INSIDE THIS ISSUE
Shorter ADT Course May Suffice for High-Risk Prostate Cancer 1
Aggressive Therapy Warranted for Gleason 10 Prostate Cancer 1
No Benefit of Adding Abiraterone to Enzalutamide in Metastatic CRPC 1
Cost Effectiveness of SelectMDx in Prostate Cancer Risk Assessment 2
Proton Therapy Trials “At Risk,” Slow to Enroll Patients 2
Doc Moyad’s No Bogus Science: “Artificially Sweetened Beverages…” 3
Aggressive Prostate Cancer Type is “Fairly Prevalent” 4
Androgen Deprivation Therapy Ups Risk of a Thromboembolic Event 4
MRI-Targeted Biopsies May Have a Role in Active Surveillance 5
Large US Study Targets Prostate Cancer in Black Men 6
Doctor Chodak’s Bottom Line 7

SEPTEMBER 2018

Hot SHEET
Us TOO INTERNATIONAL Prostate Cancer Education and Support Network

Shorter ADT Course May Suffice for High-Risk Prostate Cancer

Reducing the duration of androgen deprivation therapy (ADT) from 36 months to 18 months in men with localized high-risk prostate cancer (PCa) also receiving radiation therapy (RT) improves their quality of life (QoL) without decreasing overall survival, according to a new study.

Investigators randomly assigned 630 men to receive pelvic and prostate RT and either 18 or 36 months of ADT (short and long arm, respectively). “Five-year overall survival (OS) rates were 86% in the short arm and 91% in a long arm, a non-significant difference,” Abdenour Nabid, MD, from the Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, Quebec, Canada, and colleagues reported online in European Urology.

The investigators assessed QoL using EORTC (European Organisation for Research and Treatment of Cancer) validated tools: EORTC30 version 3.0, which is a 30-item score scale for global QoL, and PR25, which is more specific to prostate cancer and consists of 25 items, six of which assess sexual activity and sexual functioning. The investigators regrouped all 55 items into 21 scales. A QoL analysis revealed a significant difference in six scales and 13 items favoring the shorter course of ADT.

“We were not really surprised by the results; like many colleagues we think that 18 months is sufficient” (Continued on page 5)

Aggressive Therapy Warranted for Gleason 10 Prostate Cancer

Aggressive therapy with curative intent appears to be highly successful in men with Gleason score (GS) 10 prostate cancer (PCa), according to a new study published in the International Journal of Radiation, Oncology, Biology, Physics (Vol. 101, pp. 883-888, 2018).

“Our overall findings suggest that survival outcomes following definitive treatment for Gleason score 10 PCa are quite good, with five-year overall survival (OS) rates approaching 80% regardless of treatment modality,” said study investigator Amar U. Kishan, MD, from the Department of Radiation Oncology at the University of California, Los Angeles.

The team did not find any robust differences in outcomes associated with any specific upfront treatments, although external beam radiation therapy (EBRT) plus brachytherapy (BT) with long-term androgen-deprivation therapy (ADT) appeared to be associated with superior distant metastasis-free survival (DMFS). Overall, multimodality treatment with an emphasis on both local and systemic control is critical for men with GS 10 disease, according to the researchers.

Because of the rarity of GS 10 PCa, there has not been a great deal of investigation into the long-term clinical outcomes and overall prognosis for this patient population. Dr. Kishan and his collaborators examined a cohort of 112 men with biopsy-proven GS 10 disease. Definitive treatments included radical prostatectomy (RP), EBRT, or EBRT plus BT, given from January (Continued on page 6)

No Benefit of Adding Abiraterone to Enzalutamide in Metastatic CRPC When PSA is Increasing

The PLATO trial failed to show benefit of adding abiraterone/prednisone to ongoing enzalutamide vs. abiraterone/prednisone in men with metastatic castration-resistant prostate cancer (mCRPC) exhibiting rising PSA during enzalutamide treatment. Results were reported online ahead of print in the Journal of Clinical Oncology by Attard, et al.

The trial enrolled 509 men from 51 sites in North America, Europe, and Australia. In period 1, men received open-label enzalutamide 160 mg daily. Those with no PSA increase at weeks 13 and 21 continued treatment until PSA progression (≥ 25% increase and ≥ 2 ng/mL above nadir, the minimum PSA) and were then randomized in the double-blind period 2 to abiraterone acetate 1,000 mg daily and prednisone 5 mg twice daily with either enzalutamide or placebo. A total of 251 men were randomized to the combination group (N=126) or to the control group (N=125).

The primary endpoint was progression-free survival (PFS) evidenced by scans or unequivocal clinical progression or death during study. Median PFS was 5.7 months in the combination group and 5.6 months in the control group (hazard ratio [HR] 0.83, P=0.22, not a statistically significant difference). Reduction in baseline PSA of ≥ 50% occurred in 1% vs. 2% of patients. Median time to PSA progression was 2.8 months in both groups. No differences between groups were observed in rate of pain (Continued on page 5)
Cost Effectiveness of SelectMDx in Prostate Cancer Risk Assessment

Govers T, Caba L, Resnick MJ, J Urology, Article in Press, 2018

Purpose: SelectMDx is a panel of urinary biomarkers used in conjunction with traditional risk factors to individualize risk prediction for clinically significant prostate cancer. In this study, we characterize the cost-effectiveness of SelectMDx in a population of U.S. men with elevated PSA.

Materials and Methods: We developed a Markov decision-analytic model to simulate the chain of events and downstream outcomes associated with ultrasound-guided prostate biopsy and a strategy where SelectMDx is implemented prior to biopsy. The primary outcome was health outcomes, measured in quality-adjusted life years (QALY) and secondary outcome was health care costs from the Medicare payer perspective. Multiple one-way sensitivity analyses were performed to characterize model robustness.

Results: The expected mean QALY per patient under the current standard was 10.796 at a cost of $11,060 over an 18-year horizon. Incorporating SelectMDx resulted in expected mean QALY per patient and cost to be 10.841 and $9,366, respectively, representing an average 0.045 QALY gained at a cost-savings of $1,694 per patient. Extrapolating these data to a conserva-
tive estimate of 311,879 men per year undergoing biopsy, one would expect SelectMDx to result in an incremental 14,035 QALY gained at a cost-savings of $528,323,026 for each yearly cohort. The SelectMDx strategy dominated the current standard across a wide range of sensitivity analyses.

Conclusions: Routine use of SelectMDx to guide biopsy decision-making improves health outcomes and lowers costs in U.S. men at risk for prostate cancer. This strategy may optimize value of prostate cancer risk assessment era of increasing financial accountability.

Proton Therapy Trials “At Risk,” Slow to Enroll Patients

“The big question about proton beam (PB) radiotherapy (RT) – ‘is it any better than conventional RT?’ – is being addressed in seven ongoing randomized clinical trials sponsored by the National Cancer Institute (NCI). But these trials, which cover cancers of the breast, lung, prostate, esophagus, liver, and brain, are all enrolling more slowly than expected,” report a trio of experts.

“The trials are ‘at risk’ mainly because of this poor accrual,” say justin poor accrual,” say justin poor accrual,” say Justin Bekelman, MD, of the University of Pennsylvania, and Andrea Denicoff, MS, RN, and Jeffrey Buchsbaum, MD, PhD, from the NCI. Their report was published online ahead of print on July 9 in the Journal of Clinical Oncology.

The trials are essential to compare the efficacy and toxicity of the newer, experimental PB therapy to conventional photon-based RT, which includes intensity-modulated RT (IMRT). However, there are problems with getting patients to receive PBRT.

The authors talked to physicians, patient advocates, and insurers and reviewed commercial insurers’ coverage policies. “Nearly all commercial insurers and state Medicaid plans do not cover PB therapy for the indications under study,” they report. PB therapy has not been proven superior and is more expensive, claim insurers.

On a positive note, the authors found that Medicare “typically does cover the treatment through local coverage determinations, which may include clinical study participation requirements.” Another hopeful sign is that some insurers, including Cigna, Independence Blue Cross, and Blue Cross Blue Shield of Florida, cover PB therapy for selected cancers under study or have established coverage with study participation policies.

In other good news, some proton centers, including those at the University of Pennsylvania, the Mayo Clinic, and the University of Maryland, offer discounts to patients in which the price of PB therapy is equal to that of IMRT. Other centers, such as Northwestern Proton Therapy and Seattle Cancer Alliance, have payment programs in which the center absorbs the treatment cost if PB therapy is not covered upon appeal to an insurer.

“These compromises from both insurers and PB centers signal progress,” say the report authors, “but they are uncommon. Overall, the situation is at an impasse.”

The result is very slow enrollment. For example, in the breast cancer trial of 893 clinically-eligible patients screened through September 2017, 582 (65%) had insurance policies that did not cover PB therapy.

(Continued on page 3)
Artificial sweeteners have become similar, at times, to political beliefs. You have to take a side! Often, after lecturing around the globe, I have people run up to me, almost knock down another person in front of them, and literally ask me with incredible vigor (veins bulging on the forehead) the following: “are you for or against artificial sweeteners?” And, I get about five-seven seconds to answer the question before I get interrupted and then I calmly take another sip of my diet Mountain Dew (I know I am going to Hell for drinking it). What gets missed in all the passion is the inability to see first and foremost what the clinical end result of the artificial sweetener utilization will be in the next few months or year(s). If you use artificial sweeteners, overall you are moving toward a healthier place such as an improved weight/waist, then great, but if your artificial sweetener is just there to B.S. yourself that you are becoming healthier overall, when you are not, then you need to throw them out.

Recently, one of the more comprehensive prospective studies (actually part of randomized trial CALGB 89803) on diet and colon cancer recurrence after conventional treatment found that: “Higher artificially-sweetened beverage consumption may be associated with significantly reduced cancer recurrence and death in patients with stage III colon cancer.” What the heck?! Also, the authors (same ones to find benefits for coffee=yeah!) seemed to suggest that one of the potential reasons for the benefit (if true or just luck) could be due to the “substitution for sugar-sweetened alternatives” with artificial sweeteners. In other words, it appeared that even some unhealthy patients were potentially moving toward a healthier place in this study with the use of artificial sweeteners.

I have seen people lose 50 pounds going off sugar sweetened beverages and going on diet products, and I have also seen people gain lots of weight on artificial sweeteners. Yet, why did such an important study in the world of cancer appear to receive little or no attention! I mean the National Institutes of Health (NIH) was involved in this study and there appeared to be NO nefarious outside company that pushed these results or this observation (quite the contrary). These awesome researchers just found what they found! In prostate cancer, minimal human research has looked at this issue and many of the studies have been inconclusive. Regardless, this is an important study to discuss in the cancer world since, as every year passes, it is becoming accepted that diet and lifestyle plays some role in colon cancer recurrence or prognosis. And, in prostate cancer we also believe that there is some dietary role, but we don’t know how strong or weak it is or where it might work best. What we do know is that if a person takes on a comprehensive lifestyle change that moves her or him toward a better place mentally and/or physically then that should be lauded and supported.

The idea that we have to place artificial sweeteners in some category as all good or bad is partly to blame for the passionate misdirected discourse that surrounds them. Regardless, I loved this study, but not many other people seemed to, and perhaps that is the problem, at times, with nutritional research, especially in the area of cancer. My job is to report the evidence regardless of my personal belief of what diet(s) cancer patients should follow.

So, Dr. Moyad do you think it is okay to use artificial sweeteners now, or are artificial sweeteners simply evil and bad for me? The answer to this long question is “YES!”

PS: Happy Prostate Cancer Awareness Month! Emphasis on the word “Happy!”

References:
2. Moyad MA, 33+ years of doing the same damn thing.

Proton Therapy Trials “At Risk” (Continued from page 2)

Bekelman is the principal investigator in this breast cancer trial, and his home institution, the University of Pennsylvania, owns and operates a PB therapy center.

So, as seven clinical trials drag on, no answers are generated about comparative efficacy and toxicity of the two rival RT technologies. “If we can complete the trials in a timely fashion, the results will enable patients to make more informed treatment decisions,” said Denicoff in a press statement.

PB therapy has been aggressively marketed by centers, but, to date, only one randomized trial in lung cancer has reported final efficacy results. (The lung cancer trial was not among those in the current study). In that trial, PB therapy was no better than standard RT.

“One thing is certain about PB therapy: it costs more. Average Medicare reimbursement per treatment course,” say the report authors, “is approximately $10,000 to $20,000 more for PB therapy than for conventional IMRT, depending on indication.”

“The NCI and the Patient-Centered Outcomes Research Institute (PCORI) have made ‘major investments to fund’ these seven randomized trials,” say the report authors. “However, those investments evidently did not include paying for patient treatment with the various technologies.”

To address this shortcoming, the report authors propose a set of three solutions:

The first emphasizes the need for insurance. The trio says that all stakeholders should come together to establish insurance coverage with a trial participation program for patients who enroll in the NCI- or PCORI-funded randomized RT trials.

The second is to improve enrollment rates and recognize clinicians who are good at enrolling patients.

The third solution is to engage patients more deeply so that they want to enroll.

However, even with patient-friendly trials, enrollment “would be even more fruitful if there was a clear solution to restrictive insurance coverage for PB therapy,” say the report authors.

Medscape Medical News
12 July 2018
Aggressive Prostate Cancer Type is “Fairly Prevalent”

Many clinicians who treat men with prostate cancer (PCa) may be unfamiliar with “treatment-emergent small-cell neuroendocrine prostate cancer” (t-SCNC).

That’s because it has been considered a rare phenomenon, estimated to occur in about 1% of men with metastatic castrate-resistant PCa (mCRPC). However, a new study found that it is present in nearly one fifth of men with mCRPC.

Rahul Aggarwal, MD, from the University of San Francisco, California, and colleagues found that among 202 men with progressive mCRPC who were consecutively enrolled at five US centers, the overall incidence of t-SCNC was 17%.

The new finding was published online July 9 in the Journal of Clinical Oncology. The researchers note that t-SCNC, which may be a disease subtype, is associated with resistance to the androgen receptor (AR)-targeting agents abiraterone and enzalutamide, as well as to other hormonal treatments.

Notably, detection of t-SCNC was associated with shortened overall survival among men with prior AR-targeting therapy for mCRPC (hazard ratio, 2.02; 95% confidence interval, 1.07 - 3.82). Median overall survival was 44.5 months in men without t-SCNC and 36.6 months in those with t-SCNC, among those who had prior use of abiraterone and/or enzalutamide (P=0.027).

The finding that prior use of abiraterone and enzalutamide was tied to diminished survival among the men with t-SCNC should not be a complete surprise to clinicians, the authors suggest.

"Therapeutic resistance [to abiraterone and enzalutamide] is a near-universal phenomenon, frequently heralded by a more aggressive clinical course," they write.

"The main take home point is that t-SCNC is fairly prevalent and that there are no hallmark clinical characteristics that can be used to identify this high-risk disease subset," Aggarwal stated.

It is probable that increasing use of abiraterone and enzalutamide may be leading to increased incidence of t-SCNC, but our study did not definitely address this question," he added.

The study could not address the issue because only a minority of patients had no previous exposure to abiraterone or enzalutamide.

Specifically, 148 (73%) of the men in the study had prior disease progression on abiraterone and/or enzalutamide. Other study patients had disease progression on older forms of hormonal therapy, including luteinizing hormone-releasing hormone agonists, such as leuprolide, as well as first-generation antiandrogens, such as bicalutamide, nilutamide, and flutamide.

In the study, the 202 men underwent a total of 249 metastatic tumor biopsies, including those of the bone, liver, lymph nodes, and other soft tissues. The median time from diagnosis of mCRPC to biopsy was 17.6 months.

Of the 202 men, 160 (79%) had sufficient tumor present in a biopsy specimen to permit histologic classification. t-SCNC was found in 27 of the 160 (17%).

This subtype resembles de novo small-cell prostate cancer, a highly aggressive histologic variant present in less than 1% of untreated prostate cancers at diagnosis.

The study authors say that “it is not clear” whether the treatment-emergent variant is the same disease entity as de novo small-cell prostate cancer. As a result of this uncertainty, researchers have given this variant its own moniker: t-SCNC.

Other reports have attempted to define the prevalence and characteristics of this treatment-emergent variant but have been hampered by a lack of prospective data. However, one series of 150 men (with mCRPC and evaluable metastatic biopsy specimens) was prospective and, as noted above, tallied an incidence of t-SCNC of about 1% (0.7%) (Cell. 2015;161:1215-1228).

Aggarwal and his coauthors explain that this 2015 study is the best available comparator — but not a great one — because of multiple methodologic differences.

Aggarwal placed the current study in a larger context: “This was one of the first large, multicenter, prospective studies to analyze the incidence of t-SCNC in mCRPC using data from sequentially enrolled patients who did not previously carry a diagnosis of t-SCNC.

“The implication for clinical practice,” said Aggarwal, “is that metastatic biopsies should be considered broadly in men with mCRPC who have tumors that are safely accessible for biopsy.

"We observe an increasing prevalence of men who undergo tumor biopsy, but it remains an underutilized diagnostic tool outside of the academic setting," he added.

Metastatic biopsies allow for (Continued on page 8)
MRI-Targeted Biopsies May Have a Role in Active Surveillance for Prostate Cancer

MRI-targeted biopsies pick up as many higher-grade tumors as do systematic biopsies during active surveillance (AS) for prostate cancer (PCa), according to results from the ASIST trial.

“The main value of MRI in men on AS is early identification of large high-grade cancers missed on the diagnostic biopsy,” stated Dr. Laurence Klotz from Sunnybrook Health Sciences Center, in Toronto, Canada. “It doesn’t preclude systematic biopsies, nor should it be used alone as a trigger to intervene.”

AS is the current standard of care for most men with low-grade PCa, and some studies have suggested that MRI can reliably exclude higher-grade PCa in men on surveillance.

Dr. Klotz and colleagues evaluated the effectiveness of MRI-targeted biopsies vs. conventional systematic biopsies in identifying high-grade PCa in their randomized trial of 273 men diagnosed with low-risk PCa within the past year.

MRI identified regions of interest for biopsy in 64% of men, with 26% of targets considered anterior (a location that is less reliably evaluated by transrectal ultrasound), the team reports online in European Urology.

The primary outcome, the proportion of men whose confirmatory biopsy was upgraded to grading group 2 or higher, did not differ significantly between the MRI arm (21%) and the systematic-biopsy arm (23%); results were similar after central pathology review (33% versus 27%, respectively).

Upgrading was seen in 14% of men in the MRI arm on targeted biopsy alone, but this was not a statistically significant improvement over systematic biopsy.

The groups did not differ significantly in progression-free survival, time to radical intervention, or progression. There were significant differences between the three study sites in the upgrading rates of targeted biopsies, likely reflecting different levels of expertise with the targeted biopsy technique, the researchers note.

“MRI is a useful adjunct, but (a) negative MRI doesn’t preclude a systematic biopsy, (b) systematic biopsies still need to be done in men having a targeted biopsy, and (c) in low-grade PCa, presence of a region of interest should not, on its own, be an indication for treatment (i.e., one can’t assume it is high-grade cancer),” Dr. Klotz concluded.

Dr. Sanoj Punnen from Sylvester Comprehensive Cancer Center at the University of Miami, Florida, told Reuters Health by email, “The thought is that MRI can help localize cancer within the prostate, and there are lots of data that shows using MRI and targeted biopsy finds more high-grade cancer than typical random biopsy. This is mainly in the diagnostic setting, but even in AS we have seen studies showing the benefit of MRI.”

“However, in this randomized controlled trial, we failed to see a difference in the detection of aggressive cancer between an MRI-based approach and standard of care random biopsy,” he said. “This was a surprise to me. However, when you look at the cohort we have to realize it is restricted primarily to low-risk and therefore these patients were very selected.

(Continued on page 8)

Shorter ADT Course (Continued from page 1)

in most of these cases,” Dr. Nabid stated.

The short and long study arms included 320 and 310 men, respectively. After a median 9.4 year follow-up, 290 men died, 143 in the short arm and 147 in the long arm. The median ADT duration for all patients was 17.9 months in the short arm and 35.4 months in the long arm. The 10-year cumulative incidence of biochemical failure was 31% in the short arm compared with 25% in the long arm. In adjusted analyses, men in the long arm had a significant 29% decreased risk of biochemical recurrence compared with those in the short arm.

“To my knowledge, no other study compares 36 versus 18 months of ADT in high-risk PCa,” Dr. Nabid said.

Neil Desai, MD, Assistant Professor of Radiation Oncology at the University of Texas Southwestern Medical Center in Dallas, said these data are important and will change clinical practice in select cases. “Patients in this study better reflect those who now present in the clinic. It gives us more flexibility to personalize treatment and update patients on outcomes in a more contemporary setting of PSA-detected high-risk disease, as compared to locally advanced presentations of high-risk disease in older trials,” Dr. Desai said.

“The detailed data on compliance and testosterone recovery in particular can only give us a better ability to refine our therapy intensity to what a patient is on board with doing. So, yes, for me it is practice-changing for some of my patients,” he added.

Renal & Urology News
25 July 2018

Adding Abiraterone (Continued from page 1)

progression, objective response rate, or time to first use of subsequent antineoplastic therapy.

Grade ≥ 3 adverse events occurred in 45% of the combination group vs. 37% of the control group. A higher incidence of events was seen in the combination vs. control groups and included high blood pressure (10% vs. 2%), and increased liver enzymes (ALT [6% vs. 2%]) and AST [2% vs. 0%].

The investigators concluded, “Combining enzalutamide with abiraterone acetate and prednisone is not indicated after PSA progression during treatment with enzalutamide alone; hypertension and elevated liver enzymes are more frequent with combination therapy.”

The ASCO Post
2 August 2018

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 important information on recognizing and managing anxiety, depression and prostate cancer.

www.ustoo.org/anxiety-and-depression
Aggressive Therapy Warranted for Gleason 10 Prostate Cancer

(Continued from page 1)

2000 to December 2013. Of the 112 men, 26, 48 and 38 had RP, EBRT, and EBRT with a BT boost, respectively. Researchers used Kaplan-Meier method to estimate OS, cancer-specific survival (CSS), and DMFS. The median follow-up was 4.9 years (3.9, 4.8 and 5.7 years for RP, EBRT, and EBRT plus BT, respectively). In this cohort, significantly more men (98%) who had EBRT alone received upfront ADT than men who had EBRT plus BT (79%). ADT duration, however, was similar (24.0 vs. 22.5 months). Propensity score adjusted five-year OS rate was 80, 73, and 83% for the RP, EBRT and EBRT plus BT groups, respectively. Adjusted five-year CSS rates were similar among groups: 87, 75, and 94% for RP, EBRT, and EBRT plus BT, respectively.

Men in the EBRT plus BT group had a significant 60% decreased risk of distant metastases compared with the EBRT group. Dr. Kishan said, “these data may provide useful prognostic benchmark information that can benefit physicians and patients.”

“Patients with localized Gleason score 10 disease should be offered aggressive local therapy. This could either mean a definitive RT approach, with long-duration ADT and possibly a BT boost, or a definitive surgical approach,” Dr. Krishan stated. “If the latter is pursued, I would strongly suggest that it still be a multimodal approach. The bottom line is that these patients deserve the chance for curative treatment, whatever the backbone of that treatment might be.”

Yair Lotan, MD, Professor and Chief of Urologic Oncology at the University of Texas Southwestern Medical Center in Dallas, said the study is a valuable addition to the medical literature because very few studies have focused specifically on GS 10 patients. “The study is relatively small and not randomized. So the outcomes data are valuable as a benchmark, but cannot be used to recommend one therapy over another,” Dr. Lotan said. These new data suggest that many patients can be cured by aggressive local therapy if they do not have metastatic disease. “The controversy is whether the risks of RP or even RT are worthwhile if the disease will recur systemically anyway, but these results and others suggest that the risk is worthwhile since many men can be cured,” he said.

William Catalona, MD, Professor of Urology at Northwestern University Feinberg School of Medicine in Chicago, said that the use of propensity matching reduces biases, but these analyses have significant limitations.

“It is questionable to what extent valid conclusions can be drawn from this study, especially concluding that RT plus ADT is more effective than RP for Gleason 10 prostate cancer,” Dr. Catalona said. “The differences observed may be due merely to biases for which a complete adjustment is not possible by propensity-based analysis.”

“I think the work is important as it addresses treatments for the most aggressive forms of PCa,” said Mark Garzotto, MD, Professor of Urology and Radiation Medicine at Oregon Health & Science University in Portland, and Director of Urologic Oncology at Portland VA Medical Center. “This study shows that there are many acceptable modalities for these patients, including RP and RT.”

However, he pointed out that the five-year OS rate “was only around 80% for the entire group.” Data from the Surveillance, Epidemiology and End Results (SEER) program show five-year OS for local and regional PCAs at about 99%.

“So men with Gleason 10 cancer are doing poorly with standard therapies according to this study,” Dr. Garzotto said. “My guess is that many of these patients have micrometastatic disease at presentation, and that some of the newer imaging modalities will demonstrate these. I would strongly recommend that physicians include a thorough discussion about the availability of clinical trials for these patients.”

Renal & Urology News
20 July 2018

Large US Study Targets Prostate Cancer in Black Men

Black men in the U.S. have higher rates of aggressive prostate cancer (PCa) than other males. Now, a $26.5 million study is underway to understand why. The National Institutes of Health (NIH) and the Prostate Cancer Foundation (PCF) have launched the study to investigate social, environmental and genetic factors behind this disparity.

“No group in the world is hit harder by PCa than men of African descent, and, to date, little is known about the biological reasons for these disparities, or the full impact of environmental factors,” Dr. Jonathan Simons said in a NIH news release. He’s president and CEO of the PCF.

Compared to other racial and ethnic groups in the US, black men disproportionately experience aggressive PCa—meaning tumors that grow and spread quickly. Black American men have about a 15% chance of developing PCa vs. roughly a 10% chance for white men, according to the news release.

Black men also have a higher PCa death risk than white men, 4 vs. 2%, respectively. The NIH agencies supporting the new research are the US National Cancer Institute (NCI) and the US National Institute on Minority Health and Health Disparities. A team of scientists nationwide will conduct the research.

“Understanding why African-American men are more likely to be diagnosed with aggressive PCa than men of other racial and ethnic groups is a critical, unanswered question in cancer disparities research,” said Dr. Ned Sharpless, director of the NCI. “This large, collaborative study can help the cancer research community better understand and address these disparities,” he said.

The study aims to enroll 10,000 black men with prostate cancer. It will investigate (Continued on page 8)
Doctor Chodak’s Bottom Line


Editor’s Note: Us TOO has invited 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.

P1, “Shorter ADT Course…”
How long is ADT needed for men with high-risk prostate cancer? That question has been under investigation for quite some time. The radiological societies deserve great credit for conducting well-done sequential studies. The latest study randomized men to receive either 36 or 18 months of ADT. So far, overall survival at both five and 10 years are not significantly different. Also, quality of life was better in the men receiving the shorter duration. With this more mature data, new patients with high-risk disease who will receive external radiation can safely be offered the shorter course of therapy. It has the same chance of controlling their cancer with side effects being reduced.

The Bottom Line: The new standard of care for men with high-risk prostate cancer who receive external radiation should be limited to 18 months of ADT.

P1, “Aggressive Therapy…”
Do we know the best treatment for men with Gleason 10 prostate cancer? The answer is no because no well-designed study has been performed and, in general, these tumors are not that common. A non-randomized study by Kishan and co-workers is included in this Hot SHEET and there are two main takeaways. First, it is unclear from this study whether radical prostatectomy, external radiation with or without ADT or external radiation with brachytherapy boost is superior. The second point is that despite local and some systemic therapy, the overall survival at five years is only about 80%, which means that any of these local therapies is inadequate in about 20% of men. Clearly, studies are needed with more aggressive therapy for some of these men but, without a randomized trial, the efficacy will be difficult to interpret.

The Bottom Line: More work is needed to determine if a more aggressive therapy for Gleason 10 cancer can reduce mortality from this disease.

P1, “No Benefit of Adding…”
For men with metastatic castrate resistant disease undergoing treatment with enzalutamide, there is apparently no benefit from adding abiraterone acetate. That is the finding of the PLATO study, which compared men receiving enzalutamide alone or in combination with abiraterone. Progression-free survival was not significantly different between the two groups. Furthermore, side effects were more common in men getting both drugs. So, we know that additional therapy is needed for men getting enzalutamide but the best option needs to be determined.

The Bottom Line: Men with castrate resistant metastatic disease who are treated with enzalutamide do not benefit by adding abiraterone.

P2, “Cost Effectiveness…”
Use of genetic tests to help guide decision-making is growing in popularity. Two questions, however, are how much added information is provided and are they worth the cost? Several of these tests have been studied in men with an elevated PSA to find out if the test can help men avoid a biopsy. The report by Gavors, et al. is a mathematical analysis of the potential to save money and spare men from a biopsy because they have a low chance of high-grade disease. This and several other genetic tests improve the area under the curve compared to traditional criteria such as PSA, free PSA, DRE and age but none of them is able to predict all men with high-risk disease. Are they worthwhile and worth the cost? That also is unclear. However, if a man wants to avoid a biopsy, even if his risk of high-grade disease is low, but not zero, then the added information can be helpful, as long as the individual understands that these tests will miss some high-grade cancers. Longer follow-up will reveal whether or not following the results of this test will lead to a simple delay in diagnosis or a missed opportunity of curing high-grade cancer.

The Bottom Line: Genetic tests such as SelectMDx may be able to spare some men from a prostate biopsy but it will miss a small percentage of high-risk cancers.

P2, “Proton Therapy Trials…”
There has been considerable hype regarding the theoretical benefits of proton radiation compared to conventional radiation therapy. As happens all too often, new technologies receive FDA approval because they are safe but without the requirement of proven benefit. Several randomized trials evaluating the efficacy of Proton therapy are now underway, but accrual appears to be slow, in part, because several insurance companies do not cover the therapy. I personally think something is wrong here. Why should a patient, or even an insurance company, pay for someone to have a treatment that, at this time, has not been proven to offer better results? Shouldn’t the proton centers foot that bill? When a drug company wants to test a new drug, insurance companies do not pay the cost until the drug is shown to be effective. The drug company pays for the drug during the evaluation. So why does this inconsistency exist? A good answer is definitely lacking.

The Bottom Line: The added benefit of Proton therapy for prostate cancer remains unclear and studies are in progress to obtain the needed data, but who should be paying for men to participate in these trials?

P4, “Aggressive…” Is a biopsy of a metastatic site necessary to manage men with advanced disease? The answer may be “yes” because of an apparent increase in the presence of treatment-emergent small cell neuroendocrine prostate cancer or t-SCNC. This histological variant is known to be very aggressive and does not respond to the newer hormonal drugs enzalutamide and abiraterone. Whether using either of these two drugs increases the likelihood of finding t-SCNC is unclear at this time. The androgen receptor splice variant, AR-V7, also has been shown to identify men who will not respond to abiraterone, so perhaps this test should be done in those with castrate resistant disease and who should

(Continued on page 8)
MRI-Targeted Biopsy  
(Continued from page 5)

Also, while about 60% of men had an MRI-visible lesion, about 20% were indeterminate lesions, which often have a low hit rate.

“However, the criteria for observation is expanding and we are doing surveillance in more intermediate-risk patients, where MRI may have the most benefit,” said Dr. Punnen, who was not involved in the trial.

“Furthermore, additional studies like this with broader inclusion criteria need to be done to validate these findings and help identify which group of patients benefits the most from MRI.”

Reuters Health  
30 July 2018

Visit the Us TOO Prostate Cancer Clinical Trial Finder at www.ustoo.org/HCP-Clinical-Trials

Aggressive PCa Type  
(Continued from page 4)

a better understanding of the histologic subtype (t-SCNC vs standard adenocarcinoma), as well as more genetic information about the tumor.

“It is important to try to identify the distinct subsets of mCRPC,” said Aggarwal, “including those with t-SCNC, those harboring tumors with DNA repair defects, and potentially other subcategories, for purposes of new drug development and application of therapies with a higher degree of specificity for the tumor subtype.

“Two transcription factor proteins found to be overactivated in t-SCNC in the study population are targets of drugs already in clinical trials, with several more in preclinical testing,” Aggarwal said in comments online. “However, no treatments targeting such factors or mutations in PCa are currently available for use in the clinic.”

Medscape Medical News  
16 July 2018

Black Men  
(Continued from page 6)

possible links between aggressive disease and social/environmental factors such as discrimination, early life adversity, and segregation.

The researchers will also analyze DNA and tumor samples to identify gene variants associated with aggressive prostate cancer. Then they’ll explore how those gene variants may interact with the social/environmental factors.

The scientists hope that unraveling all these complex interactions will allow for the development of tailored approaches to prevention, diagnosis, and treatment.

HealthDay News  
23 July 2018

The Bottom Line: Finding t-SCNC cells in metastatic sites may identify patients who are not good candidates for the newer androgen receptor targeted drugs enzalutamide and abiraterone and probably apalutamide, but more research is needed.

Join us for our next live event and webinar: Prostate Cancer Pathways for Patients and Caregivers on Saturday, September 29, at Englewood Hospital in Englewood, NJ. Certified sexuality counselor and author, Dr. Anne Katz will join us for a special presentation on sex and intimacy related to prostate cancer. To register to attend the event in person or watch the webinar with live video and audio, visit: www.mainstreamchicago.com/ustoo-pathways-new-jersey

Hot SHEET Personal Subscriptions Available

We can deliver the Hot SHEET newsletter right to your home or office. Support the creation and distribution of the Hot SHEET with a suggested annual subscription donation of $35 for 12 issues (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 helps men with prostate cancer learn to fight this disease.

The power of Us TOO is in helping men, and those who love them, by transforming resignation into determination and fear into hope.
Between the Sheets...
Prostate cancer treatment can be life-saving. But the aftermath of treatment side effects can have a devastating impact on the quality of life for a man and his partner. The common side effects of erectile dysfunction (ED) and incontinence can be temporary or ongoing. Regardless of the duration, they pose a challenge to maintaining a satisfying sex life that may be part of a couple’s intimate relationship. Without acknowledgement and resolution, these issues can develop into a wedge that can fracture a couple’s physical and emotional bond at a point when it needs to be strong and sustainable.

The value of Us TOO is in addressing the unmet or underserved needs of the prostate cancer community. Based on recent survey results from Us TOO support group leaders across the country, we recognize the need to address the impact that prostate cancer has on sexual health and intimacy. In addition to updated content on the Us TOO website, we are pleased to introduce Between the Sheets as a new, regular feature of the Us TOO Hot SHEET newsletter.

This column will provide the platform for experts in the field to help men and women by providing answers to questions about sexual health and intimacy challenges that can result from prostate cancer treatment.

Our first column was compiled with the help of Dr. Anne Katz, Certified Sexuality Counselor and Clinical Nurse Specialist at CancerCare Manitoba. She has educated thousands of healthcare providers and cancer survivors about cancer, sexuality and survivorship. She is the editor of the Oncology Nursing Forum, an avid blogger for ASCO Connections, and the author of 13 books on the topics of illness, sexuality and cancer survivorship. (www.drannekatz.com)

Dr. Katz will be a featured presenter at the Prostate Cancer Pathways for Patients and Caregivers event and webcast in Englewood, NJ, on Saturday, September 29. (See the event ad on the opposite side of this sheet. Register at www.mainstreamchicago.com/ustoo-pathways-new-jersey).

QUESTION FROM PROSTATE CANCER SURVIVOR:
When I received my prostate cancer diagnosis, my wife was my rock as we met with the doctor and decided on treatment. I’m now struggling with managing post-treatment side effects of ED and incontinence. It’s taking a toll on our marriage and my sense of being a man. While I have never loved her more, I’m not able to perform sexually like I used to and we don’t talk about it. It pains me that we’re not able to be intimate and I sense that she’s withdrawing from me. How do we move forward?

RESPONSE FROM DR. ANNE KATZ:
This is a common problem - the sexual changes as well as incontinence - but also the feelings you are experiencing about your relationship and how you see yourself as a man. Sexuality is an important component of male self-esteem and self-image, and changes in this area often precipitate a crisis of confidence.

Men often use sex as a way of showing their love for their partner, but when problems occur - such as after treatment for prostate cancer - they have trouble finding ways to express this. You have included this in your question: “We don’t talk about it.”

Relationships are dependent on communication especially when there is a challenge, such as loss of sexual function. When you don’t talk about what is going on (or what is NOT happening!), the other person starts to make assumptions, just as you are doing when you say that you sense that your spouse is withdrawing. She may be keeping her distance because she doesn’t want you to think that she is initiating something sexual and you will be upset if you can’t respond like before. She may be withdrawing because she is trying to protect herself - and you! She may be blaming herself for something and thinks that YOU are avoiding her because you are not doing what you would normally do to create and maintain the connectedness that is the true meaning of intimacy and is the result for many couples of coming together sexually.
How can you move forward? It’s simple, but complex - YOU NEED TO TALK TO EACH OTHER, OPENLY AND HONESTLY. She needs to know what you are thinking and feeling and how you are interpreting her reactions and response to you. You need to listen (and believe) what she tells you about her thoughts and feelings. You both need to lean in TOWARDS each other just as you did when you were learning about your diagnosis and treatment options. If you can’t talk to each other without help, then find some help - a couple’s counselor or marriage therapist or sex therapist can help you to talk in a safe environment. Once you have talked you can then discuss WHAT you want to do about the situation - explore medical therapies that may help with erections, pelvic floor physiotherapy for the incontinence, or other ways of experiencing sexual pleasure that do not require an erection. The key element is that you have to SHARE and do this TOGETHER.

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: ustooBTS@ustoo.org

Or mail your letter to:
Us TOO International
Between the Sheets
2720 S. River Road, Suite 112
Des Plaines, IL 0018

Prostate Cancer Pathways for Patients and Caregivers
an Educational Event
& Webcast Series from

Us TOO
SUPPORT • EDUCATION • ADVOCACY

Saturday, September 29
Englewood Hospital
Chiang Auditorium
350 Engle Street
Englewood, NJ 07631

The event will be webcast live on the internet for those unable to attend in person.

To register, visit:
www.mainstreamchicago.com/ustoo-pathways-new-jersey
or contact Terri at 877-978-7866 or terril@ustoo.org.

☑ Men’s health
☑ Overview on prostate cancer
♥ Sex and intimacy related to prostate cancer
☑ Content for newly diagnosed, recurring, and advanced patients

Presenters: Dr. Anne Katz of CancerCare Manitoba; Dr. Stacy Loeb of NYU Langone Health; Dr. Charles G. Drake of the Herbert Irving Comprehensive Cancer Center; and Dr. Mazyar Ghanaat of Englewood Health