benefits are durable. (Source: Journal of Urology, September 3, 2015)

Prostate Cancer Diagnosis and Suicide Risk. Men who have prostate cancer are at increased risk of suicide and accidental death within the first year of diagnosis compared with their counterparts diagnosed with other solid malignancies, according to a new study. The risk also is increased when definitive treatment was recommended but not received. Men with PCa have a 4-fold increased risk of suicidal death within 3 months of diagnosis compared to men who have other solid cancers.

Quoc-Dien Trinh, MD, et al, Harvard Medical School, noted that while substantial research has demonstrated a relatively higher risk of suicidal death among PCa patients compared with the 'cancer-free' population, they say that their study is the first to directly compare the risk of suicidal death in men with PCa to those with other solid cancers. Their findings suggest the need for close monitoring and coordination with mental health professionals in at-risk men with potential curable disease.

The study included 524,965 men diagnosed with PCa and 956,576 men diagnosed with other solid cancer. The investigators found that the risk of suicidal or accidental death was lower among men with PCa than those with other cancers , except within the first year of diagnosis. For example, from 0–3 months after diagnosis, PCa patients had a 4-fold increased adjusted relative risk of either suicidal or accidental death compared with their counterparts with other solid cancers. Among men who were recommended treatment but did not receive it or refused it, those with PCa had a significant 32% increased risk of a suicidal death and 44% increased risk of accidental death.

The authors discussed possible reasons for the higher suicidal and accidental risks observed in their study. Although the higher risk may be partly attributable to unmeasured baseline differences between patients with PCa and those with other solid cancers, Trinh and colleagues cited studies suggesting it may also reflect a disproportionately high immediate psychosocial impact of the PCa diagnosis, fueled by perceived anxiety of treatment-related adverse effects in younger men and uncertainty regarding watchful waiting in older patients. Clinical depres-

sion associated with a PCa diagnosis, distress secondary to treatment indecision, or treatment-related adverse effects such as urinary incontinence and erectile dysfunction that impair quality of life may contribute to a heightened suicidal risk, the authors stated. Patients diagnosed with PCa experience negative intrusive thoughts and significant decrements in physical, mental, and social aspects of their lives, particularly within the first 6 months of diagnosis, according to the investigators.

The new findings corroborates those of previous studies. Although the increase in absolute risk of suicide was modest, the researchers concluded that their findings reflect the severe psychological stress that prostate cancer patients may experience upon diagnosis. (Source: Renal and Urology News, August 28, 2015)

Prostate Cancer, Salvage Radiation, and Survival. Patients experiencing biochemical failure — defined as an increase in prostate-specific antigen (PSA) level — after prostatectomy for prostate cancer often receive salvage radiation therapy (SRT) to control the disease and prevent metastases. However, despite SRT, some patients still exhibit biochemical failure. Now, a long-term, single-center study by Kim, et al., Texas Oncology, Waco, TX, has demonstrated that outcomes for 61 men who experienced a biochemical recurrence after surgery, including a subset of 34 men who experienced failure twice (once after surgery and once after SRT), are robust.

The median overall survival was 13.6 years for the men in the study who had two biochemical recurrences and 14.7 years for the men who had just the one recurrence after surgery. Furthermore, the 10-year prostate cancer-specific, metastasis-free, and castration-resistant-free survival rates were all in excess of 70% for the men who had two biochemical recurrences. This new retrospective data might be of service to clinicians in discussions with anxious patients because there is a paucity of prospective data about this clinical scenario, the authors suggest.

The extensive follow-up period makes the study one of the longest in the literature. Median follow-up was 126 months after SRT and 112 months after SRT failure. Most studies have a median follow-up of less than 90 months after SRT. "Because of our long-term follow-up, we were able to make observations in those patients who recurred despite SRT," the authors write.

Although their study was of a single group of men, and thus not comparative in any way, the authors observe that another study on natural history after PSA failure demonstrated that the median time to distant metastasis was 8 years after PSA failure after radical prostatectomy (without SRT), and roughly one in three patients developed distant metastases within 5 years without radiation therapy. The study suggests that SRT is effective in preventing prostate-cancer-specific mortality and decreases the rate of distant metastases, according to the researchers

The new study also raises the issue of the timing of radiation therapy after prostatectomy. PSA levels determine what's next for these patients, according to an independent observer.

Patients with adverse pathologic features, such as seminal vesicle invasion, positive surgical margins, and extraprostatic extension without evidence of disease recurrence (i.e., undetectable PSA levels), are candidates for adjuvant radiation therapy (ART), according to the ob-

server. Patients who show increases in PSA at any time after surgery are candidates for SRT, she explained.

The new study findings do not challenge the existing guidelines. The study provides food for thought, but is not practice-changing," according to the observer. Nevertheless, in this study, the authors indicated that 70% of their patients would have been candidates for ART based on their pathologic stage and margin status. They emphasize that without concrete evidence from randomized clinical trials, one must seriously consider the advantages and disadvantages of ART versus SRT. The decision of whether to use ART or SRT remains an area of active debate, and prospective randomized trials are currently underway to attempt to answer this question. (Source: Journal of Clinical Oncology , July 19, 2015 - online; via Medscape Medical News, August 10, 2015)

Combination Treatment for Advanced Prostate Cancer. Chemotherapy at the start of hormone therapy can extend the lives of men with prostate cancer that has spread beyond the gland, a new study finds. Over nearly 29 months of follow-up, men with advanced prostate cancer who received the combination therapy lived almost 14 months longer than men who received only hormone therapy (58 months versus 44 months), researchers said.

"Men who have hormone-sensitive metastatic prostate cancer should speak with their doctors about having this combination treatment to significantly prolong their survival," said lead researcher Dr. Christopher Sweeney at Harvard Medical School. For 50 years, hormone therapy has been the standard care for these patients. Adding chemotherapy to hormone therapy is worth doing because even though it's not a cure, it does improve survival and quality of life, Sweeney said.

The study randomly assigned 790 men with prostate cancer, average age 63, to chemotherapy plus hormone therapy or hormone therapy alone. In addition to the survival benefit, men who received the combination of chemotherapy and hormone therapy saw their cancer remain dormant for more than 20 months before it began to progress, compared with close to 12 months among those who only received hormone therapy, the researchers found.

The side effects of the chemotherapy were mild, in general. Fatigue, low white blood cell count and infection were the most common side effects. One man died from an unknown cause, though researchers said the death may have been due to the chemotherapy. The man probably should not have been in the trial in the first place, Sweeney said. One of the criteria for the treatment is that patients should be able to handle the chemotherapy. If they have other conditions such as liver or kidney disease, they should not be getting chemotherapy.

Dr. Anthony D'Amico, chief of radiation oncology at Brigham and Women's Hospital in Boston, said, "This is an important study that will change practice." In the study, the greatest benefit was seen in men who had four or more tumors outside the prostate, but D'Amico, who wasn't involved with the research, believes chemotherapy will also help men with fewer tumors. "It will probably work across the board," he said. Other studies have confirmed these findings.

"This drives home the point that we should change practice," he said. "It's not curing prostate cancer," he said. "But it's certainly increasing the time people have." (Source: New England Journal of Medicine, August 5, 2015, via Health Day News, August 5, 2015)

Relaxed PSA Guidelines and Aggressive Tumors. Relaxed guidelines on prostate cancer screening may delay diagnosis and treatment of aggressive tumors, a new study suggests. In 2011, the U.S. Preventive Services Task Force recommended against routine prostate specific antigen (PSA) testing, to curb over-diagnosis and overtreatment of prostate cancer. Since then, PSA screening has dropped by 28 percent, the researchers report.

Barocas, et al., Vanderbilt University, commented that "On the positive side, there is a lot of prostate cancer that we don't need to know about." These are low-risk cancers that most men will not die of, and the treatment can be more harmful than the cancer. "To that extent, the guideline had a beneficial effect," Barocas said.

"On the negative side, we seem to be missing intermediate and high-risk cancers in men who would be eligible for treatment," he said. "Those are missed opportunities to identify disease and treat it." The report will be published in the December 2015 issue of the *Journal of Urology*.

Dr. Kirsten Bibbins-Domingo, vice chair of the U.S. Preventive Services Task Force, said, "When the task force reviewed the evidence on PSA screening for prostate cancer in 2011, what we found is that there is a very small potential benefit and significant potential harms." Most prostate cancers found by PSA screening are slow-growing and not life-threatening, she explained. "However, there is currently no way to determine which cancers are likely to threaten a man's health and which will not," she said.

Barocas disagreed, saying that "The policy of screening no one is throwing the baby out with the bathwater. Some men are at high risk for prostate cancer and should be screened.. These include men with a family history of prostate cancer, and black men. In addition, screening should be combined with treatment. Low-risk cancer need not be treated but watched, while high-risk cancer should be treated, Barocas said.

Another expert made another point. Since 2011, when the guideline was published, new techniques, including MRI and ultrasound, have been developed that can diagnose prostate cancer more accurately and distinguish between low- and high-risk cancers. These techniques may need to be taken into account in modifying the guideline, said Dr. Anthony D'Amico, chief of genitourinary radiation oncology at Brigham and Women's Hospital and Dana-Farber Cancer Institute in Boston.

Using the U.S. National Cancer Database, Barocas and colleagues looked at the effect of the new guidelines on the number of new prostate cancer diagnoses between January 2010 and December 2012. The researchers found that the number of prostate cancer diagnoses dropped more than 12 percent (1,363 cases) in the month after the draft guideline was issued. It continued to drop to an overall decline of 28 percent in the year after the draft guideline was issued. The diagnoses of low, intermediate and high-risk prostate cancers all decreased significantly, but diagnoses of prostate cancer that had spread beyond the prostate did not change, they found. The decreases were similar for all ages, races, income and insurance.

the year after the guidelines were published, diagnoses of new low-risk cancers dropped nearly 38 percent and continued to fall more rapidly than diagnoses of more aggressive cancer. This suggests that for low-risk cancer, the guideline had its intended effect, Barocas said. In addition, prostate cancer diagnoses fell by 23-29 percent among men over 70 and by 26 percent

among men who were not likely to live long enough to benefit from early diagnosis and treatment, the researchers found.

However, researchers also found a drop of 28 percent in diagnoses of intermediate-risk cancer and a 23 percent drop in diagnoses of high-risk cancer one year after the guideline was published. "These findings are consistent with what we hoped would not happen," D'Amico said. It is likely that such men will develop more advanced prostate cancer before it is diagnosed and be less likely to be cured, he added. "This is a warning that we are not picking up patients who are curable," D'Amico said. (Source: Health Day News, September 22, 2015)

Patient Understanding of Cost/Benefit and End-of-Life Treatments (Canada). Cost of medications for castrate-resistant prostate cancer (CRPC) range from $24,000 to $93,000 per year. The Canadian system is unique where the medications are provided free of charge rather than at a cost to the patients as is the case in the United States.

A group from Toronto conducted surveys to assess: patients' general understanding of castrate-resistant prostate cancer (CRPC); patient opinions on costs/benefit of currently marketed CRPC drugs; and to assess if/when patients would forego CRPC drug therapy in a medical system where most drugs are provided free of charge. Patients were also asked if they would refuse any further treatment in exchange of one-time end-of-life premium of $50,000.

One hundred and three patients completed the survey. CRPC was not understood by 79% of respondents. Most felt abiraterone was helpful and should be offered to all patients (71%). 65% felt enzalutamide should be offered for abiraterone failures despite any evidence of efficacy. Only 30% felt alpharedin was helpful at all.

Despite any evidence, a majority (58.2%) felt combination medications should be given even if the costs exceeded $250,000. However, out-of-pocket scenarios shifted opinions. If patients had to pay, only 29% were willing to exceed $40,000. More than 60% of patients would forego any therapy for a $50,000 one-time premium. Better educated/higher income patients were more likely to undervalue the benefit of CRPC drugs and take the end-of life premium.

The researchers concluded that a large gap exists between patient understanding of CRPC prognosis and drug value. Patients overvalue drugs when paid by third parties but see less value if they have to pay "out-of-pocket." More realistic discussion between CRPC patients and their doctors about benefits of CRPC drugs are needed. (Source: Presentation. Amer Uro Assn Annual Meeting, May 15-19, 2015, via Uro Today)

Artificial Urinary Sphincter versus theTransobdurator Sling. This study compared continence outcomes in patients with post-prostatectomy stress urinary incontinence treated with a salvage artificial urinary sphincter versus a secondary transobturator sling. It retrospectively reviewed the records of patients undergoing salvage procedures after sling failure from 2006 to 2012. Postoperative success was defined as the use of 0 or 1 pad, a negative stress test and pad weight less than 8 gm per day. We performed the Wilcoxon test and used a Cox regression model and Kaplan-Meier survival analysis.

A total of 61 men presenting with sling failure were included in study, of whom 32 went directly to an artificial urinary sphincter and 29 received a secondary sling. Of the artificial urinary

sphincter cohort, 47% underwent prior external beam radiation therapy versus17% of the secondary sling cohort . Average preoperative 24-hour pad weight and pad number were higher in the artificial urinary sphincter cohort. Median follow-up in artificial urinary sphincter and secondary sling cases was 4.5 and 4 months, respectively. Overall treatment failure was seen in 55% of patients (16 of 29) with a secondary sling vs 6% (2 of 32) with an artificial urinary sphincter.

In summary, patients who experienced failure with a primary sling, and who then had a secondary sling procedure were up to 6 times more likely to have persistent incontinence versus those who underwent artificial urinary sphincter placement. These data are useful for counseling patients and planning surgery. The study currently recommends placement of an artificial urinary sphincter for patients in whom an initial sling has failed. (Source: Journal of Urology, September 14, 2015)

Radical Prostatectomy versus Brachytherapy (Canada). Radical prostatectomy (RP) and low-dose-rate brachytherapy are two of the most common modalities for prostate cancer treatment, but studies comparing these two treatment modalities are scarce.

This study examined patterns of recurrence and estimated the local recurrence rate after brachytherapy using a prospective population-based database. At a median follow-up of 5 years, 109 of 2,223 patients treated with brachytherapy developed biochemical relapse. Thus, the crude rate of any disease relapse was 4.9%. Of these 109 patients with relapse, the site of first recurrence was established in 48 cases, in which 18 of 2,223 (0.8%) were local, and 30 of 2,223 (1.3%) were distant. Of the remaining 61 of 2,223 patients, 93% had digital rectal exams, 30% had post-treatment biopsies, 74% had bone scans, and 56% had CT imaging of the abdomen and pelvis, all of which failed to identify a site of recurrence.

It was necessary to determine the local recurrence rate after brachytherapy. We concluded that the local recurrence rate after brachytherapy in British Columbia could be as low as 0.8% or as high as 4.9%, but most likely ranged from 1.8-2.7%.

For comparison, we estimated the rate of local relapse after RP in British Columbia, based on surgical pathology and data from randomized control trials. This suggests that the local recurrence rate after RP for pT2 disease in British Columbia is approximately 7.5%. In all likelihood, this 7.5% is an underestimate of the true local recurrence rate after RP because it does not account for local relapses that would have been salvaged in the observation arm, nor for the isolated local relapses that postoperative RT would not have cured.

The limitations in the estimates of local recurrence rates after brachytherapy and after RP need to be considered. There were several technical considerations in calculating local recurrence rates. Also, several assumptions were made for which there was no direct evidence. In the context of the limitations of our study design, this population-based analysis indicates that the local recurrence rate after brachytherapy appears to be as low or lower than that following RP in our jurisdiction. Further research is required to determine whether this finding can be generalized to other institutions and populations.

Androgen Deprivation and the Risk of Venous Thromboembolism - (UK). Few observa-

and venous thromboembolism (VTE) in patients with prostate cancer (PCa).

This study attempts to determine whether the use of different types of ADT in patients with PCa is associated with an increased incidence of VTE. A population-based cohort study was conducted using the UK Clinical Practice Research Datalink. The cohort consisted of men newly diagnosed with PCa between April 1, 1998, and March 31, 2014 who were hospitalized for VTE associated with current and past ADT use compared with nonuse. A secondary analysis was conducted to assess the risk with current use of specific types of ADT.

The cohort included 21,729 patients, of whom 609 were hospitalized for VTE during follow-up. Current ADT use was associated with an 84% increased risk of VTE , but there was no association with past use. In the secondary analysis, most types of ADT were associated with a high risk of VTE. Residual confounding is possible given the observational nature of the study.

Conclusion: This study investigated whether androgen deprivation therapy was associated with the risk of blood clots in a cohort of patients with prostate cancer. It found that the risk was nearly doubled in patients who used ADT compared with those who never used it. This treatment should be reserved for patients for whom the benefits outweigh the risks. (Source: European Urology, June 29, 2015, via UroToday, June 29, 2015)

CT Scans and Cellular Damage in Patients. Cellular damage occurs when people undergo computed tomography (CT) scans, but whether or not this causes cancer or any other health problems is unclear. Nguyen, et al., Stanford Cardiovascular Institute, California, examined the blood of 67 people before and after they had undergone cardiac computed tomographic angiography. After the scans, the research did show an increase in DNA damage in cells, as well as cell death. There was also increased expression of genes involved in the repair or death of cells, the researchers found. Most cells damaged by the CT scan were repaired.

The report noted that researchers didn't find any DNA damage in healthy people who were of average weight who had the lowest doses of radiation during their CT scans. Still, the team noted that a CT scan exposes patients to at least 150 times the amount of radiation from a single chest X-ray. And in 2007, the U.S. National Cancer Institute predicted that 29,000 future cancer cases could be linked to the 72 million CT scans performed in the country that year alone."We now know that even exposure to small amounts of radiation from scanning is associated with cellular damage," study author Patricia Nguyen, MD, an assistant professor of cardiovascular medicine at Stanford, said in a university news release. However, she added that it's still not clear from this study whether or not this causes cancer or any negative effect to the patient. The findings should encourage physicians to use CT scan dose-reduction strategies. (Source: Healthday News, July 24, 2015)

Active Surveillance: The Swedish Experience. Active surveillance (AS) is an important strategy to reduce prostate cancer overtreatment, but its use is variable worldwide, including the United States, where historically, it has been underutilized.

By contrast, Sweden has complete data on 98% of prostate cancer cases nationwide, and, since 2007, Sweden had classified AS and watchful waiting separately in the country's National Prostate Cancer Register. These contemporary, complete, records provided a useful source for researchers. Loeb, et al., New York University, conducted a close examination of trends in AS

management for favorable-risk prostate cancer. Their data were presented at the recent American Urological Association (AUA) Annual Meeting, held in New Orleans, May 14-19, 2015.

Between the years 2007-2011 in Sweden, 59% of men with very low risk; 41% of low risk; and 16% of intermediate-risk prostate cancers were managed with AS.

In her AUA presentation, Dr. Loeb provided updated statistics on the use of AS for newly diagnosed low and intermediate risk disease in Sweden. From 2011-2013, 16,478 men were diagnosed with very low-, low-, or intermediate-risk prostate cancer in Sweden. For the study population (n=15,478), complete data on tumor features and primary treatment were available.

The investigators used descriptive statistics and tests for trend to evaluate the use of AS in the study period across clinical risk categories (very low, low, and intermediate risk), then estimated the proportion of men who met six published criteria for AS who actually received AS. Results of the study revealed that 84% of very low-risk prostate cancer and 66% of low risk were receiving active surveillance as of 2013.

The researchers concluded that prompt treatment is very important for life-threatening cases. Early diagnosis and treatment is the only way to cure men with life-threatening disease. But for men with low-risk disease, we should be better about very careful patient selection for treatment, to try to reduce the burden on patients. The United States has traditionally been lagging in this regard, Dr. Loeb added. “The often quoted number is that less than 10% in the U.S. were receiving surveillance, but those numbers are very old at this point. There is a publication of SEER Medicare from 2006 to 2009 saying that the percentage of men receiving active surveillance was about 19% of low-risk patients.” This number is starting to increase. The effort in the U.S. is finally starting to catch up with what has been achieved already in Sweden.
(Source: Uro Today, May 20, 2015)

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(A Decade of Change - continued from page 1)

In 2004, the U.S. Food and Drug Administration (FDA) approved docetaxel after the publication of two random-controlled trials, one of which was led by a PCF clinical investigator.

Over the past decade, the FDA has approved the pure luteinizing hormone–releasing hormone antagonist degarelix (Firmagon); the first immunotherapy for prostate cancer, sipuleucel-T (Provenge); and a taxane-based chemotherapy, cabazitaxel (Jevtana). The FDA also approved denosumab (Prolia/Xgeva) as a treatment to increase bone mass in patients at high risk for fracture receiving androgen-deprivation therapy (ADT).

Enzalutamide (Xtandi) has been approved to treat men with metastatic castration-resistant prostate cancer that has spread or recurred, even with medical or surgical therapy to minimize testosterone. Enzalutamide was approved for patients who have previously been treated with docetaxel.

In May 2013, the FDA approved radium Ra 223 dichloride (Xofigo) to treat symptomatic late-stage metastatic castration-resistant prostate cancer that had spread to bones, but not to other organs. “Provenge and radium 223 dichloride have helped a lot for patients in the late stages of the disease,” Dr. D'Amico told *Cancer Therapy Advisor*. “In the future, we hope to do more than just extend life more than several months in late stage disease.”

Yair Lotan, MD, professor of urology and chief of urologic oncology at University of Texas Southwestern Medical Center, in Dallas, TX, said no one agent has been a home run, even though there have been significant advances in the past decade.

“The advancements of the past decade have been mostly small incremental changes. Each of the new therapies provides modest survival benefits, 3 to 4 months,” Dr. Lotan told *Cancer Therapy Advisor.* “There is still a desperate need for effective therapy for patients with castrate-resistant prostate cancer and it is unclear whether this will be provided by novel targeted therapies.”

Tomasz Beer, MD, who is chair for prostate cancer research and the deputy director of the Oregon Health & Science University, Portland, OR, said clinicians should be cautious when analyzing the 5- and 10-year survival numbers. He said while treatment improvements are partly responsible for better outcomes, a part of this trend reflects early diagnosis and stage migration. “Having said that, there have been major advances; the most notable of which is the development of two new drugs that target androgen receptor signaling, abiraterone and enzalutamide. But in total six agents that extend survival have been approved, approximately five in the last 5 years. That is real progress,” Dr. Beer told *Cancer Therapy Advisor.*

He added “Further, and importantly, we have learned that earlier use of chemotherapy in metastatic, but hormone-responsive disease substantially magnified the benefits of chemotherapy. Taken together, the early application of chemotherapy coupled with compelling new androgen receptor signaling inhibitors have transformed the management of advanced disease.” Measuring circulating tumor cells (CTC) following first-line therapy is changing how patients are managed. This past year, researchers reported that detection of androgen-receptor splice variant 7 messenger RNA (AR-V7) in CTC from men with advanced prostate cancer may be associated

with resistance to enzalutamide and abiraterone. “The biggest changes in the landscape of advanced prostate cancer include discovery of CTC, genetic testing on them (AR-V7), improvement in overall survival from various drugs like abiraterone, enzalutamide, radium-223, sipuleucel-T, and cabazitaxel. The most striking data are from the ECOG-3805 trial, which changed the standard of care for de novo metastatic prostate cancer by adding six cycles of docetaxel to ADT. This significantly changed the overall survival,” said Saby George, MD, an assistant professor of oncology at Roswell Park Cancer Institute, in Buffalo, NY.

Novel agents that work by different mechanism and are matched to genetic signatures may soon significantly change the management of metastatic prostate cancer. Gerald Andriole, MD, chief of urologic surgery at Washington University School of Medicine in Saint Louis, MO, said experimental therapeutic vaccines and check-point inhibitors are showing promise and may soon be part of the armamentarium.

Recently, researchers discovered that cytotoxic T lymphocyte antigen 4 (CTLA-4) is a receptor on the surface of T cells that blocks the immune response by inhibiting T cell activation. Now, studies are looking at whether an antibody (anti–CTLA-4) can block the “immune checkpoint” protein.

"More complete obliteration of the androgenic pathways has played a major role for men with advanced prostate cancer. Going forward, efforts to better understand the role of immunotherapy with vaccines, checkpoint inhibitors, and other approaches, hold great promise, and may be applied to men with earlier stages of prostate cancer," Dr. Andriole told *Cancer Therapy Advisor*.

Dr. George said there is a strong possibility that prostate cancer could become a manageable chronic disease. However, he said it is important that clinicians not give their patients false hope. Dr. George said many patients may mistakenly have too high of expectations based on recent reports about precision medicine and what it can and cannot do.

“Precision medicine is a loose term. The clinical development of second-line hormonal manipulation like enzalutamide and abiraterone are examples of how to optimize the targeting of the androgen receptor signaling axis. There needs to be a lot more development to make this disease a chronic disease. Cure is an elusive term in advanced prostate cancer as of today,” Dr. George told *Cancer Therapy Advisor*. (Source: Cancer Therapy Advisor, September, 2015)

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♦ WRNMMC US TOO COUNSELORS ♦ (As of November 1, 2015)

(THESE PERSONS ARE WILLING TO SHARE THEIR EXPERIENCES WITH YOU. FEEL FREE TO CALL THEM.)

SURGERY

Tom Assenmacher	Kinsvale, VA	(804) 472-3853	
Jack Beaver	Falls Church, VA	(703) 533-0274	1998 (Open RP)
Rob Calhoun	Annapolis, MD	(410) 293-6635	2011 (Robotic Surgery)
Gil Cohen	Baltimore, MD	(410) 367-9141	
Richard Dorwaldt	San Antonio, TX	(210) 310-3250	(Robotic Surgery)
Michael Gelb	Hyattsville, MD	(240) 475-2825	(Robotic Surgery)
Robert Gerard	Carlisle, PA	(717) 243-3331	
Tony Giancola	Washington, DC	(202) 723-1859	2008 (Radical Prostatectomy)
Ray Glass	Rockville, MD	(301) 460-4208	
Monroe Hatch	Clifton, VA	(703) 323-1038	
Tom Hansen	Bellevue, WA	(425) 883-4808	1998 (Robotic Surgery)
Bill Johnston	Berryville, VA	(540) 955-4169	
Dennis Kern	San Francisco, CA	(415) 876-0524	
Sergio Nino	Dale City, VA	(703) 590-7452	
Ed Postell	Collegeville, PA	(610) 420-6765	(Robotic Surgery)
George Savitske	Hellertown, PA	(703) 304-3081	2000 (Open RP)
Artie Shelton, MD	Olney, MD	(301) 523-4312	
Jay Tisserand	Carlisle, PA	(717) 243-3950	

PROSTATE CANCER AND SEXUAL FUNCTION

James Padgett	Silver Spring, MD	(301) 622-0869	
George Savitske	Hellertown, PA	(703) 304-3081	

RADIATION

Leroy Beimel	Glen Burnie, MD	(410) 761-4476	1987 (External Beam Radiation)
Bob Bubel	Grand Junction, CO	(970) 263-4974	2010 (Proton Beam Radiation)
Harvey Kramer	Silver Spring, MD	(301) 585-8080	1998 ((Brachytherapy)
Joseph Rosenberg	Kensington, MD	(301) 495-9821	2009 (Brachytherapy)
Barry Walrath	McLean, VA	(571) 969-8269	2001 (Brachytherapy)

WATCHFUL WAITING

Tom Baxter	Haymarket, VA	(703) 753-8583	Active Surveillance

SPOUSE SUPPORT

Renate Bubel	Fairfax, VA	(703) 280-5765
Karen Collins	Mechanicsburg, PA	(717-766-6464
Betty Kramer	Silver Spring, MD	(301) 585-8080
Ellen Rosenberg	Kensington, MD	(301) 495-9821
Nancy Wallrath	McLean, VA	(703) 915-8108

OTHER THERAPIES/MULTIPLE THERAPIES

Howard Bubel	Fairfax, VA	(703) 280-5765	1995,1996 (Hormonal, Cryosurgery, Sexual Function
Arthur E. Clough	Kerryville, TX	(830) 896-8826	1993 (Surgery and Radiation)
Pete Collins	Mechanicsburg, PA	(717) 766-6464	2007, 2009 (Surgery, Radiation, Hormonal)

♦ MEETING ANNOUNCEMENT ♦

THURSDAY, NOVEMBER 5, 2015

7:00 - 8:30 PM

AMERICA BUILDING (2D FLOOR)
ROOM 2525
(DIRECTLY ABOVE THE LAB/PHARMACY)

WALTER REED NATIONAL MILITARY MEDICAL CENTER

♦ SPEAKER ♦

TIMOTHY J. TAUSCH, MD

DEPARTMENT OF UROLOGY, WRNMMC

TOPIC

"PROSTATE CANCER SURVIVORSHIP:
URINARY INCONTINENCE AFTER THERAPY"

Gate/Parking: If you enter the base through South Gate (Gate 2) off Rockville Pike/Wisconsin Avenue, take the first right (Palmer Road South). On your left will be the Emergency Room. Continue to follow signs to the America Building and the America parking garage.

Security: A military ID card is required to get on base. Persons without a military-related ID card who are attending the meeting are required to register in advance in order to gain entry. To register, contact the CPDR front desk at 301-319-2900 at least four business days prior to Thursday, May 7, 2015, to arrange entry. Have a photo ID card ready when arriving at the gate