Overactive Bladder Linked to Androgen Deprivation Therapy for Prostate Cancer

Androgen deprivation therapy (ADT) for prostate cancer is associated with an increased risk of overactive bladder (OAB), a finding consistent with an inhibitory role of androgen in modulating male voiding dysfunction, according to a new study.

Compared with ADT recipients, healthy men and men receiving alpha blockers for benign prostatic hyperplasia (BPH) had a significant 98% and 30% decreased risk of OAB, respectively, after adjusting for numerous potential confounding factors. Increased ADT duration increased the cumulative risk of OAB.

Since ADT is still the pivotal treatment in advanced prostate cancer, OAB which might occur after ADT should be taken into consideration during patient care, a team led by Chen-Li Cheng, MD, PhD, of Taichung Veterans General Hospital and Chung Shan Medical University in Taichung, Taiwan, concluded in *Anticancer Research* (Vol. 39, pp. 305-311, 2019).

Using the Taiwan National Health Insurance Research Database, Dr. Cheng and colleagues compared 2,629 men receiving only ADT for newly diagnosed prostate cancer with 20,464 controls without cancer divided into three groups: 14,151 men with BPH treated with an alpha blocker (BPH-alpha blocker group); 1,056 men with BPH primarily treated with a 5-alpha reductase inhibitor (BPH-5ARI group); and 5,258 healthy men.

There were 109 OAB cases in the PCA group, three cases among healthy controls, 501 cases in BPH-alpha blocker group, and 58 cases in the BPH-5ARI group. 

(Continued on page 8)

Prostatectomy Beats Surveillance Long Term – or Does It?
The 29-Year Follow-Up Makes Data Hard to Interpret

Long-term follow-up of prostate cancer patients randomized to radical prostatectomy (RP) or surveillance (“watchful waiting” [WW]) showed a substantial and statistically significant survival advantage for the surgical procedure, Swedish researchers said.

Specifically, among participants in the Scandinavian Prostate Cancer Group Study Number 4 (SPCG-4) followed for up to 29 years, men who underwent RP added a mean of 2.9 years to their life expectancy after 23 years, according to Anna Bill-Axelson, MD, PhD, Uppsala University, Uppsala, Sweden, and colleagues.

The researchers found a relative risk of 0.55 (95% Confidence Interval [CI] 0.41-0.74) for prostate cancer death in those undergoing RP vs. surveillance, as they reported online ahead of print in the *New England Journal of Medicine*.

But a U.S. prostate cancer specialist told MedPage Today that the very length of the study complicates the interpretation, since current diagnosis and treatment is markedly different than when the trial began. “It would be very difficult for a newly diagnosed patient to determine where he fits in this study,” said James Mohler, MD, of Roswell Park Comprehensive Cancer Center in Buffalo, New York.

In SPCG-4, 695 men with localized prostate cancer.

(Continued on page 5)

Prostate Cancer – New, Quicker Test to Assess Metastasis Risk

Men with prostate cancer (PCa) are at risk of metastatic tumors forming. A newly developed test can assess this risk more quickly than existing tests and is also cheaper to run.

According to the National Cancer Institute, about 11.2 percent of men will receive a prostate cancer diagnosis at some point in time.

In 2015 — the most recent year for which data are available — an estimated 3,120,176 men in the United States were living with PCa. Individuals with a first-time PCa diagnosis and those who have undergone previous treatment for this form of cancer need to receive tests to determine their risk of metastasis.

If the risk of cancer spreading is high, the doctor may advise the person to proceed with a more aggressive type of treatment.

Researchers from the Albert Einstein College of Medicine in New York City, NY, have collaborated with colleagues from other research institutions to develop a new test for the assessment of metastasis risk. The new test, they say, is cheaper and faster than other methods currently available, and it requires only small tissue samples.

The new test detects copy number alterations (CNAs), which are changes in the genome that drive the spread of cancer tumors. By

(Continued on page 6)
Short-Term Androgen Suppression and Radiotherapy Versus Intermediate-Term Androgen Suppression and Radiotherapy, With or Without Zoledronic Acid, in Men with Locally Advanced Prostate Cancer (TROG 03.04 RADAR): 10-Year Results from a Randomised, Phase 3, Factorial Trial


The Lancet Oncology 19 December 2018; Epub

Background: Optimal duration of androgen suppression (AS) for men with locally advanced prostate cancer (PCa) receiving radiotherapy (RT) with curative intent is yet to be defined. Zoledronic acid (ZA) is effective in preventing AS-induced bone loss, but whether it prevents castration-sensitive bone metastases in locally advanced PCa is unclear. The RADAR trial assessed if adding 12 months of adjuvant AS, 18 months of ZA, or both, improves outcomes in men with locally advanced PCa who receive six months of AS and prostatic RT. We present 10-year outcomes from this trial.

Methods: For this randomised, phase 3, 2×2 factorial trial, eligible men were 18 years or older with locally advanced PCa [either clinical stage T2b–4, N0 M0 [non-invasive] tumours or T2a, N0 M0 tumours provided Gleason score was ≥7 and baseline PSA was ≥10 μg/L [ng/mL]]. We randomly allocated participants in a 2×2 factorial design by computer-generated randomization, and stratified by centre, baseline PSA, clinical tumour stage, Gleason score, and use of a brachytherapy boost in a 1:1:1:1 ratio to four treatment groups. Men in the control group received six months of neoadjuvant AS with leuprolerin and RT alone (short-term AS [STAS]); this treatment was either followed by another 12 months of adjuvant AS with leuprolelin intermediate-term AS [ITAS]), or accompanied by 18 months of ZA (4 mg every three months, intravenously) starting at randomisation (STAS plus ZA), or both (ITAS plus ZA). All men received RT to the prostate and seminal vesicles, starting from the end of the fifth month of AS (66, 70, or 74 Gy in 2-Gy fractions per day, or 46 Gy in 2-Gy fractions followed by a high-dose-rate brachytherapy boost dose of 19.5 Gy. Treatment allocation was open label. The primary endpoint was PCa-specific mortality and was analyzed according to intention-to-treat using competing-risks methods. The trial is closed to follow-up and this is the final report of the main endpoints. This trial is registered with ClinicalTrials.gov, number NCT00193856.

Findings: Between Oct 2003, and Aug 2007, 1,071 men were enrolled and randomly assigned to STAS (n=268), ITAS (n=268), STAS plus ZA (n=268), and ITAS plus ZA (n=267). Median follow-up was 10.4 years (interquartile range [IQR] 7.9—11.7). At this 10-year follow-up, no interactions were observed between AS and ZA so the treatment groups were collapsed to compare treatments according to duration of AS: six months of AS plus RT (6AS+RT) vs. 18 months of AS plus RT (18AS+RT) and to compare treatments whether or not men received ZA. The total number of deaths was 375 (200 receiving 6AS+RT and 175 receiving 18AS+RT), of which 143 (38%) were attributable to PCa (81 men receiving 6AS+RT and 62 receiving 18AS+RT). When analyzed by AS duration, the adjusted cumulative incidence of PCa-specific mortality was 13.3% (95% Confidence Interval [CI] 10.3—16.0) for 6AS+RT vs. 9.7% (7.3—12.0) for 18AS+RT, representing an absolute difference of 3.7% (95% CI 0.3—7.1; sub-hazard ratio [sHR] 0.70 [95% CI 0.50—0.98], adjusted p=0.035, a statistically significant difference). The addition of ZA did not affect PCa-specific mortality; the adjusted cumulative incidence of PCa-specific mortality was 11.2% (95% CI 8.7—13.7) with ZA vs. 11.7% (9.2—14.1) without, representing an absolute difference of −0.5% (95% CI −3.8 to 2.9; sHR 0.95 [95% CI 0.69—1.32], adjusted p=0.78, not a statistically significant difference). Although safety analysis was not prespecified for this 10-year analysis, one new serious adverse event (osteonecrosis of the mandible, in a third man who received 18 months of AS plus ZA) occurred since our previous report (<1% of 530 men who received ZA evaluated for safety) and the total number of drug-related serious adverse events increased to 12 (1% of all 1,065 men evaluable for safety). No treatment-related deaths occurred during the study.

Interpretation: 18 months of AS plus RT is more effective for locally advanced PCa than six months of AS plus RT, but the addition of ZA is not beneficial. Evidence from the RADAR and French Canadian Prostate Cancer Study IV trials suggests that 18 months of AS with moderate RT doses is an effective but more tolerable option than longer durations of AS for men with locally advanced PCa including intermediate- and high-risk elements.
Doc Moyad’s What Works & What is Worthless Column — Also Known as “No Bogus Science” Column

“Restaurants=Weight Gain City?!!”

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

Editor’s Note: Us TOO invites certain physicians and others to provide information and commentary for the Hot SHEET to enrich its content to empower the reader. This column contains the opinions and thoughts of its author and are not necessarily those of Us TOO International.

We know now more than ever before that weight gain is simply bad...actually really bad for your prostate (also not good for those sans prostate of course). It can make your prostate increase in size from that of a walnut to that of two or three walnuts (or a tennis ball, or maybe even a grapefruit. This column is making me hungry). Weight gain reduces the effectiveness of BPH or prostate enlargement drugs and appears to increase the risk of aggressive prostate cancer. Even when on hormone therapy, you want to do your best to try and prevent weight gain because it can make you heart unhealthy. Hormone therapy saves lives, or can prevent men from dying from prostate cancer. But ironically (or is that coincidentally... I was never smart enough to figure out when to use those words) — these drugs make it easier to gain weight and harder to lose weight. What a bummer! And, now it is 2019 and it is more of a pain in the glutteus maximus to lose weight than ever before! Yet, there are some situations which appear to be greater contributors to weight gain than others. So remember that and you may be able to do something against this weight gain epidemic.

A recent study in the United Kingdom that had similar results to a prior US study, again demonstrated something incredible.¹ Researchers looked at meals from 27 sit down or full-service restaurants and found more calories at the restaurants compared to fast food! The average content of a meal at regular restaurants was approaching 1,000 CALORIES! What the FORK?! It has become so darn easy to pick on the easy targets such as the fast food restaurants, but regular restaurants, over time, have become calorie or weight gain city centers and you, me and everyone else are becoming the mayors of these cities! Whether it is the excess bread, sauces, sodium, bigger portions, endless alcohol, and appetizers with the caloric content of a full meal... blah, blah, blah.

We are eating out more than ever before in the history of this planet and it has become easy to blame weight gain on so many other things. Yet, one of the best places to reduce your chances of gaining weight is to become restaurant aware. The more you eat out, the more you are likely to be exposed to a massive quantity of calories. Remember that TV show Cheers (from 1982-1993) where everybody knows your name? One of the main characters was “Norm” and he was the one heavy guy in the TV show that loved to come to the bar/restaurant every evening and we would laugh at his jokes because he was funny as heck! However, looking back on that TV show (it has been 25 years!), I can’t help but think what a soothsayer that series would become in terms of regular attendance at restaurants and weight gain in the modern world! It portended the future!

Yikes! I am not saying to stay away from restaurants, but I am saying plan ahead online and look for moderate to lower caloric options and stick with them. Otherwise you may become that guy going to your favorite restaurant regularly where everybody knows your name and laughs at all your jokes! PS. This study was released over the holidays, but I decided to wait until now to discuss it. Otherwise it would have made me sad at the annual holiday dinner that we hold every year at my favorite restaurant.

Reference:

Prostate Cancer Risk Higher in Men with IBD

Men with inflammatory bowel disease (IBD) are four to five times as likely as their peers without IBD to develop clinically significant prostate cancer (PCa), according to a new study.

“We have to study this further, but since these patients with IBD are getting frequent colonoscopies and frequent exams, it may be worthwhile to see that a good prostate exam is performed, but again, we do have to validate this in future studies,” Dr. Shilajit D. Kundu of Northwestern University Feinberg School of Medicine in Chicago told Reuters Health.

“Epidemiological research has linked IBD to PCa, but the association has not been studied in the PSA era,” Dr. Kundu noted. Screening for PCa with PSA testing is “controversial,” he and his colleagues write in European Urology, online ahead of print on December 4th.

The study team compared 1,033 male IBD patients who underwent PCa screening at their medical center in 1996-2017 to 9,306 controls who did not have IBD. Ten-year PCa incidence was 4.4% for men with IBD compared to 0.65% among controls (hazard ratio, 4.84; P <0.001, a statistically significant difference); for clinically significant PCa, incidence was 2.4% and 0.42%, respectively (HR, 4.04; P<0.001). Men with IBD also had higher average PSAes than men without IBD starting at about age 55.

“Not only do men with IBD have an increased risk of cancer, they also have an increased risk of clinically significant cancer that would warrant treatment,” stated Dr. Kundu.

“Doctors may assume that an elevated PSA in an IBD patient is related to the disease,” he added. “If a man with IBD who feels OK has an elevated PSA, we shouldn’t necessarily assume that it’s just coming from inflammation of his gut. It may be a sign that he should be checked for PCa.”

Reuters Health
31 December 2018

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Hypofractionated Radiotherapy May Benefit Patients with Localized Prostate Cancer

Dose-escalated, moderately hypofractionated intensity-modulated radiation therapy (HIMRT) may have some advantages over conventionally fractionated IMRT (CIMRT) for treating men with localized prostate cancer (PCa). A study published in The Journal of Clinical Oncology (Vol. 36, pp. 2943-2949, 2018), suggests superior cancer control for localized PCa receiving dose-escalated moderate HIMRT. It also appears more convenient, as HIMRT cuts treatment duration.

Karen Hoffman, MD, University of Texas MD Anderson, and coworkers compared CIMRT (75.6 Gy in 1.8-Gy fractions over 8.4 weeks) vs. a dose-escalated moderate HIMRT regimen (72 Gy in 2.4-Gy fractions over six weeks). Of 206 men, 72% had clinical stage cT1 PCa, 99% had a Gleason score of 6 or 7, 90% had a PSA ≤10 ng/mL, and 24% received androgen-deprivation therapy (ADT).

The researchers found that the men treated with HIMRT experienced fewer treatment failures than men treated with CIMRT (10 vs. 21, respectively) with a median follow-up of 8.5 years. The eight-year failure rates were significantly different (10.7% for HIMRT vs. 15.4% for CIMRT). The study demonstrated no differences in overall survival (OS) between the two treatment arms. The researchers noted that there was a nonsignificant increase in late grade 2/3 gastrointestinal toxicity with HIMRT (12.6% vs. 5.0%). However, the study showed that the number of men who developed toxicity was small, and all rectal bleeding resolved with treatment. The authors wrote that the risk of bleeding can be further reduced by minimizing the proportion of rectum exposed to high-dose RT.

Cancer Therapy Advisor 19 December 2018

Combination Strategy Improves Identification of Clinically Significant Prostate Cancers

Combining visual-registration and image-fusion biopsy targeting strategies provides the highest rate of detecting clinically significant prostate cancer (PCa), according to results generated from the SmartTarget biopsy trial. Multiparametric MRI improves the diagnostic sensitivity for clinically significant PCa while reducing overdiagnosis of clinically insignificant cancer, but it remains unclear which MRI-targeted biopsy method is best.

Dr. Hashim U. Ahmed of the Faculty of Medicine at University College London, and colleagues sought to determine whether visual-registration (mentally translating MRI targets onto real-time ultrasound images) is sufficient or whether it needs augmentation with image-fusion software.

Among 129 men who underwent visual-registration and image-fusion biopsies, 93 (72%) had clinically significant PCa (Gleason pattern of 3+4=7 or higher) using both biopsy strategies.

Each strategy alone detected 80 of these significant cancers, with each method identifying 13 cancers that the other missed. The combination of the two methods resulted in a 14% improvement in the detection of clinically significant PCa.

Results were similar using an alternative definition of clinically significant PCa (Gleason pattern of 4+3=7 or higher), researchers report in European Urology, online on December 6th.

Safety profiles were similar with the two biopsy strategies and no significant differences in patient-reported outcome scores were seen. Both strategies missed clinically significant cancers detected by the other strategy and so should be used in combination to optimize cancer detection, the researchers conclude.

A cost-benefit analysis is a complex question beyond this study’s scope, they add. However, our results suggest potential benefits of a faster learning curve and higher repeatability that may enable less experienced centers to increase throughput and achieve cancer detection rates equivalent to those of highly experienced centers.

Several of the authors report financial ties to SmartTarget Ltd., which is commercializing the image guidance device used in this study.

Renal & Urology News 18 December 2018

Gleason 6 PCa More Lethal in Black Men

Black Men are More Likely Than White Men to Die From Gleason 6 Prostate Cancer

Risk assessment and management of prostate cancer (PCa) in black men is controversial. To better understand the implications of Gleason score, Brandon A. Mahal, MD, of Harvard Radiation Oncology Program in Boston, and colleagues compared PCa mortality among 31,841 black and 340,286 nonblack men diagnosed with localized PCa during 2010 to 2015 using the Surveillance, Epidemiology, and End Results Prostate Active Surveillance/Watchful Waiting (SEER AS/WW) database.

“Black men were diagnosed at younger ages (median 62 vs. 65 years), and significantly more had cT1 to T2a (81.3% vs. 75.3%) and Gleason 7 to 10 disease (60.1% vs. 55.8%) than nonblack men. Despite comparable overall PCa death rates (1.4% vs. 1.4%), nearly twice as many black men with Gleason 6 died from their cancer (0.40% vs. 0.22%) over a median 36 months of follow up,” the investigators reported in the Journal of the American Medical Association. Among men with Gleason 6 disease, black men had a two-fold increased risk of death from PCa compared with nonblack men, after adjusting for potential confounders.

The team conducted similar analyses in the general SEER cohort, which included 62,736 black and 340,286 nonblack men over a longer follow-up period. Again, blacks fared significantly worse than nonblacks, especially those with Gleason 6 disease, who were 1.5 times more likely to die from PCa. PCa mortality at 12 years was 2.2% vs. 1.4% for Gleason 6 and 5.5% vs. 5.3% for Gleason 7 to 10 PCa. Investigators controlled for socioeconomic status and treatment selection differences.

“Future studies with longer follow-up will be needed to further characterize low-grade PCa in black men and determine the clinical significance of small absolute differences if they increase over time,” they concluded.

Renal & Urology News 18 December 2018
Gold Nanoparticles Could Destroy Prostate Cancer

In an ongoing clinical trial, researchers using gold nanoparticles to target prostate cancer (PCa) cells say results are promising and side effects are relatively minimal.

PCa affects around one in nine men in the US. Due to its high prevalence, researchers are constantly looking for improved treatment options. Recently, a team from the University of Texas Health Science Center at Houston (UTHealth) tried an innovative approach to PCa treatment using gold.

PCa is treatable, and results are best when doctors detect it early. However, treatment can be unpleasant and cause significant side effects. Treatment options include radiotherapy (RT), chemotherapy, cryotherapy, and radical prostatectomy (RP) which is the removal of the entire prostate gland and some of the surrounding tissue.

The cutting-edge therapy under investigation in the current study uses nanoparticles consisting of small layers of silica glass in a spherical shape. A very thin layer of gold coats each sphere. Nanoparticles seek out and enter cancer cells. A laser used by researchers stimulates the nanoparticles and makes them vibrate and pulse with extreme temperatures, which kills the cancerous tissue.

Treatment preserves surrounding tissue, including vital nerves and the urinary sphincter. This should prevent men from experiencing some common side effects of PCa treatment, such as urinary incontinence and impotence.

“The side effects of current (Continued on page 8)

Prostatectomy Beats Surveillance, or Does It? (Continued from page 1)

were randomly assigned to either RP or WW in 14 centers in Sweden, Finland, and Iceland from 1989 to 1999. Findings similar to those in the current study were reported in a 2014 follow-up analysis. Of the 695 men involved in the study, 347 were randomly assigned to the RP group and 348 to the WW group. In the new analysis, the maximum potential follow-up time was 29.3 years, and median follow-up was 23.6 years.

As of December 2017, 80% of men enrolled in the study had died. The cumulative incidence of death from all causes at 23 years was 71.9% in the RP group and 83.8% in the WW group (difference 12.0 percentage points; 95% CI 5.5-18.4). Seventy-one deaths in the RP group and 110 in the WW group were due to prostate cancer, for an absolute difference in risk of 11.7 percentage points (95% CI 5.2-18.2).

Distant metastases were diagnosed in 92 men in the RP group and 150 men in the WW group. At 23 years the cumulative incidence of metastases was 26.6% in the RP group and 43.3% in the WW group (difference 16.7 percentage points; 95% CI 6.7-23.7).

Bill Axelson and her colleagues also found that among men in the RP group, extracapsular extension was associated with a risk of death from prostate cancer that was five times that of men without extracapsular extension. In addition, a high Gleason score (>7) – which comprised about 40% of both treatment groups – was associated with a risk of death from prostate cancer that was 10 times higher than a score of 6 or lower. But the researchers did not report mortality for the two treatment groups stratified by baseline Gleason score. Adverse events such as incontinence and sexual dysfunction were also not addressed in the current report (a 2011 publication indicated similar rates of erectile dysfunction in the two groups, but a nearly fourfold higher prevalence of urinary leakage in the RP patients).

“A mean of 2.9 years of life was gained with RP,” the authors stated. “The mean number of years gained is a crude measure, since any given man who is randomly assigned to undergo the procedure either might not benefit at all or might have a much greater benefit than the mean number for the whole group indicates. However, the measure puts in perspective what is risked by delaying intervention.”

“This remains the best randomized study of RP vs. observation ever done,” Mohler told MedPage Today. “Its follow-up is long, it did not have PSA early detection bias and, even with the problems with Gleason grading and the determination of clinical pathologic stage, the group of patients seems to be largely devoid of who we would place on surveillance today.”

But Mohler, who was not involved in the study, said that because of the way that prostate cancer diagnosis and management has changed since 1989, it’s unclear what the findings mean for current patients.

“The authors raise the concern that diagnosing cancer earlier – like it is done today – might fail to show this gain in life benefit because of contamination of modern-day patients with lots of patients that don’t really need to be treated,” he said. “And that’s a very legitimate concern, so it would be wrong for patients and urologists to say that this study proves that more men should have RP... That’s why this study is so hard to interpret in 2018.”

However, Mohler noted that if a patient does have an aggressive prostate cancer, the study shows that a patient “is better off having RP than observation, in terms of preventing the development of metastasis, dying of prostate cancer, and overall survival.”

MedPage Today
12 December 2018

Video Now Available of Prostate Cancer Pathways Chicago Event

Video is now available of our Prostate Cancer Pathways for Patients and Caregivers Chicago event and webcast!

Recorded November 3 at NorthShore University HealthSystem in Skokie, IL.

- Sex and Intimacy After Treatment
- Pelvic Floor Health
- Incontinence
- Men’s Health Risks
- PSA Testing
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You can access direct links to short video segments specific to each topic at: www.ustoo.org/PathwaysChicago.
Overall Survival of Black and White Men with Metastatic Castration Resistant Prostate Cancer Treated with Docetaxel

Halabi S, Dutta S, Tangen CM, et al.
J Clin Oncol 21 December 2018, Epub

Purpose: Several studies have reported that among patients with localized prostate cancer (PCa), black men have a shorter overall survival (OS) time than white men, but few data exist for men with advanced PCa. The primary goal of this analysis was to compare the OS in black and white men with metastatic castration-resistant PCa (mCRPC) who were treated in phase III clinical trials with docetaxel plus prednisone (DP) or a DP-containing regimen.

Methods: Individual participant data from 8,820 men with mCRPC randomly assigned in nine phase III trials to DP or a DP-containing regimen were combined. Race was based on self-report. The primary end point was OS. The Cox proportional hazards regression model was used to assess the prognostic importance of race (black vs. white) adjusted for established risk factors common across trials (age, PSA, performance status, alkaline phosphatase, hemoglobin, and sites of metastases).

Results: Of 8,820 men, 7,528 (85%) were white, 500 (6%) were black, 424 (5%) were Asian, and 368 (4%) were of unknown race. Black men were younger and had worse performance status, higher testosterone and PSA, and lower hemoglobin than white men. Despite these differences, median OS was 21.0 months (95% CI, 19.4 to 22.5 months) vs. 21.2 months (95% CI, 20.8 to 21.7 months) in black and white men, respectively. The pooled multivariable hazard ratio of 0.81 (95% CI, 0.72 to 0.91) shows that, overall, black men have a statistically significant decreased risk of death vs. white men (P <0.001).

Conclusion: When adjusted for known prognostic factors, we observed a statistically significant increased OS in black versus white men with mCRPC who were enrolled in these clinical trials. The mechanism for these differences is not known.

Surrogate Marker for ADT Evaluation Proposed

The time interval free of biochemical failure (IBF) may be a promising surrogate end point in the setting of androgen-deprivation therapy (ADT) evaluation in men with prostate cancer (PCa), according to researchers at the University of Chicago. They reported online ahead of print in The Journal of Clinical Oncology that IBF may serve as a valid end point in clinical trials and may also aid in risk monitoring after initial treatment.

The investigators found that the length of the IBF could have a major bearing on trial duration. They cited several trials where findings could have been revealed three to five years earlier, if the IBF interval had been adopted and a surrogate measure used. James Dignam, PhD, the Department of Public Health Sciences, the University of Chicago, and colleagues conducted a trial with 1,520 men that compared short-term ADT (four months) with long-term ADT (28 months). They evaluated the IBF in relation to clinical end points of PCa-specific survival and overall survival (OS).

New, Quicker Test (Continued from page 1)

assessing CNAs in samples of blood or prostate tissue, specialists can get a better idea of whether or not the cancer cells are proliferating.

“We have demonstrated that CNAs can be detected rapidly and accurately with the new Next-Generation Copy Number Alteration (NG-CNA) assay,” says Dr. Harry Ostrer, the study’s lead author.

“The impact of this information is two-fold: to assure aggressive therapy at the time of diagnosis for men with metastasis-prone disease and provide a rationale for active surveillance (and not overtreatment) for men with indolent disease (disease that progresses at a slow pace).”

In the paper researchers submitted to The Journal of Molecular Diagnostics, they explain that the NG-CNA can analyze 902 genomic sites across 194 genomic regions, which it can do both faster than existing tests and at a lower cost.

“For example,” Dr. Ostrer explains, “with NG-CNA, the cost of DNA extraction, library preparation, and sequencing reagents can be $20 to $40 per sample, compared to nearly $1,000 for whole genome sequencing.”

More importantly, the team notes that results they obtain by the new test are easier to read, allowing researchers to process thousands of tissue samples in one go. NG-CNA also has a quicker turnaround time for the results, at approximately 36 hours.

Another advantage of the new method is that lower data storage is required, which, Dr. Ostrer says, would “allow our approach to move from large reference labs to smaller, more resource-constrained independent labs as needed.”

Finally, NG-CNA requires collection of a smaller sample than other tests currently in use. The sample size can be as low as 12.5 nanograms of material, which would allow specialists to use the test to analyze cell lines, biopsy samples, and surgical samples.

The researchers also explain how they tested the accuracy of NG-CNA. Previously, the team developed a new indicator of metastatic risk called the “metastatic potential score” (MPS).

Dr. Ostrer and team used NG-CNA to determine MPS in 70 surgical samples of prostate cancer. On comparing the results with those from existing tests, the researchers found that they were “highly correlated.”

The team also validated the NG-CNA test using a second group of surgical samples that they matched with biopsy tissues.

“We believe the addition of the NG-CNA assay onto a standard cancer gene testing platform will augment personalized medicine by identifying aggressive tumors and genetic mutations that are predictors of response to targeted therapies,” Dr. Ostrer declares.

Medical News Today
27 December 2018

Check out Us TOO web pages on maximizing quality of life after prostate cancer treatment:

Sexual Health and Intimacy at www.ustoo.org/intimacy and Urinary Incontinence at www.ustoo.org/incontinence
P1, “Prostatectomy Beats…”
“One of the more important studies done in men with early stage PCAs was conducted in Scandinavia. They compared radical prostatectomy (RP) to the traditional watchful waiting (WW) and found at 29 years, survival was significantly higher in men undergoing RP. But the study included men with low-, intermediate- and high-risk disease. Also, current management of men with localized PCAs has changed greatly by the use of active surveillance (AS) with delayed therapy instead of waiting for metastases to arise. The only real conclusion for today is that WW may not be good, but it does not mean that RP should always be used instead of AS.

The Bottom Line: The information available from this study is not really that useful for men diagnosed today.

P2, “Short-Term Androgen…”
“One of the more important research findings is that ADT improves survival in men with locally-advanced PCAs treated with external RT. Although some comparisons have been made, the optimal duration of ADT is still unclear, but 36 months is better than six months. In this study they compared six months of ADT to 18 months. With a median follow-up of 10.4 years, PCA mortality was 3.7% lower in the men receiving longer ADT, but they did not report overall survival, so caution is needed in drawing conclusions. This study also assessed whether adding zoledronic acid is beneficial and found it was not.

The Bottom Line: In this study 18 months of ADT offers better survival than six months, but overall survival should also be compared.

P3, “Prostate Cancer Risk…”
“Does inflammatory bowel disease (IBD) increase risk of developing significant prostate cancer (PCa)? That is the suggestion from a study by Kundu, et al. who conducted a retrospective case control analysis. They found that the incidence of “significant” PCa was 4.4% in the IBD group vs. only 0.65% for the controls. However, little information is available about the management of PSA testing, or any family history of PCAs. As is the case with all retrospective studies, numerous explanations may account for this difference. Nevertheless, it is an interesting observation.

The Bottom Line: There may be an increased risk of significant PCa in men with IBD but more validation is needed.

P4, “Hypofractionated RT…”
“Can shortening the duration of radiotherapy (RT) using hypofractionation save time in therapy without jeopardizing outcomes?” Hoffman, et al. addressed this question in a prospective, randomized trial. They found that there was no difference in overall survival but the treatment failure rate was higher in the men receiving conventional RT. Side effects were slightly higher. Unfortunately, there are some factors that might explain the results, making it premature for firm conclusions. The authors state that 99% had Gleason 6 or 7 but the abstract does not show the distribution or compare the two groups for Gleason 6 cancers. Also 24% received ADT. These differences could account for the differences seen or certainly could have created a bias in the study.

The Bottom Line: Hypofractionation could offer reduced time in therapy without compromising survival but more data are needed to rule out biases.

P4, “Combination…”
“Evidence is accumulating that multi-parametric MRI offers an increased ability to find high-risk cancers while reducing the detection of low-risk disease. Ahmed and co-workers assessed whether visual registration (mentally translating MRI targets onto real-time ultrasound images) is sufficient or whether it needs augmentation with image-fusion software. They found that both techniques miss significant cancer, so the combination is the best way to optimize detection. More data is needed to validate these findings. It would help if a blinded analysis could be done comparing detection rates at different centers.

The Bottom Line: Combined visual and image-fusion software may provide better detection of higher risk PCa but more data are needed.

P4, “Gleason 6 PCa More…”
“Now we have another uncontrolled study suggesting that African-American men with a Gleason 6 PCa have a higher risk of dying from the disease compared to Caucasians. Although authors found the relative risk was 1.5% higher, the absolute risk was less than 1 per 100 men higher. Is that difference enough to justify more aggressive therapy in men with Gleason 6 PCa? Personally, I do not think so, especially because there are so many factors to consider: How did the management differ?

What biopsy techniques were used? Was access to aggressive therapy identical? And what kind of monitoring occurred? These are all important questions that cannot be assessed from this report.

The Bottom Line: African-American men with Gleason 6 PCa may have a very small difference in their risk for dying from PCa, but more information is needed before suggesting they should be treated more aggressively.

P5, “Gold Nanoparticles…”
“In a very interesting report, gold-coated nanoparticles activated with lasers are being studied as a way to treat PCa. The results are early but, if successful, could offer an alternative therapy with less severe side effects.

The Bottom Line: Activated gold-coated nanoparticles are a novel method under investigation for treating PCa, but considerably more work needs to be done.

P6, “Overall Survival…”
“Do African-American men with mCRPC treated with docetaxel have a different overall survival compared to Caucasians?” A pooled analysis of men participating in phase III randomized trials found some differences in the groups, Black men actually had a lower risk of dying from mCRPC. However, some studies have found that men with mCRPC who had higher testosterone fared better than those with lower testosterone. So the mechanism to explain this difference is unclear. Of course, the real question is “so what?”

The Bottom Line: African-American men with mCRPC treated with docetaxel are not at greater risk of dying

(Continued on page 8)
prostate cancer treatments can be extremely traumatic,” says Dr. Steven Canfield, chair of the division of urology at McGovern Medical School at UTHealth. “This new technology holds the potential to eliminate those life-altering effects, while still removing the cancer tissue and reducing hospital and recovery time.”

Dr. Canfield notes that the first participant in this trial experienced great results and was even able to ride a bike within the first week following treatment.

Naomi Halas, who is the head of Rice University’s Laboratory for Nanophotonics, invented the gold nanoparticles this clinical trial uses. Dr. Canfield realized that nanoparticle technology had real potential and worked closely with Halas to bring it to trial.

If future trials show rewarding outcomes, this treatment option could conceivably receive FDA clearance.

Medical News Today 23 December 2018

**Gold Nanoparticles**

(Continued from page 5)

**Surrogate ADT Marker**

(Continued from page 6)

The study showed that long-term ADT was superior to short-term ADT in terms of biochemical failure (BF) and clinical end points. Men who did not develop BF for three years had relative risk reductions of 39% for OS and 73% for PCa-specific survival.

Accounting for three-year IBF status, the long-term ADT OS benefit was reduced from 12% to 6%. With PCa-specific survival, the long-term ADT benefit dropped from 30% to 6% at three years.

The study also revealed that at three years, 50% of subsequent deaths attributed to PCa occurred in men with BF compared with 19% of those who were free of BF.

Researchers concluded that IBF appears to have a clear role in clinical decision making, and may provide guidance during surveillance if treatment is warranted.

Prostate Cancer Advisor 16 December 2018

**Dr. Chodak’s Bottom Line**

(Continued from page 7)

compared to Caucasians. **P6, “Surrogate Marker...”**

One of the challenges with randomized trials in men with PCa is the long time needed to achieve overall survival results. Consequently, researchers are always looking for interim outcomes that could shorten the time until meaningful study results are achieved. Dignam, et al. conducted a study of long- vs. short-term ADT and found that biochemical failure (BCF) at three years was a valuable predictor of overall survival. Although their findings suggest a potential value of this approach, it is not clear how often an incorrect prediction would occur using their approach and more analysis is needed. Whether the FDA would consider their findings sufficient for future studies is unclear.

The Bottom Line: The three-year BCF rate may be a useful interim marker for overall survival but more data are needed to substantiate this observation before the FDA would likely use it to shorten prospective studies.

**ADT & OAB**

(Continued from page 1)

The BPH-5ARI group had a significant 49% increased risk of OA vs. the ADT group. The authors explained that reimbursement regulations require prostate size to >30 mL or the maximal voiding flow must be <15 mL/min.

“With this regulation, these men should have more severe lower urinary tract symptoms than the other three groups,” he noted. Renal & Urology News 7 January 2019
QUESTION FROM PROSTATE CANCER SURVIVOR:
Can you provide information on rejuvenation therapies for erectile dysfunction after prostatectomy such as stem cells, platelet rich plasma or low intensity extracorporeal shock wave therapy?

RESPONSE FROM DR. JEFFREY ALBAUGH:
Thank you for asking about this. New innovations are exciting and, although some of these rejuvenative therapies show potential for the future, they have not yet had sufficient research to determine if and who they may benefit and how they may be delivered with minimal side effects or harm. There are a lot of people out there who are making a lot of money from rejuvenation therapies without adequate scientific evidence to support effectiveness and safety. Some of these therapies can cost $10,000 to $80,000 or more by the time they are complete. Please be clear that the American Urological Association, the Sexual Medicine Society of North America (I am members of both organizations) and the FDA have taken a very strong stance to say that all these therapies are off-label, lack adequate research and are not approved by the FDA. They should only be performed under an institutional review board (IRB) approved study. These procedures should not be undertaken in any clinic outside of a research study. To see the specific statements about these rejuvenative procedures, go to https://www.auanet.org/guidelines/male-sexual-dysfunction-erectile-dysfunction-(2018) and http://www.smsna.org/V1/news/433-smsna-position-statement-on-restorative-therapies-for-ed.

Stem cell therapy, low-intensity extracorporeal shock wave therapy and plasma rich protein therapy for erectile dysfunction represent potential restorative modalities to promote cell rejuvenation. Each treatment is designed to possibly regenerate erectile tissue. These are exciting, new approaches to treating erectile dysfunction, but more research is needed to determine safety and effectiveness of each treatment.

Animal studies have shown promise for some of these treatments, but the human studies have been very small and limited and, in some cases, no human studies have been published. In particular, there are no randomized controlled human studies of plasma rich protein (PRP) therapy, which is sometimes referred to as the P shot. There is nothing more to say about PRP until we have published scientific human studies. There are a few small randomized studies for stem cell therapy and for short-term extracorporal shock wave therapy (LI-ESWL).

The exact mechanism of action of stem cell therapy is not understood, but it is thought to be due to immune modulation leading to secretion of cytokines and growth factors to decrease inflammation and promote healing. Animal studies have shown promise with stem cell therapy, but there are only four small studies published on using it for erectile dysfunction. In men post radical prostatectomy, there are no randomized placebo controlled studies, but only two small studies (Metz, et al., 2018). Careful, methodic research is needed to determine both safety and efficacy to identify the best treatment protocol that may or may not help men with erectile dysfunction after prostate cancer treatment while minimizing harm. This research is just not accomplished yet.

Low-intensity shock wave therapy for erectile dysfunction is another treatment being investigated for treatment of erectile dysfunction. The mechanism is still being determined, but it is thought to decrease inflammation while causing cell membrane micro-trauma resulting in the release of blood flow promoting factors. It has been used for erectile dysfunction caused by blood flow problems (vaculogenic ED) specifically. From the limited small studies, it seems to work best in mild vasculogenic erectile dysfunction and younger patients do better with the treatment (Zhihuz, L., et al., 2017 & Zou, Z., et al, 2017). There was only one study (not a randomized controlled study) using the therapy in men after radical prostatectomy with a small improvement in erectile function scores at one month after treatment and very minimal improvement in the average score one year after treatment (Frey, Sonksen & Fode, 2016). Given the lack of any randomized placebo controlled studies in men treated for prostate cancer, further research is needed to determine if this treatment will have any positive effect on erectile function in these men and there is no good evidence to support this to date.

It is exciting to know there are completely different treatments for erectile dysfunction currently under scientific investigation. We all must be patient until definitive treatment regimens are determined that are both effective and safe. In addition, we need to know exactly which patients may benefit from these treatments and then ultimately we need them to be accessible to the men who will benefit from treatment. Please only participate in IRB approved research studies with these new experimental/investigational therapies.

You can access the new edition of my book or download a free copy of my original book at www.drijeffalbaugh.com.

Do you have a question about sexual health or intimacy? If so, we invite you to send it to Us TOO. We’ll select questions to feature in future Between the Sheets columns.

Please email your question to: ustoBTS@ustoo.org

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