INSIDE THIS ISSUE

Us TOO® PROSTATE CANCER EDUCATION & SUPPORT

HOTSHEET

DECEMBER 2013

THE PHASE 3 PREVAIL TRIAL OF ENZALUTAMIDE MEETS BOTH CO-PRIMARY ENDPOINTS OF OVERALL SURVIVAL AND RADIOGRAPHIC PROGRESSION-FREE SURVIVAL IN CHEMOTHERAPY-NAIVE PATIENTS WITH ADVANCED PROSTATE CANCER

Medivation, Inc. and Astellas Pharma Inc. announced that the Independent Data Monitoring Committee (IDMC) has informed the companies of positive results from a planned interim analysis of the global Phase 3 PREVAIL trial of enzalutamide (ENZ) in more than 1,700 men with metastatic prostate cancer progressing despite androgen deprivation therapy and having not received chemotherapy. Given the observed benefits in the trial's co-primary endpoints of overall survival (OS) and radiographic progression-free survival (RPFS), and considering the observed safety profile, the IDMC concluded ENZ demonstrated a favorable benefit-risk ratio. The IDMC recommended the study be stopped and men treated with placebo be offered ENZ. Additional data from the Phase 3 PREVAIL results, including safety data, will be submitted for presentation at an upcoming medical conference.

The IDMC informed the companies of the following results:

- Men treated with ENZ showed a statistically significant OS advantage

(Continued on page 3)

PROSTATE CANCER TOPS THE LIST OF INHERITABLE CANCERS

One legacy that most men could do without is an inherited risk for prostate cancer, but a massive cohort study shows that for some men, genetic history hints at oncologic destiny.

Data on both identical (monozygotic) and fraternal (dizygotic) twins from the comprehensive birth-to-death registries in Denmark, Finland, Norway, and Sweden show that a man whose monozygotic twin has prostate cancer has a 32% risk for the disease himself, whereas a dizygotic twin whose brother has prostate cancer has only a 16% risk, said Jaakko Kaprio, MD, PhD, professor of genetic epidemiology at the University of Helsinki. Results were presented at the American Society of Human Genetics (ASHG) 63rd Annual Meeting, on 23 October 2013.

The estimated heritability of prostate cancer – the degree to which genes contribute to risk – was 58% (95% confidence interval, 52–63), which is the highest for any malignancy studied, Dr. Kaprio reported at the American Society of Human Genetics 63rd Annual Meeting.

Dr. Kaprio's team looked at data on 133,689 monozygotic and dizygotic pairs as part of the Nordic Twin Registry of Cancer. They used time-to-event analysis to estimate heritability and familial cancer risk.

(Continued on page 4)

EXPERTS PROPOSE WAYS TO BOOST ENROLLMENT IN CANCER TRIALS

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

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

Being able to enroll in a clinical trial should not be dependent on living in a large city that has a teaching hospital either, he told Medscape Medical News. "Clinical trials need to be offered to patients everywhere, including rural areas, not only to patients at major cancer centers." Clinical trials are the foundation for advancing cancer care, yet so few cancer patients are able to participate, he added. "This is a big problem for society."

Dr. Meropol co-chaired a recent symposium, sponsored by the NCI and ASCO, to develop recommendations for overcoming issues related to the accrual of cancer patients in clinical trials. The symposium, entitled Cancer Trial Accrual Symposium: Science and Solu-

(Continued on page 4)

THIS ISSUE OF THE US TOO PROSTATE CANCER HOTSHEET IS MADE POSSIBLE BY CHARITABLE CONTRIBUTIONS FROM

Genentech
IN BUSINESS FOR LIFE

Takeda MILLENNIUM
THE TAKEDA ONCOLOGY COMPANY

BAVARIAN NORDIC

AND PEOPLE LIKE YOU!

5003 FAIRVIEW AVE. DOWNER'S GROVE, IL 60515
PHONE: (630) 795-1002 / FAX: (630) 795-1602

WEBSITE: WWW.USTOO.ORG

INCREMENTAL DETECTION RATE OF PROSTATE CANCER BY HI-REAL TIME ELASTOGRAPHY TARGETED BIOPSIES IN COMBINATION TO A CONVENTIONAL 10 CORE BIOPSY IN 1024 CONSECUTIVE MEN

Salomon G, Drews N, Autier P, et al

BJU Int 15 October 2013; Epub

Objectives: To quantify the incremental detection rate of a targeted biopsy in addition to a randomized 10-core biopsy.

Material and Methods: This retrospective study analyzed 1024 patients who consecutively underwent a 4-core real time Elastography targeted biopsy (RTE) in addition to a randomized 10-core transrectal ultrasound (TRUS) guided biopsy in a primary or rebiopsy setting. Overall detection rate and detection rate of 10-core randomized, RTE guided biopsy and incremental detection rate have been calculated.

Results: Overall, randomized and RTE targeted biopsies detection rates were 46.2 % (n=473), 39.1 %(n=400) and 29.0 % (n=297) for the combination, the 10 core and RTE-4 core biopsy scheme, respectively. RTE-4 core targeted biopsies found an additional 73 patients (increase in overall detection rate by 7.1%). Of those, 34 patients harbored significant Gleason 4 or 5 PCa, diagnosed by RTE-4 biopsy only. Moreover, PCa with a Gleason grade of 4 or 5 was detected by RTE-4 biopsies in 30 patients, who showed low grade PCa ≤ Gleason 3 only in systematic 10 core biopsy. These were not detected by the 10-core randomized biopsies. Therefore, RTE-4 core targeted biopsies incremented men diagnosed with PCa by 18.3%. Incremental detection rate was better in re-biopsy patients (24.8%) compared to patients having their first biopsy (14.7%).

Conclusions: RTE targeted biopsies seems to be an appropriate method to increase detection rate of PCa. Nevertheless, RTE targeted biopsies missed a high proportion of patients with PCa and should therefore be considered as an addition to randomized biopsies.

MEN (AGED 40-49 YEARS) WITH A SINGLE BASELINE PROSTATE-SPECIFIC ANTIGEN BELOW 1.0 NG/ML HAVE A VERY LOW LONG-TERM RISK OF PROSTATE CANCER: RESULTS FROM A PROSPECTIVELY SCREENED POPULATION COHORT

Christopher J. Weight CJ, Kim SP, Jacobson DJ, McGree ME, Karnes RJ, St. Sauver J

Urology 19 October 2013, Epub

Objective: To study the use of a baseline prostate-specific antigen (PSA) and digital rectal examination in men (aged 40-49 years) in predicting long-term prostate cancer risk in a prospectively followed, representative population cohort.

Patients and Methods: Since 1990, a random sample of men in Olmsted County (aged 40-49 years) has been followed up prospectively (n = 268), with biennial visits, including a urologic questionnaire, PSA screening, and physical examination. The ensuing risk of prostate cancer (PCa) was compared using survival analyses.

Results: Median follow-up was 16.3 years (interquartile range 14.0-17.3, max 19.1). For men with a baseline PSA <1.0 ng/mL (n = 195), the risk of subsequent Gleason 6 PCa diagnosis by 55 years was 0.6% (95% confidence interval [CI] 0%-1.7%) and 15.7% (95% CI 6.5%-24.9%) for men with a baseline PSA ≥1.0 ng/mL. No man with a low baseline PSA developed an intermediate or high risk PCa, whereas 2.6% of men with a higher baseline PSA did (95% CI 0.58%-4.6%).

Conclusion: Men (aged 40-49 years) can be stratified with a baseline PSA. If it is below 1.0 ng/mL, there is very little risk for developing a lethal PCa, and as many as 75% of men might be able to avoid additional PSA screening until 55 years. Conversely, men aged 40-49 years with a baseline PSA level >1.0 ng/mL had a significant risk of CaP diagnosis and should be monitored more closely.

FOR THE FIRST TIME ORIGINS OF LETHAL PROSTATE CANCER TRACKED

For the first time, researchers have traced the development of lethal prostate cancer, from the primary cancer to metastases, in a man who died from the disease. The innovative effort was enabled by whole-genome sequencing and molecular pathological analyses.

The research provides "proof-of-concept of the potential importance of molecular staging and grading strategies, in conjunction with existing pathological criteria, to accurately inform clinical decision making in precision medicine," write the authors, led by Michael C. Haffner, MD, from Johns Hopkins University in Baltimore, MD. The work was published in the November issue of the *Journal of Clinical Investigation* (Vol. 123, pp. 4918–4922, 2013).

The patient in question was diagnosed with prostate cancer when he was 47 years old. His entire primary tumor and a single involved lymph node metastasis was removed with radical prostatectomy, but an elevated PSA level 5 years after the surgery suggested the disease was systemic. He received the investigational prostate cancer vaccine GVAX, androgen ablation, systemic chemotherapy, and localized radiation. Despite these treatments, the patient died at the age of 64 from castrate-resistant prostate cancer, 17 years after his initial presentation.

The researchers used tissue samples taken throughout the progression of the cancer and at the time of death to identify the origin of the lethal clone. They were surprised to find that the lethal clone originated from a small low-grade focus in the primary tumor, and not from the larger higher-grade primary tumor or from the lymph node metastasis resected at prostatectomy.

Dr. Haffner and his group note that prostate cancer is highly heterogeneous, with manifestations that range from indolent localized tumors to widespread metastases. "Given recent controversies surrounding overtreatment of prostate cancer, there is a critical need to understand the features of the primary tumor that are associated with progression to lethal disease," they write.

(Continued on page 8)

PHASE 3 PREVAIL TRIAL OF ENZALUTAMIDE *(Continued from page 1)*

compared with men given placebo (p <0.0001). ENZ provided a 30% reduction in risk of death compared to placebo (Hazard Ratio [HR] = 0.70; 95% confidence interval [CI], (0.59-0.83).

- ENZ treatment demonstrated a statistically significant RPFS advantage compared with placebo (p <0.0001). ENZ provided an 81% reduction in risk of radiographic progression or death compared with placebo (HR = 0.19; 95% CI, 0.15-0.23).
- The percentage of men alive in the ENZ arm was 72% vs 65% in the placebo arm at the time of the interim analysis. ENZ treatment resulted in a calculated point estimate for median OS of 32.4 months (95% CI, 31.5 months-upper limit not yet reached) vs 30.2 months (95% CI, 28.0 months -upper limit not yet reached) for men receiving placebo. Because the trial will be stopped early with the majority of men still alive, the estimated median survivals are not as precise as the HR. The HR takes into account available information about the trial endpoint from all men whereas the median is a single point estimate of a much smaller number of men at risk.
- The median RPFS was not yet reached (95% CI, 13.8 months-upper limit not yet reached) in the ENZ arm and was 3.9 months (95% CI, 3.7-5.4) in the placebo arm.
- Given the OS benefit and the observed safety profile, the IDMC considered the overall benefit-risk ratio to favor the ENZ arm and recommended unequivocally that men receiving placebo be offered ENZ.

Of the 1,715 men treated in the blinded PREVAIL study, two men were reported by investigators to have had a seizure event. The full analysis of the safety data will become available upon final database lock and unblinding.

"To my knowledge, the benefits in OS and RPFS reported in the PREVAIL trial are unprecedented in this patient population," said Tomasz M. Beer, MD, FACP, professor of medicine and deputy director of the Knight Cancer Institute at Oregon Health & Science University, and the co-principal investigator of the PREVAIL study.

"Achieving statistically-significant and clinically meaningful results in both co-primary endpoints - OS and RPFS is an important outcome for patients and we are excited by the results of the Phase 3 PREVAIL trial," said David Hung, MD, founder, president and CEO, Medivation. "I extend my sincere thanks to the patients, physicians, study teams and other collaborators around the world, who have been instrumental in helping us achieve this important milestone."

Sef Kurstjens, MD, PhD, Chief Medical Officer of Astellas added, "we are committed to being at the forefront of the fight against prostate cancer by providing patients with treatment options to help them manage their disease."

Discussions with regulatory agencies will begin in early 2014.

Company news release, 22 October 2013

CLINICAL BENEFITS OF NON-TAXANE CHEMOTHERAPIES IN UNSELECTED SYMPTOMATIC METASTATIC CASTRATION-RESISTANT PROSTATE CANCER PATIENTS AFTER DOCETAXEL: THE GETUG P02 STUDY

Joly F, Delva R, Mourey L, et al

BJU Int 1 November 2013 [Epub]

Objective: To evaluate the overall benefits of non-taxane chemotherapies in a non-selected population including unfit patients presenting with symptoms and pain.

Patients and Methods: This randomised phase 2 study reports data from 92 patients (52% > 70 yrs-old; 40% with performance status II) previously treated with taxane-based chemotherapy and collected at 15 centres in France. Patients received intravenous mitoxantrone (MTX), oral vinorelbine (VN), or oral etoposide (EP) associated with oral prednisone. Palliative benefit (pain response without progression of the disease), biological and tumoral responses, and toxicity profile as well as geriatric assessment (in elderly population) were analysed on an intention-to-treat basis.

Results: The palliative response rate was 17% for the whole population, and reached 29% when considering the MTX arm. The control of pain was achieved in 40% of the patients. The median overall survival was 10.4 months, and was longer in palliative responders. Few grade 3-4 toxicities were observed. The subgroup analysis of elderly patients showed similar results regarding the number and dose-intensity of treatments, efficacy and safety.

Conclusion: In a population including frailty and/or elderly patients, who are poorly represented in most of the clinical studies, non-taxane chemotherapy may remain a relevant option for metastatic prostate cancer having relapsed after a docetaxel-based regimen. While new treatment options are now approved, decision-making process should take into account the expected benefit/risk ratio based on the patient status.

BOOSTING ENROLLMENT IN CANCER TRIALS *(Continued from page 1)*

tions, brought together more than 350 cancer research experts, including clinical investigators, researchers of accrual strategies, research administrators, nurses, research coordinators, patient advocates, and educators. The recommendations were published online October 15 in the Journal of Oncology Practice.

Less than 5% of cancer patients actually get to participate in clinical trials. Much has already been written about barriers to enrollment in trials, Dr. Meropol said. One important one is at the patient level.

"Patients fear randomization or getting a placebo. Or they simply are unaware that clinical trials exist," he said. Barriers to accrual at the patient and community level, at the physician and provider level, and at the site level (where clinical trials are organized) were addressed at the symposium. "All of these areas need to be targeted. If we do this, we will accelerate accrual to trials and advance cancer care," said Dr. Meropol.

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

At the physician and provider level, there is a lot doctors can do to promote access to clinical trials, Dr. Meropol said. "We need to do a better job talking to our patients about clinical trials in a culturally sensitive way," he noted. "We need to educate physicians how to talk to patients."

The recommendations for physicians and providers include developing evidence-based training initiatives to improve communication and disseminating the availability of local trials to primary care providers. One way to do this is with information technology, such as registries and electronic health records.

At the organizational level, where clinical trials originate, it is imperative that we create a culture that acknowledges the importance of clinical trials and gives incentives for accrual, Dr. Meropol said. Recommendations at this level include promoting accrual via leadership best practices, such as establishing a culture of commitment to clinical trials and adopting formal quality-improvement processes to increase the efficiency of opening and conducting trials.

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

Medscape Medical News, 25 October 2013

HEREDITARY CANCER

(Continued from page 1)

The magnitude of the genetic contribution to prostate cancer found in this study is higher than the estimated 42% seen in a previous study of Nordic twins. Dr. Kaprio explained that this difference can be attributed to the fact that his team expanded the original cohort to include data from Norway, had 10 additional years of follow-up data, and had an aging cohort, with a resultant increase in incident cancers.

This study raises important questions about the interplay between genetics and environment in cancer, said Richard Stevens, PhD, professor of cancer epidemiology at the University of Connecticut Health Center in Farmington, CT. The study supports the presence of genetic polymorphisms in prostate cancer that can cumulatively contribute to risk.

"The specific polymorphisms we're aware of – familial syndromes – account for very little breast cancer or prostate cancer. There are other genes where allelic variation and risk is moderate. There must be a lot of those genes with moderate risk; you put them together and it makes you more susceptible," Dr. Stevens said.

Medscape Medical News, 29 October 2013

TESTOSTERONE TREATMENTS LINKED WITH HEART RISKS

Testosterone treatments may increase risks for heart attacks, strokes and death in older men with low hormone levels and other health problems, a big Veterans Affairs study suggests. The results raise concerns about the widely used testosterone gels, patches or injections heavily marketed for low sex drive, fatigue and purported anti-aging benefits, the authors and other doctors said.

Previous studies on the supplements' health effects have had mixed results, with some research suggesting potential heart benefits but none of the studies has been conclusive. The new study was published Tuesday in the Journal of the American Medical Association (JAMA Vol. 310, pp. 1829–1836, 2013).

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

Nearly 26 percent of men using testosterone had one of the bad outcomes within three years of the heart test, compared with 20 percent of nonusers. Men who used testosterone were 30 percent more likely to have a heart attack or stroke or to die during a three-year period. It's unclear how the hormone might increase heart risks but possibilities include evidence that testosterone might make blood substances called platelets stick together, which could lead to blood clots, the study authors said.

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

An editorial in the journal stated that it is uncertain if the study results apply to other groups of men, including younger men using the hormone for supposed

(Continued on page 6)

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

"Eat the rainbow or pick more brightly colored fruits and veggies to get more health benefits" WRONG! BUZZER B.S. (Bogus Science) Alert! SORRRRRY!!"

Mark A. Moyad, MD, MPH, Univ. of Michigan Medical Center, Dept. of Urology

Editors' note: Us TOO has invited certain physicians and others to provide information and commentary for the *HotSheet* to enrich its content to empower the reader. This column contains the opinions and thoughts of its author and is not necessarily those of Us TOO International.

Bottom Line:

There is such an obsession with the quality of fruits and veggies consumed that few folks really refer to the research, which actually suggests it is the QUANTITY up to a certain point and not the quality that can lower the risk of some diseases (such as heart disease) and may impact cancer in my opinion.

In one of the largest epidemiologic studies to date to examine the issue of fruits and veggies and heart disease, a higher intake of fruits and veggies was associated with a lower risk of heart disease (only about 17% -- not dramatic but enough to be semi-excited).[1] Over 71,000 women from the Nurses' Health Study and over 42,100 men from the Health Professionals Follow-Up-Study were followed for over 20 years and over 6000 cases of heart disease cases were diagnosed. It was also interesting that this study documented the effect of a threshold for fruits and veggies whereby up to 5 servings a day provided more protection and beyond 5 servings the impact was basically the same! Yeah! Yeah! This makes me happier than a primary care doctor only having to see 150 patients a day in the current medical system rather than 175 a day (they are over worked and under paid my friends).

Interestingly only 1 other study has looked at fruit and veggie variety and heart disease and again no difference was found for diversity or variety.[2] I will not lie, this study makes me happy because for years I have been writing about how sick and tired I am of "experts" telling folks to eat the rainbow or get as much diversity in your fruits and veggies as possible in order to take advantage of all of the antioxidants! It is sort of like telling people to eat dark chocolate or only drink dark beer because of the antioxidants! I simply have never bought into this line of thinking because it is hard enough to get several servings of fruits and veggies a day (THE NATIONAL AVERAGE IS 3 SERVINGS on a good day, FOLKS)!

What happened to the poor old celery, cucumber, or how about kale? They might not be brightly colored but they have a lot to offer. When you look at an avocado from the outside (boring city!) but when you break it open (Yummy City and you are the mayor). So, while the big push is for bright colors and more expensive fruits and veggies I say the research suggests you should JUST PICK WHAT YOU LIKE because the message is to get them regularly and not be consumed by which ones are best for you! Gee, I wonder why I did not see this story on the nightly news because so many bone headed experts have been feeding this line to the public for years and I cannot imagine them getting up now and saying "Ooopps I got it wrong folks-just eat the fruits and veggies you like."

So, the next time you see me I will be eating a lot of celery and cucumbers with my Buffalo Wild Wings, and I will have a Molson Canadian Beer or Pabst Blue Ribbon and regular chocolate! VIVA CELERY! VIVA CUCUMBERS! VIVA KALE! VIVA EATING THE FRUITS & VEGGIES YOU LIKE AND NOT THE ONES THE "EXPERTS" LIKE FOR YOU!

References:

1. Bhupathiraju SN, Wedick NM, Pan A, et al. Am J Clin Nutr, 2 October 2013, Epub ahead of print.
2. Oude Griep LM, Verschuren WM, Kromhout D, et al. Pub Health Nutr 15:2280-2286, 2012.

STUDY EXPOSES OVERUSE OF RADIOTHERAPY SERVICES WHEN UROLOGISTS PROFIT BY SELF-REFERRAL

IMRT use is 2 ½ times greater when self-referrer's financial incentives are involved

A comprehensive review of Medicare claims for more than 45,000 patients from 2005 through 2010 found that nearly all of the 146 percent increase in intensity- modulated radiation therapy (IMRT) for prostate cancer among urologists with an ownership interest in the treatment was due to self-referral, according to new research, "Urologists' Use of Intensity-Modulated Radiation Therapy for Prostate Cancer," published in *The New England Journal of Medicine* (NEJM) last month (N Engl J Med Vol. 369, pp. 1629–1637, 2013). This study corroborates the increased IMRT treatment rates among self-referrers reported in the Government Accountability Office's (GAO) August 2013 report, "Medicare: Higher Use of Costly Prostate Cancer Treatment by Providers Who Self-Refer Warrants Scrutiny."

Authored by Jean M. Mitchell, PhD, economist and professor at the McCourt School of Public Policy at Georgetown University, the NEJM manuscript provides an intricate analysis of treatment patterns by urologists before and after they acquired ownership of IMRT services, compared to the treatment patterns of non-self-referring urologists and urologists who practice at National Comprehensive Cancer Network® (NCCN®)-designated cancer centers (also non-self-referrers).

The two cohorts for the NEJM study data, obtained through Medicare claims from January 1, 2005 through December 31, 2010, include Medicare patients in 26 geographically dispersed states who were (1) treated at 35 self-referring urology groups in private practice matched to a control group of 35 non-self-referring urology groups in private practice, for a total of 38,765 patients; and (2) treated by 11 self-referring urology groups in private practice within close proximity to and matched directly to non-self-referring urologists at 11 NCCN® centers, for a total of 6,713 patients. Patient records were followed for a period of six months from the initial prostate cancer diagnosis to track treatment choices. Sixty percent of the self-referring urologists established their IMRT services during the period from January 1, 2008 through January 15, 2010.

A difference-in-differences analysis was used to isolate the impact of self-referral on changes of IMRT utilization over time, according to self-referral status. This approach controls for initial differences in practice patterns during the pre-ownership period as well as secular trends that affect the use of IMRT and are unrelated to ownership status. The analysis found that:

- IMRT utilization among self-referring groups increased from 13.1 percent to 32.3 percent once they became self-referrers, an increase of 19.2 percentage points (146 percent). In contrast, IMRT utilization by non-self-referring urologists who were peers practicing in the same community-based setting was virtually unchanged—with a modest increase of 1.3 percentage points. Therefore, the difference-in-differences analysis reveals that self-referral accounts for 93 percent of the growth in IMRT.

- IMRT utilization among the subset of 11 self-referring urology practices near NCCN® centers increased from 9 percent to 42 percent, an increase of 33 percentage points (367 percent), from the pre-ownership to the ownership period, compared to an insignificant increase of 0.4 percentage points at the NCCN® centers.

- In addition to increased IMRT utilization, the data demonstrate decreases in utilization of other effective, less expensive treatment options by self-referring urologists. For example, brachytherapy decreased by 14.9 percentage points to just 2.7 percent of patients receiving this treatment in self-referring urology practices. These results are in stark contrast to non-self-referring urologists, for whom the study reports "virtually no change in practice patterns."

The NEJM report concludes that "men treated by self-referring urologists, as compared with men treated by non-self-referring urologists, are much more likely to undergo IMRT, a treatment with a high reimbursement rate, rather than less expensive options, despite evidence that all treatments yield similar outcomes."

ASTRO Chairman Colleen A.F. Lawton, MD, FASTRO, voiced the Society's grave concerns regarding this study's results. "ASTRO urges Congress to promptly pass the 'Promoting Integrity in Medicare Act of 2013' (PIMA), introduced August 1, 2013, by Rep. Jackie Speier (D-Calif.) and Rep. Jim McDermott (D-Wash.). PIMA will close the self-referral loophole for radiation therapy, advanced imaging, anatomic pathology and physical therapy services, resulting in better care for patients and billions of Medicare dollars saved that could offset the costs of repealing the Medicare physician payment formula (sustainable growth rate – SGR).

Press release, 30 October 2013

TESTOSTERONE TREATMENTS

(Continued from page 5)

anti-aging benefits. "There is only anecdotal evidence that testosterone is safe for these men," said editorial author Dr. Anne Cappola, a hormone expert at University of Pennsylvania and an associate journal editor.

"In light of the high volume of prescriptions and aggressive marketing by testosterone manufacturers, prescribers and patients should be wary" and more research is needed, she wrote. AbbVie, Inc., a manufacturer of one heavily marketed testosterone supplement, AndroGel, issued a statement in response to the study, noting that testosterone treatments are approved by the Food and Drug Administration, and the risks are listed in the product insert.

"We encourage discussion between physicians and patients that leads to proper diagnosis based on symptoms, lab tests and a patient's other health needs," AbbVie said.

Associated Press, 5 November 2013

DOCTOR CHODAK'S BOTTOM LINE *(Ref Key: article #, page #, column #)*

Gerald Chodak, MD Author, Winning the Battle Against Prostate Cancer , Second Edition www.prostatevideos.com

Editors' note: Us TOO has invited certain physicians and others to provide information and commentary for the *HotSheet* to enrich its content to empower the reader. This column contains the opinions and thoughts of its author and is not necessarily those of Us TOO International.

a1p1c1 The PREVAIL study provides more good news for men with progressive castrate resistant metastatic prostate cancer. The study compared enzalutamide to a placebo in men who had become resistant to medical or surgical castration. It showed a significant increase in survival and a delay in time to radiographic progression. These findings led to early termination of the study and we can expect Medivation-Astellas to apply to FDA for this indication soon. Based on the results, we also can expect the FDA to approve it for this group of patients. If and when that occurs, patients and their doctors will face the challenge of figuring out which drug to use first when the disease progresses while on androgen suppression. So far we do not know whether there are any advantages to starting abiraterone before or after enzalutamide. Hopefully those studies will be done so doctors and patients know the best sequence. Until then, we can appreciate the importance of this new finding.

The Bottom Line: Enzalutamide offers significant patient benefit to men with metastatic disease when androgen deprivation therapy is no longer effective.

a2p1c2 Family history is a known risk factor for prostate cancer. Men with one first degree relative with the disease have a two-fold risk while those with 2 family members have a 4 to 8-fold risk. Now a study of twins found that a monozygotic twin has a 32-fold higher risk than average and a dizygotic twin has a 16-fold increased risk. Twins of men with prostate cancer should be made aware of this information. The challenge is whether testing them earlier will result in a greatly improved survival. That can only be assessed by a proper trial, which is unlikely to ever get done.

The Bottom Line: Twins of brothers with prostate cancer have a very dramatic increased risk of getting the disease.

a3p1c3 Perhaps the most important article in this month's *HotSheet* addresses the problem of patient participation in clinical trials. Unless patients are willing to enroll, studies cannot be done and lowering morbidity and mortality from prostate cancer cannot occur. The reasons for low participation are varied but they start with most doctors not informing their patients of available studies. Another major reason is a fundamental fear of patients that they will be deprived of a life-saving therapy. More work is needed to provide doctors and patients with better information so studies are completed in a timely manner and new therapies can become available sooner.

The Bottom Line: More work is needed to educate patients and doctors about available clinical trials and patients should recognize that the benefits of participating in clinical trials in most cases outweigh the risks.

a5p2c3 Should men undergo a baseline-screening test between the ages of 40-49? This question is partly addressed in the article by Weight and co-workers. They found that if the PSA was under 1.0 ng/mL then no cancers were detected with a median follow-up of 16.3 years; however, almost 16% were diagnosed with a Gleason 6 cancer during that time if the PSA was greater than 1.0 ng/mL. At first glance, these results suggest a benefit from routine testing. Unfortunately, there are several limitations in the analysis. First, this study does not talk about the impact of finding those cancers and treating them. How many men had to be treated to prevent one of them from dying from cancer? Does it save lives? Also, how many men would get have to undergo biopsies? Unless a randomized study is done in men under 50, it is not possible to tell if routine testing in this age group would result in more good than harm.

The Bottom Line: Screening men between ages 40-49 may identify some men at low risk for eventual cancer but it is unclear if it will save lives or will overtreat too many men.

a6p3c1 One of the most fundamental questions about prostate cancer is how many cancer cells must be present in the prostate before one can spread outside the gland. The study by Haffner and co-workers provides some interesting insight into the answer. They found that a man who died 17 years after diagnosis had the source of his metastases from a small, low-grade focus in the original tumor. What is unclear is how often does this occur? Also, if it happens often, then it would be easy to understand why screening is not more effective; the bad cancers spread before they are readily detectable but the less dangerous ones are easier to find although they don't really need to be treated.

The Bottom Line: This case report may provide an explanation why bad cancers may not benefit from routine screening; they spread before they can be detected.

a7p4c1 Is there a role for non-Taxane chemotherapy in men failing docetaxel? That is the question addressed in the study by Joly et al who studied the effect of Mitoxantrone, vinorelbine or etoposide in older, less healthy men. Although they found an overall palliative response rate of 29%, only Mitoxantrone has been studied in a proper controlled trial and it was approved for palliation. Perhaps a randomized study would be appropriate to find out if the other drugs offer a significant benefit but unless that is done, this study does not support using any of those drugs before cabazitaxel is first used, because the latter has been found to improve survival in men who progressed while taking docetaxel.

The Bottom Line: Assessing if there is a role for vinorelbine or etoposide requires a randomized study to determine if either is a worthwhile therapy.

a8p5c1 Is testosterone replacement safe for men with low levels of this hormone? It seems that advertisements promoting this treatment have greatly expanded. Although low levels may cause a decreased libido and decreased energy, the long-term safety has not been well studied. The article by from the VA hospital suggests that men on testosterone replacement therapy were at increased risk for stroke or heart attack compared to men with low testosterone that were not treated. The problem with the study is it is a retrospective analysis and little

(Continued on page 8)

DOCTOR CHODAK'S BOTTOM LINE *(Continued from page 7)*

information is available from a prospective study about the risk from this treatment. For now, men should be informed about this potential risk and decide whether or not to receive treatment.

The Bottom Line: The long term safety of testosterone replacement in men with cardiovascular disease is uncertain and more studies are needed to identify if a risk truly exists.

a10p6c1 When men meet with their doctor to discuss managing their prostate cancer, they expect to get balanced, unbiased information. Unfortunately, that may often not be the case. A recent study suggests that doctors who own their own radiation equipment are more likely to recommend radiation therapy (RT) than someone who does not own the equipment. The study was well done using an interesting method for its analysis, but one that makes it easy to see that the recommendations made by urologists change when they own their own radiation equipment. Once doctors acquired their equipment, they had a much greater increase in the percentage of men receiving RT compared to doctors in a similar region of the country who were not part owners of the equipment. The American Urology Society has been quick to attack the article and defend urology ownership, but sadly, it does not change the fact that men should be careful when advised to undergo external beam RT. Of course, biases may also exist if a doctor specializing in surgery, cryosurgery or brachytherapy recommends one of those treatments. If RT is recommended, a patient should request a second opinion or ask his doctor the following questions to help make sure that the option he is given is in his best interest:

- Doctor, do you have part ownership in the radiation equipment since there is a radiation center closer to my home than the one you want me to go to?
- Why am I not a good candidate for a different treatment?

The Bottom Line: Doctors owning their own radiation equipment may be over treating patients with external RT when more appropriate options may be available. Men should recognize that every recommendation could be biased when the doctor has a personal gain.

LETHAL PROSTATE CANCER

(Continued from page 3)

However, the generalizability of these findings is not clear, because this is the first prostate cancer case in which it was possible to carry out such detailed longitudinal characterization of the lethal cell clone, from the primary cancer to distant metastases, the authors note.

In an accompanying commentary, A. Rose Brannon, PhD, and Charles L. Sawyers, MD, from the Memorial Sloan-Kettering Cancer Center in New York City, commended Dr. Haffner and his group for reporting "such a fascinating anecdote." They note that the effect of this work "will only be realized if we can collect and assemble this type of data across hundreds of cases."

"The growing penetration of genomic sequencing into clinical medicine has led to increased calls for the creation of various types of medical 'data commons' that will allow comparisons between individual cases. Perhaps we are entering an era in which 'N of 1' cases are here to stay," they conclude.

Medscape Medical News, 25 October 2013

HOTSHEET PERSONAL SUBSCRIPTIONS AVAILABLE!

If you are unable to attend chapter meetings or print from our website to get the latest issue or prefer an original copy, we can deliver the newsletter right to your home or office. Receive 12 issues for a 1-year subscription of $35 (includes shipping and handling). To obtain an order form or to order online, go to: <www.ustoo.org/Hot_Sheets.asp>, or call 1-800-808-7866 (1-800-80-UsTOO).

US TOO INTERNATIONAL:

Our Mission

Be the leading prostate cancer organization helping men and their families make informed decisions about prostate cancer detection and treatment through support, education and advocacy.

US TOO INTERNATIONAL

See blue. SEA Blue.

SUPPORT • EDUCATE ADVOCATE

US TOO INTERNATIONAL TAX DEDUCTIBLE DONATION

Name: _____ Company: _____

Address: _____ Suite/Unit #:_____

City: _____ State: _____ ZIP: _____ Country: _____

Phone: ( ) _____ Fax: ( ) _____ Email: _____

Please accept my enclosed tax-deductible donation to Us TOO International, a non-profit 501(c)(3) organization.

Amount: _____ $50 _____ $75 _____ $100 _____ $200 Other: $ _____ Check # _____

VISA/MC/AMEX/DISC # _____ Expiration Date: _____ /_____ CVV#: _____

Signature _____ Date: _____

☐ Check here if you wish to remain anonymous Annual Report donor recognition listing

US TOO INTERNATIONAL, 5003 Fairview Ave., Downers Grove, IL 60515