Notable Differences with Three Prostate Cancer Genomic Tests

There are “notable differences” in the oncologic outcomes predicted by the three leading prostate cancer genomics tests, according to a small retrospective study of Oncotype Dx, Prolaris, and Decipher clinical usage.

“You can do a Prolaris test on one man and tell him you think he should undergo active surveillance (AS), and then do an Oncotype Dx on the same man and tell him he may need treatment,” senior author Joseph Wagner, MD, from the Hartford Healthcare Medical Group in Connecticut, reported at the American Urological Association (AUA) 2018 Annual Meeting.

The comparative study also “highlights the difficulty of interpreting genomic tests for prostate cancer,” Wagner and his colleagues write in their meeting abstract. “I need a lot of help figuring out how to use these tests,” Wagner acknowledged during a meeting press conference.

“Traditionally, clinicians have used Gleason score (GS), PSA level, clinical staging, the number of positive needle cores, and related measures to risk-stratify men with biopsy-confirmed disease and to help with subsequent treatment and management decisions, including AS,” he explained. “But it is now becoming increasingly common for clinicians to use genomics tests, also known as molecular tests, to predict outcomes and guide treatment for favorable-risk prostate cancers (including very low-, low-, and intermediate-risk [GS 3+4]).”

“Genomics tests incorporate both traditional measures and (Continued on page 4)

Black Men Do Well in Prostate Cancer Trials

Outcomes as Good as in White Men, and Contrast with a Dismal Record in Clinical Practice

If black men with advanced prostate cancer get aggressive care in clinical trials, they do as well as whites and perhaps better, two studies presented here suggested. The findings are a stark contrast to outcomes seen in the general population, where African Americans have higher rates of prostate cancer than whites, are diagnosed at a later stage, and have higher mortality, researchers said at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting.

The studies — one prospective and the other a retrospective pooled analysis of nine clinical trials — showed that black men with metastatic castration-resistant prostate cancer (mCRPC) receiving standard chemotherapy or hormone therapy, do just as well as their white counterparts.

In fact, there’s a hint in the retrospective study that black men might do better once adverse prognostic factors such as age, performance status, and PSA levels are taken into account, according to Susan Halabi, PhD, of Duke University in Durham, NC, and colleagues.

In their analysis, median survival was identical at 21 months for both whites and blacks, but after adjustment for prognostic factors, blacks had a 19% lower risk of death. The risk was even lower when the researchers restricted their analysis to studies conducted only in the U.S., which had a higher

(Continued on page 4)

No Survival Bump for Localized Prostate Cancer with More Frequent PSA Tests

Undergoing more frequent PSA screening after radical prostatectomy (RP) or primary radiotherapy (RT) for localized prostate cancer was not associated with improved overall survival (OS), regardless of disease risk, according to results of the AFT-30 study (abstract 6503) presented at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting.

“Based on our study results, PSA testing every three to six months may represent overutilization of care,” said Ronald Chen, MD, of the University of North Carolina at Chapel Hill. "This study provides empiric data to inform future guidelines and clinical practice.”

The ideal PSA screening frequency for men who have completed treatment for localized prostate cancer is unknown. Current guidelines recommend post-treatment PSA surveillance, but the frequency of screening varies from once a year to four times a year. Intense post-treatment surveillance has the potential to cause harm, and it is unknown whether more frequent surveillance improves survival.

Chen and colleagues wanted to gain more insight into the appropriate frequency of PSA screening, find out if this frequency should vary by aggressiveness of disease or the type of primary treatment received, and deter

(Continued on page 4)
IsoPSA Test Could Reduce Overdiagnosis/Overtreatment in Prostate Cancer

A new blood-based diagnostic test (IsoPSA) for prostate cancer (PCa) that evaluates structural changes in PSA, instead of measuring the protein blood levels, could reduce unnecessary biopsies and identify the right men that need treatment.

The research, published in *European Urology*, was conducted in five academic and community urology centers in the United States. The study sample was heparin-plasma, collected from 261 men scheduled for a prostate biopsy between August 2015 and December 2016, following a suspicious digital rectal exam or rising PSA levels.

“Despite criticism, PSA has transformed the landscape of early detection, screening, and management of PCa in the last few decades,” said Eric Klein, MD, chair of Cleveland Clinic’s Glickman Urological & Kidney Institute. “Unfortunately, PSA is tissue-specific, not cancer-specific, leading to overdiagnosis and overtreatment of biologically insignificant PCa that is widely recognized as a key limitation in its clinical utility.”

The advantage of this study was that men were their own control, because researchers could compare the IsoPSA test against the PSA test in the same patient. Results showed a 53.3% prevalence of PCa in the study cohort, with a 33.7% prevalence of high-grade PCa. Importantly, there was no significant correlation between IsoPSA and serum PSA levels, and IsoPSA outperformed the PSA test for both endpoints that were measured. For a cutoff selected to recommend biopsy, IsoPSA demonstrated a 48% reduction in false-positive biopsies, and for a cutoff selected to identify men at low risk of high-grade disease, there was a 45% reduction in the false-positive rate.

Another study author, Mark Stovisky, MD, also at the Cleveland Clinic Glickman Urological & Kidney Institute, expressed hope that IsoPSA, requiring only a blood draw, would have good clinical utility once validated.

*Am Journal of Managed Care* 15 May 2018

Laser Focal Ablation of Prostate Cancer Improves Outcomes

Partial gland ablation of low-risk prostate cancer (PCa) using laser energy and a photosensitizing drug significantly decreased the risk of disease progression compared with active surveillance (AS), according to four-year outcome data from the first and only prospective randomized controlled trial evaluating focal therapy for PCa.

Trial results, were presented at the 2018 American Urological Association (AUA) Meeting by Inderbir Singh Gill, MD, Chair and Distinguished Professor of Urology at the University of Southern California Keck School of Medicine and Executive Director of the USC Institute of Urology. Ablation was done using the laser procedure – vascular-targeted photodynamic therapy (VTP).

“Partial gland ablation with VTP decreases progression of low-risk cancer to grade group 2 or higher, and therefore reduces conversion to radical therapy [compared with AS] minimizing the morbidity associated with radical therapy,” Dr. Gill said. “That is clinically meaningful for a large majority of men.”

VTP was recently approved in Europe for PCa focal therapy in men with low-risk disease based on two-year data published last year in *Lancet Oncology*, but it remains investigational in the United States. “The procedure involves intravascular administration of paezeliporfin, which circulates in the bloodstream. When exposed to light, the drug releases free radicals, causing occlusion of the microvasculature, resulting in ischemic coagulative necrosis,” explained Dr. Gill. Laser fibers are placed in the prostate at the site requiring ablation by the transperineal route. Laser light is administered for 22 minutes. Dr. Gill and collaborators randomly assigned 413 men with low-risk PCa to VTP or AS. VTP recipients had significantly lower rates of crossover to radical therapy at three years (7 vs. 33%) and four years (24 vs. 53%). Compared to AS patients, the VTP recipients had a reduction in absolute risk of 30 and 29% at three and four years, respectively. Both cohorts had similar four-year rates of metastasis-free cancer-specific, and overall survival.

Dr. Gill noted within five to 10 years of starting AS, 30 to 60% of men will convert to radical therapy, which is associated with high rates of erectile dysfunction and urinary incontinence. “If we can keep these men from converting to radical therapy... it will substantially improve their quality of life.”

Presented at the AUA 2018 Annual Meeting, abstract LBA23.

*Renal & Urology News* 23 May 2018
Humans are basically water. What the H.E.-DOUBLE-TOOTHPICK does that mean Moyad?! It means the human body is 66% water and blood, brains, lung, (just name another organ) ... are also primarily made up of water! Wow! Can someone please grab me a towel, or at least a paper towel?! Yet, somewhere in the internet educational world, a general health recommendation began to take hold, which is drinking eight glasses of water every day for the rest of your life was healthy? Say what?!

So, some groovy researchers decided to look into this whole eight glasses of water thing and reviewed peer-reviewed published literature since 1972 and they found something interesting. They found there was very good evidence to suggest that drinking more water can exacerbate symptoms of overactive bladder (OAB), but in patients with a history of kidney stones who drank this amount of water could prevent another kidney stone. Overall, there was no evidence to support drinking more water in a variety of medical situations.

However, they did find that dehydration could make some conditions worse, including chronic constipation and headache intensity. Still, it is easy to forget that humans get 20-25% of their water intake, on average, from food. So, watermelon, peaches, celery (by the way, I love celery way more than life itself because you can dip it in anything), radishes, broccoli, cucumbers, raw carrots, blah, blah, blah.

Some of the healthiest foods are primarily water (80-95% water content by weight). Still, each person has different water requirements and the kidneys are great at letting you know if you are getting enough water because your urine is usually clear in color when hydrated and generally dark yellow when not hydrated.

And, as we get older, our body’s alert system for dehydration does not work as well, so knowing the color of your urine is a good thing. I like to stare at my urinary stream often because I am not normal and because I want to know if I am hydrated. So, the whole eight glasses of water per day thing is again probably a good rule to prevent kidney stones, but please be careful if you have OAB (many women and men reading this column are impacted by this condition).

Oh, and in case you were wondering like I was, one of the first looks at the weight of the prostate was published long ago (1979). This proportion was determined to be about 80-85% and did not change much by age! So, at least the prostate knows how to stay hydrated throughout life!

I have to go now and stare at my urine again because all this talk of water makes me want to use the bathroom and/or set sail to Iceland in a cruise ship and/or listen to the song ‘Age of Aquarius’ by the 5th Dimension.

References:

* H.E.-DOUBLE-TOOTHPICK

"Hell" spelled out, referring to the fact that lowercase "l" looks like a toothpick.

No Immediate Treatment for Low-Risk Prostate Cancer

Record numbers of men with low-risk prostate cancer (PCa) are opting for conservative management such as watchful waiting (WW) or active surveillance (AS) rather than immediate treatment, a Veterans Affairs (VA) analysis indicates. With WW, men defer treatment until symptoms worsen, whereas AS relies on regular follow-up visits to monitor for any signs of disease progression.

The VA analysis found a sharp increase in this practice over the last decade. In 2005 it found that 27% of men aged <65 years and 35% of men ages ≥65 years were managed conservatively. In 2015, that number had increased to 72% of men aged <65 years and 79% of men aged ≥65 years (P <0.0001 for both endpoints, a statistically significant result).

The findings appeared in a research letter published online May 15th in JAMA.

The VA database was analyzed for men diagnosed with low-risk PCa between 2005 and 2015. Low-risk PCa was defined as a PSA level ≤10 ng/mL, a Gleason score ≤6, and clinical stage cT1/T2 disease. “Among 125,083 veterans with low-risk PCa, mean age was 64 years...and mean PSA was 5.4 ng/mL,” the investigators note.

Over the 10-year period, 48% of men were managed conservatively, 30% with WW, and 18% with AS. “On multivariable analysis, more recent diagnosis, increasing age, black race, unmarried status, higher PSA and higher comorbidity were associated with greater odds of conservative management,” the study authors note.

“Where the men were treated was also influential. For example, conservative management occurred in roughly 39, 24, 21 and 14% of men treated in the South, West, Midwest and Northeast, respectively,” researchers noted.

When asked to comment, Stacy Loeb, MD, from New York University in New York City suggested that “the successful uptake of conservative management in the VA system is due to several factors. One of these might be that the VA is publicly funded with salaried physicians, so there is little financial incentive to overtreat patients.”

Marc Garnick, MD, Gorman Brothers professor of medicine, Harvard Medical School and Beth Israel Deaconess Medical Center said that “the change in management of low-risk PCa at the VA has also been seen nationally.

“I think results simply reflect national practices,” Garnick noted. “National practices, in turn, reflect what is now recommended in the most recent guidelines,” he added.

Medscape Oncology
17 May 2018
**Differences with Genomic Tests**Continued from page 1

Instead, the team concluded that the majority of patients (21 of 22) met the NCCN criteria for AS and that the analysis “suggests Polaris is most apt to confirm this [NCCN] recommendation while Oncotype DX is more likely to go against it.”

“The lack of statistical significance and the k scores indicate that the results might be the result of chance,” said Wagner. “However, they do show that there are potential differences in the test outcomes.” He acknowledged that the study was not scientifically rigorous and was intended more to provoke questions about the utility of the tests.

Because there are no head-to-head studies of these genomics tests, “there has been very little reason, necessarily, to choose one over another,” said Stacy Loeb, MD, from New York University in New York City, who moderated the press conference. “There’s no clear evidence of a superior test.”

“Clinicians tend to use the test that is preferred at their institution, if they use one at all,” Loeb explained.

The tests cost $5,000 to $6,000, most of which is covered by Medicare and private insurance. However, when asked by a reporter if these costly tests have ever been shown to actually improve outcomes, such as disease-specific or overall survival, Loeb answered “no.”

Dr. Wagner reports financial ties to Genomic Health. Dr. Loeb reports financial ties to Lilly, MDx Health, General Electric, Genome Dx, Astellas, Sanofi, Minomic, and Boehringer Ingelheim.

Presented at the AUA 2018 Annual Meeting, abstract PD06-09.

**PSA Test Frequency**

(Continued from page 1)

mine if more intense surveillance was associated with improved survival.

The study used medical records data of 10,476 men from the National Cancer Data Base. All men were diagnosed with localized prostate cancer between 2005 and 2010 and had undergone RP or RT. Of these men, 4,088 had low-risk disease, 3,241 had intermediate-risk disease, and 3,148 had high-risk disease. The median age of men was 64 years.

The median number of PSA screens one year post-treatment was two for all groups, regardless of risk or treatment. Two years’ post-treatment, the median number of screens was two, regardless of risk or treatment group. However, by year two the proportion of men undergoing three or more PSA screens decreased compared with year one.

OS across all groups was eight years or longer. There was no significant association between frequency of PSA surveillance and OS in any of the risk or treatment groups.

**Blacks in Clinical Trials**

(Continued from page 1)

black enrollment.

“In all of the trials in the analysis, the primary outcome was overall survival after treatment with a standard chemotherapy regimen, docetaxel, and prednisone. All told, the studies had more than 8,000 men enrolled, but 85% were white and just 6% were black. Combining the studies allowed researchers to tease out difference in outcomes by race,” Halabi stated.

In the second study, Daniel George, MD, also of Duke, and colleagues, looked at hormone therapy – abiraterone acetate and prednisone – in a prospective analysis designed to see if whites and blacks had a different response. (Results of that study are discussed on page 6 of this month’s Us TOO Hot SHEET).

Both authors noted that it has historically been difficult to get black men into clinical trials of prostate cancer therapy, and stressed that it is important to change that.

“The bottom line,” according to ASCO expert Robert Dreicer, MD, of the University of Virginia School of Medicine in Charlottesville, VA “is that African Americans have potentially better survival on conventional therapy. But,” he said, “it’s still not clear why trial outcomes are better than what’s seen in general clinical practice. What is clear is that these men need to get to an oncologist and get treated.”

Presented at the 2018 Annual ASCO meeting, abstract LBA 5005
Prostate Cancer Survival Odds Worse for Smokers

Prostate cancer (PCa) patients who smoke are more likely to have tumors return, spread to other parts of the body, and become fatal than nonsmokers, a new study suggests.

Researchers examined data from previous studies with a total of 22,549 men with PCa that hadn’t spread to other parts of the body. The cancers were treated with either surgery or radiation.

Overall, nearly one in five men were current smokers. During a median follow-up of six years, vs. men who never smoked, current smokers were 40% more likely to have tumors return after treatment and more than twice as likely to have cancer spread beyond the prostate. Smokers were also 89% more likely to die from cancer.

“PCa diagnosis, even when it is not associated with tobacco smoking, is a teachable moment for patients to quit smoking,” said senior study author Dr. Shahrokh Shariat of the Medical University of Vienna in Austria. The study was published online May 24 in JAMA Oncology.

“Former smoking was associated with higher risk of relapse, but not with spread or cancer-specific death, which underlines the importance of smoking cessation in improving disease outcome,” Shariat said. “In fact,” he added, “men who had stopped smoking more than 10 years earlier ‘were not significantly different than men who had never smoked.”

“We know that tobacco smoking produces more than 70 carcinogens,” Shariat said. “It’s not clear exactly how smoking might lead prostate cancer to develop or make it more aggressive or more fatal. One possibility is that smoking causes inflammation, which in turn encourages tumors to grow, or that nicotine leads malignancies to spread,” Shariat said.

The smaller studies in the current analysis that looked at cancer-related deaths had a total of 7,924 participants. Overall, 654 men, or about 8%, died during a median follow-up of nearly eight years.

The current study wasn’t a controlled experiment designed to prove whether or how smoking influences the odds of dying from PCa. Researchers also based the analysis on smoking status when men were in treatment, and it’s possible some men might have stopped or started smoking after that.

“Smokers also might be less compliant with treatment than nonsmokers,” said Dr. Stephen Freedland, author of an accompanying editorial and the Director of the Center for Integrated Research on Cancer and Lifestyle at Cedars-Sinai Medical Center in Los Angeles, CA. “But because the study looked at men undergoing aggressive treatment, it’s unlikely that noncompliance influenced patient outcomes,” Freedland said by email.

“Cigarettes themselves have chemicals that can cause cancer,” Freedland said.

“This is more clear in the lung where the smoke is inhaled,” Freedland added. “However, the fact that PCa death is linked with smoking means (these cancer-causing) chemicals are not just present in the lungs but absorbed in the body and make their way to the prostate and, as such, they probably make their way into every organ in our bodies.”

Reuters Health
6 June 2018

This “Metastasis-Blocking” Compound Could Conceivably Stop the Spread of Cancer

Using a new approach, scientists located a compound that stops the spread of breast, pancreatic, and prostate cancers in mice. Researchers from the National Institutes of Health (NIH) and Northwestern University Feinberg School of Medicine in Chicago, IL collaborated on the study and published a paper in the journal Science Translational Medicine.

The compound, which they call metarrestin, destroys a unique structure inside the nucleus of cancer cells that can spread and form new tumors. In describing how it works, co-corresponding study author Sui Huang, who works as an associate professor of cell and molecular biology at Northwestern University Feinberg School of Medicine, likens it to a “dirty bomb against cancer.”

“It could potentially result in a better outcome for patients with solid tumor cancers with high potential to spread to other organs,” she adds. Once at the metastatic stage, cancers are very difficult to treat with current methods. Metastatic disease accounts for around 90% of cancer deaths and this figure has not changed much in half a century.

“Many drugs,” explains co-corresponding study author Dr. Juan Jose Marugan, group leader of the Chemical Genomics Center at the NIH’s National Center for Advancing Translational Sciences in Rockville, MD, “are aimed at stopping cancer growth and killing cancer cells. But so far, no drug designed specifically against metastasis has been approved,” he added.

Metarrestin destroys a little-understood structure inside the nucleus of cancer cells known as the “perinucleolar compartment (PNC).” Tests on lab-cultured cancer cells and cells sampled from human tumors have shown that “PNCs selectively form in cells from solid tumors.”

In earlier work, Prof. Huang and her team found that the likelihood of cancer spread was greater when tumor cells had more PNCs. This led the team to wonder whether attacking PNCs might reduce cancer spread and improve patients’ prospects.

In this study, scientists used “high-throughput screening and chemical optimization” to assess which compound, of at least 140,000, might have the greatest power to destroy PNCs in metastatic cancer cells. They whittled down the list to 100 compounds, and then they identified one that destroyed PNCs in metastatic prostate cancer cells.

A modification of the compound became metarrestin, which “significantly inhibited metastasis” in mice grafted with human pancreatic, breast, and prostate cancer. Treated mice also lived longer than untreated mice. Researchers intend to contact the Food and Drug Administration for a New Drug Application later this year to conduct investigational trials, after they have run more preclinical tests and collected the required data.

MedicalNewsToday
8 May 2018

Find Your Clinical Trial at the Us TOO Prostate Cancer Clinical Trial Finder
www.ustoo.org/HCP-Clinical-Trials
Abiraterone May Be More Effective in Black Men with Advanced Prostate Cancer Than in White Men

In a prospective clinical trial of 100 men with metastatic castration-resistant prostate cancer (mCRPC), response to abiraterone treatment was greater and longer-lasting in black men than in white men. Black men were more likely to have a decline in PSA and had a five-month longer median time to PSA worsening than white men (16.6 vs. 11.5 months). The study was featured in a press briefing presented by Daniel George, MD, Professor of Medicine and Surgery at the 2018 American Society of Clinical Oncology (ASCO®) Annual Meeting. This is the first prospective study to compare outcomes of abiraterone for advanced prostate cancer in black men and white men, according to the authors. The findings confirm prior retrospective observations suggesting a stronger cancer response to abiraterone in black men. In most clinical trials, the percentage of minority participants is disproportionately lower than the representation of the same racial group in the general population. (Black men were also under-represented in the clinical trial that led to the approval of abiraterone for this indication.) As a result, there is insufficient evidence about possible differences in treatment efficacy and side effects by race.

The Abi Race clinical trial enrolled 100 men with mCRPC, of whom 50 self-identified as white and 50 self-identified as black. The men received a standard treatment regimen for this disease – abiraterone acetate and prednisone – until the cancer worsened or unacceptable side effects arose. Cancer worsening was assessed through imaging scans (radiographic progression-free survival [rPFS]) and by measuring PSA level in the blood (PSA PFS).

The time to radiographic disease progression was similar between the two cohorts, but there were differences in PSA response by race. Abiraterone was more effective at both lowering PSA and delaying PSA progression in black men than in white men. Median PSA PFS was 16.8 months in black men and 11.5 months in white men. After abiraterone treatment, a greater percentage of black than white men had a PSA decline of 90% or more (48 vs. 38%), 50% or more (76 vs. 66%) and 30% or more (86 vs. 76%).

In addition, more white men than black men (eight vs. four) had no PSA decline. Based on imaging scans, black men did not have worse outcomes than white men – the median rPFS was the same for black men and white men (16.8 months). Most side effects were similar by race. However, 40% of white men experienced fatigue vs. 26% of black men. Also, 36% of black men experienced a low potassium level in blood vs. only 18% of white men. A low potassium is a complication directly related to the effect of abiraterone on adrenal hormones, which can be life-threatening if not corrected.

“Black men are more than twice as likely to die of prostate cancer as white men and are generally thought to have worse prostate cancer outcomes. Our study suggests that when black men and white men with advanced prostate cancer are given the same hormone treatment, this is not the case,” said Dr. George and colleagues.

ASCO Expert Robert Dreicer, MD, MS, MACP, FASCO commented, “Racial and ethnic minorities continue to be underrepresented in clinical trials. This study should serve as a call for the entire cancer research community to make trials much more inclusive. When it comes to cancer treatments, people are not all alike, and it’s important to understand how different groups respond to different therapies,” he said.

Presented at the 2018 ASCO Annual Meeting, abstract LBA5009.

The ASCO Post
1 June 2018

Adjuvant Docetaxel Fails in Higher-Risk Prostate Cancer

Adjuvant docetaxel without prednisone failed to improve biochemical disease-free survival in men with intermediate- or high-risk prostate cancer (PCa) who have undergone radical radiotherapy (RRT) with androgen deprivation therapy (ADT), according to results of the Scandinavian Prostate Cancer Group’s multinational phase III SPCG-13 trial.

Findings were presented by Pirko-Liisa I. Kellokumpu-Lehtinen, MD, of University of Tampere, Finland at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting, abstract 5000. According to Kellokumpu-Lehtinen, chemotherapy was known to be effective in metastatic breast cancer, colorectal cancer and PCa when this trial was planned over 10 years ago. However, the survival benefit in castration-resistant prostate cancer (CRPC) was only 2.5 months. At the time, adjuvant chemotherapy was used for breast and colorectal cancers due to clinical studies that had shown a survival benefit. This trial was designed to answer the question whether adjuvant chemotherapy after RRT for PCa would improve outcomes.

In the trial, men were randomly assigned to either six cycles of adjuvant docetaxel at 75 mg/m² every three weeks without prednisone (Arm A, N=187) or to surveillance (Arm B, N=188). All men were required to have neoadjuvant/adjuvant ADT. Men were followed for five years, with a PSA test every three months for two years then every six months. The primary endpoint of the trial

(Continued on page 8)

Resources Address Anxiety, Depression and Prostate Cancer

Many men who are diagnosed with prostate cancer, or are managing the disease, experience some level of anxiety and/or depression. Caregivers may also be affected. The psychosocial challenges surrounding treatment choices and side effect management can have a negative impact on the prostate cancer journey. Anxiety and depression aren’t always effectively treated, in part because the symptoms may not be recognized.

We encourage you to visit the Us TOO web page for information on recognizing and managing anxiety, depression and prostate cancer.

www.ustoo.org/anxiety-and-depression

US TOO INTERNATIONAL PROSTATE CANCER EDUCATION & SUPPORT Hot SHEET – JULY 2018
P1, “No Survival Bump…” A question that has never been properly assessed is how often do men need PSA tests following local therapy for prostate cancer. A recent presentation by Chen, et al. suggests that more frequent testing did not translate into better outcomes. One may expect that testing frequency may need to be individualized. Since few men with low-risk disease will ever progress, frequent testing seems to be unnecessary. Men with high-risk disease are certainly at greater risk for progression. However, that also does not mean that testing them more often will translate into a better survival.

The Bottom Line: Optimal testing frequency of post-therapy PSA was not properly assessed but better outcome has not been seen.

P1, “Notable Differences…” As active surveillance gains acceptance around the U.S., doctors are looking for ways to improve patient selection rather than relying only on the biopsy, Gleason score and DRE. Genetic tests would appear to offer an excellent opportunity and three are available: the Oncotype, Prolaris, and Decipher tests. Unfortunately, they have not been compared to each other. Now we have a small retrospective study in a group of 22 men that had at least two of these tests. While the Prolaris test was most consistent with the NCCN guidelines, the small sample size and uncontrolled format leaves the results open to question. A larger, better, controlled trial would be needed. The weakness of all three tests is that they provide a percentage risk not an actual risk. Either a patient’s cancer will or will not progress, but these tests provide only an odds ratio. That means if any of the tests give a low probability of progression, some men may still feel that any risk is too much to accept. Alternatively, those with a 30-40% risk may still feel the odds are in their favor (60-70% not progressing) and they may choose a conservative approach. Clearly genetic testing is evolving, but the true value of any of them remains unclear.

The Bottom Line: The added value of genetic testing beyond the NCCN criteria remains uncertain.

P1, “Black Men Do Well…” Historically, African-American men do not have high enrollment in most prospective clinical trials. Consequently, doctors are not sure if treatments need to be modified because of their higher prostate cancer mortality rate. A study presented at the 2018 annual AUA meeting suggests that African-Americans do not have worse outcomes compared to Caucasians, and there is a hint they may do better. A pooled analysis of nine clinical trials showed similar overall survival and when certain risk factors were considered, they actually did better. Clearly, doctors need to understanding why African-American men are reluctant to enroll in clinical trials, but at least based on this analysis, they can be reassured that they do not need a more aggressive therapy.

The Bottom Line: African-American men with advanced prostate cancer do not have worse outcomes when enrolled in clinical trials and this information needs to be disseminated to that community in order to increase enrollment in future trials.

P2, “IsoPSA Test…” A long-standing goal for prostate cancer screening has been to improve the accuracy of the test used to detect the cancer. One possibility is the IsoPSA Test, which measures different forms of PSA. Early results suggest there are fewer false positives and a reduction in finding non-life threatening cancers. A next step is to assess its utility as a screening test, possibly comparing it to PSA.

The Bottom Line: IsoPSA is showing promise as an alternative to PSA for prostate cancer screening.

P2, “Laser Focal Ablation…” Focal therapy of localized prostate cancer is like a ball rolling downhill that can’t be stopped, with a growing belief in its value despite an absence of the right studies. The most recent study by Gill, et al. is prospective and randomized, but the outcome may not be sufficient. At three and four years, they found that the conversion rate to definitive therapy was much lower after vascular-targeted photodynamic therapy compared to active surveillance. Thus far, the rate of metastases was similar and no information was provided about survival. Some concerns about this are the following: First, we know that many men come off AS, not because of disease progression, but rather because they can no longer tolerate the approach. The abstract does not report that information. If any focal therapy is really a psychological treatment, we should question if that is a good enough justification to do it. Second, the abstract does not present information about post-therapy biopsies, to determine how often the cancer is eradicated. It would also be important to know what percentage of men have cancer in other parts of the gland that was not treated with focal therapy.

The Bottom Line: Focal therapy using photodynamic therapy appears to lower the conversion rate to definitive therapy, but many questions remain unanswered.

P5, “Prostate Cancer…” As if men did not need a good reason to stop smoking, we now have another uncontrolled study by Shariat, et al. suggesting that smokers have a greater likelihood of dying from their disease than non-smokers or those that stopped more than 10 years ago. This is consistent with several other uncontrolled studies and it is unlikely that we would ever see a prospective trial. It is curious that smokers will undergo aggressive therapy to try to improve their survival while not also taking other actions that could improve their health. One wonders why this is so often the case?

The Bottom Line: Smokers appear to have a higher risk of dying from prostate cancer, even after definitive therapy compared to non-smokers.

P6, “Abiraterone…” In an-
Adjuvant Docetaxel (Continued from page 6)

was a rising PSA of 2 ng/mL or more above the nadir (lowest post-RRT) PSA value.
The majority of men (78.2%) completed all six cycles of
docetaxel in Arm A, with only eight men who received no
docetaxel at all.
Toxicity was moderate. Serious side effects related to
docetaxel occurred in 52% of men. Most were cytopenias (low blood cell counts), and
febrile neutropenia (fever with a low white blood cell count) of any grade occurred in
16.1% of men. There were no treatment-related deaths.
No disease progression occurred in 69% of men in Arm A and 69.7% of men in Arm B
over the five year period. In
the whole study population, the primary endpoint was
achieved in 30.7% of men,
but there was no difference
in the primary endpoint be-
tween the two arms.
“...the biochemical progression rate in both arms at five-
year follow-up was ‘lower
than expected,’”
Kellokumpu-Lehtinen re-
ported. “The Kaplan-Meier
curves for biochemical pro-
gression-free survival did not
separate at all,” she said. In
univariate and multivariate analyses, Gleason sum was
the only predictive factor for progression. T stage or ran-
domization arm did not have a
prognostic effect.
Subgroup analysis showed a
trend favoring docetaxel for
Gleason score tumors >8,
however, the P value was not statistically significant
(P=0.059, P<0.05 is statistically
significant).
“...As we know, docetaxel was
shown effective in hormone-
naive metastatic prostate
cancer in the STAMPEDE and
CHARTED trials, but why not in
[the adjuvant setting] needs further preclinical and
clinical studies,” Kellokumpu-
Lehtinen concluded.
Cancer Network
10 June 2018

The Bottom Line (Continued from page 7)

other study, abiraterone acete-
tate plus prednisone was
compared prospectively in
African-American and Cauca-
sian men with metastatic
castrate resistant disease.
Although the study needs to
mature further to see the
effect on overall survival,
thus far, African-American
men had a better disease-
free survival. There were
some differences in the side
effect profile. Again, this is
important information that
needs to be publicized to
encourage more African-
American men to participate in
clinical trials.
The Bottom Line: In men
with mCRPC, African-
American men appear to
have a better progression-
free survival than Caucasian
men with some differences in
the incidence of side effects.
P6, “Adjuvant Docetaxel...”
Recent studies have shown
that many men with meta-
static prostate cancer have a
higher survival with ADT plus
docetaxel compared to ADT
alone. This might suggest a
benefit from adding chemo
to high-risk men after radical
radiation therapy (RRT). Un-
fortunately, a randomized
study by Kellokumpu-
Lehtinen, et al. has failed to
show a reduction in the re-
currence rates at five years.
It is possible that with longer
follow-up, differences may
be observed but, for now,
chemotherapy should not be
recommended.

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information on prostate cancer.
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