Quality of Life Takes Huge Hit After Prostate Cancer Treatment

Prostate cancer (PCa) treatments take a huge toll on multiple quality of life (QoL) domains and the impact may be greater than reported in clinical trials, according to results of the European Uomo Patient Reported Outcomes Study (EUPROMS).

The results show that QoL is negatively impacted by any treatment for PCa other than active surveillance (AS), which “should be prompted as the first option for treatment for those men where it can be offered safely,” Dr. André Deschamps, Europa Uomo Chairman, reported in a presentation at the European Association of Urology (EAU) Virtual Congress.

The findings are based on 2,943 men treated for PCa from 24 European countries who completed a 20-minute online survey that used validated QoL questionnaires.

Their mean age was 64 at diagnosis and 70 when they completed the survey, meaning they were reporting QoL six years after treatment. Two-thirds of the men received one treatment for PCa, 22% received two treatments, 10% received three, and 2% received four or more.

Overall, half of the men reported that loss of sexual function was a “big” (28%) or “moderate” (22%) problem in the years following treatment.

“We often hear that decline in sexual functioning is a relatively small problem for PCa patients. This survey paints a different picture,” Dr. Deschamps, of Erasmus University Medical Centre Department of Urology, said in a conference statement.

(Continued on page 2)

Genomic Profiles of Prostate Cancers Differ Between Men of African and European Ancestry

The genomic profiles of prostate cancers in African-American men and men of European ancestry show several differences, researchers report.

“This study strongly supports the idea that samples from African-American men need to be included in future molecular studies and clinical trials for new prostate cancer (PCa) therapies,” stated Dr. Joshua D. Campbell of Boston University School of Medicine by email.

African-American men have a higher incidence of PCa, present with more advanced disease at an earlier age, and have increased mortality from the disease compared with European Americans. Whether genomic alterations differ between these groups and contribute to clinical outcomes remains unclear.

Dr. Campbell and colleagues evaluated PCa genomic alterations associated with race and investigated tumor genomic features in primary and metastatic disease in 250 African-American men and in 611 European-American men from four publicly available data sets.

Tumors from African-American men showed significantly higher frequencies of somatic mutations in ZFHX3 (6.0 vs. 2.1%), ETV3 deep deletions (6.3 vs. 2.3%), and deletions in ZFHX3 (8.8 vs. 3.4%) and NKX3-1 (10.5 vs. 5.4%).

In contrast, deletions in PTEN were significantly less com-

(Continued on page 3)
Beyond PSA: New Prostate Cancer Screening Options

In the wake of more than a decade of controversy over PSA testing, research is emerging pointing to new approaches for stratifying prostate cancer (PCa) risk. Two noninvasive tests — an assessment of spermine levels in urine and a blood test that combines free and total PSA and the (−2)-pro-PSA isoform (p2PSA) — are much safer than historically risky biopsy and what is now considered to have been unnecessary surgery.

“We’ve ‘cured’ a lot of men,” Franklin Gaylis, MD, from the University of California, San Diego, stated. “Even some men who didn’t need to be cured. Now we are working to solve this dilemma,” he said. “It’s time we determine who do you screen, [who do you] not screen, and how aggressively?”

Urine Spermine Test More Accurate Than PSA

Data from a highly predictive test that assesses spermine levels in urine were presented by Peter Ka-Fung Chiu, MD, from the University of Hong Kong, at the virtual European Association of Urology (EAU) 2020 Congress. Normal spermine levels are inversely associated with both PCa and high-grade PCa (HGPCa).

To investigate the predictive value of spermine for any PCa or HGPCa (Gleason 7 or above), the researchers recruited 556 men from two centers and collected 30 mL of urine prior to prostate biopsy.

They analyzed data from 390 men using decision-curve analyses for PCa and for HGPCa. The multivariate spermine score — which considers age, prostate volume, PSA level, and spermine line — provided net clinical benefit over PSA alone and over spermine score alone.

“At 90% sensitivity, this risk score actually had a negative predictive value of 96.7% and avoided about 50% of unnecessary biopsies,” Chiu explained. “This test predicts PCa and high-grade PCa well, without the need for prior prostate massage, offering improved predictive performance.”

PHI Reduces Need for MRI Screening

Another test, the PHI prostate cancer biomarker, is as predictive as multiparametric (mp)MRI, both with and without PSA scoring. PHI scores from 554 men from five centers added to either PSA density or mpMRI improved the prediction of risk for ≥GG2 cancers to more than 0.81 and for ≥CPG3 cancers to more than 0.85, according to data from the multicenter PRIM (PHI to Refine MRI) study group published in *BMC Medicine* and presented at EAU.

With a PHI cut-off of 30, mpMRI referrals could be cut by 25%, and unnecessary biopsies could be cut by 40%, the PRIM group reports. PHI (Continued on page 8)

QoL Takes Huge Hit After Prostate Cancer Treatment

The men also reported that different treatments had different effects on QoL. Radiation therapy (RT) had the biggest reported impact on sexual function and radical prostatectomy (RP) had the biggest reported impact on urinary incontinence. “The impact of RT on sexual function was reported as worse than RP, but both had a severe impact,” Dr. Deschamps told *Reuters Health*.

Fatigue and insomnia scores were highest with RT and chemotherapy. “RT doubled the fatigue a patient experienced vs. surgery, whereas chemotherapy tripled the fatigue score,” he noted. “Fatigue and insomnia rates were higher than we were expecting. Results for incontinence and sexual function confirmed that data gathered in clinical environments are an understatement,” Dr. Deschamps said. “I hope healthcare professionals will give a better indication to men before treatment and make sure that after treatment all possible help is given to minimize effects.”

The survey also found that the best QoL scores are seen when PCa is detected in an early, curable stage.

“This means efforts toward early detection and awareness are essential to avoid unnecessary deterioration in QoL. Wherever it is possible and safe, AS should be considered the first line treatment to ensure best QoL,” Dr. Deschamps said in the statement.

“Our findings provide patients and health care professionals with a snapshot of the impact of treatments. We hope they will be used to set realistic expectations of the effects of the different treatments for PCa on QoL,” he added.

Dr. Deschamps added, “This is the first time ever that such a study has been done. EAU has recognized this by giving us the opportunity to speak in one of the four game changing sessions.”

Presented at the 2020 EAU Virtual Congress, 17 July 2020

*Reuters Health Information*
27 July 2020
I love to say that I think we (prostate cancer [PCa] researchers) can learn a lot from breast cancer research and vice versa. A recent preliminary paper from a past notable chemotherapy clinical trial of locally advanced breast cancer “attribato la mia attenzione” (aka “caught my eye” in Italian – I like to impress my audience with my ever-evolving Googled temporary language skills). 1 Basicall, women in this study in the higher weight categories were less likely to respond to treatment, but why?

This study did some analysis and found that women treated specifically with docetaxel were potentially less likely to receive an effective response from the drug compared to lean individuals. Researchers suggest that since docetaxel is “lipophilic” or absorbed or drawn in by adipose (fat) tissue, that perhaps the tumors are not able to receive as much drug in someone that weighs more vs. someone that weighs less. However, as the drug is currently given, it is believed the dosage does adequately fit the body type (so to speak), but is this method super precise for these types of drugs and does this really account for the pharmacokinetics of this unique drug?

It seems some preliminary PCa research is also now debating the impact of weight, weight gain, and amount of adipose tissue (actually visceral fat) on docetaxel efficacy and this is a controversial subject. 2,3 Regardless, another recent study of weight or weight gain in the years following a prostate cancer diagnosis is fascinating. In my world it is known as the “Cancer Prevention II Nutrition Cohort” and included 8,330 total PCa patients, of which 6,749 of them had lower-risk/localized tumors (Gleason 7 or less).4 Researchers found weight gain could impact prognosis and other risks, regardless of treatment. They concluded, “...postdiagnosis weight gain may be associated with higher mortality from all causes and PCa.” It also included increased risk of cardiovascular disease mortality.

Postdiagnosis weight gain more than 5% of body weight or more than 10 pounds vs. more stable weight post-diagnosis was associated with a worse cancer prognosis, increased cardiovascular problems, and simply less longevity. It is not easy making all of us better understand the potentially profound negative impact of unhealthy weight gain on treatment and its impact on quality and quantity of life. Weight maintenance and weight loss is a total pain in the gluteus maximus... it is so very difficult today, which means it requires as much attention, awareness, and education compared to almost anything else we all write about in cancer newsletters, which is why we should be obsessed with talking about it and potential solutions for it.

Weighing in on weighty weight issues are needed more than ever and there is no time to wait (pun not intended) for more research to tell us it needs to be prioritized as much as anything else during PCa awareness month!

Genomic Profiles of PCa Differ Between Men of African and European Ancestry (Continued from page 1)

mon in African-American men (5.3%) than in European-American men (15.3%), the researchers report online in Clinical Cancer Research.

In a separate analysis of 3,454 men with localized and metastatic PCa, frequencies of several genomic alterations were significantly higher in tumors from African-American men than in European-American men. These include CCND1 amplification, HGF amplification, KMT2D truncation, MYC amplification, SPOP point mutation, and overall alterations in KEL, NOTCH2, and PTCH1. There were no significant differences between African-American and European-American men in currently clinically actionable genes.

“We were able to find genes that were more frequently mutated in PCa from African-American men including ZFHX3, ETV3, and MYC,” Dr. Campbell said. “These associations had not been previously reported, although other studies had already found that some genes were less frequently mutated in tumors from this population (e.g., the TMPRSS2-ERG fusion and PTEN deletions).

“We found that the frequency of mutations in DNA repair genes and other genes that are targets of current therapeutics are similar between men with African ancestry compared to other groups,” he said. “This suggests that current PCa therapies should benefit in people of both African and European ancestry as long as they are applied equitably.”

Dr. Timothy Rebbeck of Harvard T. H. Chan School of Public Health and Dana Farber Cancer Institute, in Boston, who earlier reviewed variation in PCa genetics by race, ethnicity and geography, told Reuters Health, “We have known for a while that there are differences in genomic features of prostate tumors. The fact that this study reported differences is therefore consistent with the literature, but it was interesting to see in this paper that many of the clinically relevant molecular events do not differ by race.

“This work needs to be confirmed before the data can be translated to clinical practice, but if there are similarities in molecular profiles across races for relevant therapies, this could guide therapeutic decisions,” said Dr. Rebbeck, who was not involved in the new research. “However, these data don’t provide data on treatment responses, so studies that extend these molecular differences to actual treatment responses or outcomes still need to be done.”

 Reuters Health Information 11 August 2020
Both the authors and Kutikov point out that male gender and age are two main risk factors for a lethal COVID-19 infection and for PCa. The authors also state that “older age and comorbidities (hypertension, diabetes, obesity, and smoking) that adversely affect COVID-19 are also lethal for PCa.”

“There appears to be a ‘perfect storm’ of COVID-19 risk, consisting of age, race [among black men], sex, comorbidities, and cancer among many men with PCa,” explained senior author Ashutosh Tewari, MD, also of Mount Sinai, in an interview. “Being a large hospital in New York City, Mount Sinai was ‘the epicenter of the epicenter’ in the early weeks of the pandemic,” he said. “There was a convergence between [the type of man] who showed up in the ICU and who showed up in my PCa clinic,” observed Tewari, who, like many staff at Mount Sinai, eventually provided care to COVID-19 patients. “I also saw first-hand that men were more likely to get infected, to be hospitalized, to be in an ICU, and to die,” he continued.

Tewari eventually was infected himself and spent two weeks in the ICU before being released; his wife and daughter also contracted the COVID-19 virus.

During his interview with Medscape Medical News, Tewari slightly moderated the call for testing among patients with PCa. “Have a low threshold for testing is what I am suggesting,” he said. “[Men with PCa should] get tested if they have even slight fear that they have been exposed.”

A Shared Biology?
As noted above, the New York team posits that there may be biological mediators of the sex differences seen with COVID-19. In their review of these, they note research suggesting that in men with PCa, the use of androgen deprivation therapy (ADT) may be protective against COVID-19, as reported by Medscape Medical News in another article. Clinical trials to further explore the link between COVID-19 and PCa and ADT are underway. For example, a trial on the use of bicalutamide, an antiandrogen, among men with COVID-19 is being conducted in Baltimore. And the US Department of Veterans Affairs launched a phase II trial for the use of the hormone suppresser degarelix (a GnRH analog that blocks luteinizing hormone and thereby reduces androgens) for COVID-19-infected male patients.

Tewari said men with PCa need to be “super cautious” in following CDC guidelines to avoid COVID-19 and doctors need to reach out to them via telehealth for ongoing monitoring. He advises physicians to encourage behavior change for the sake of improved health and comorbidities.

“Men usually don’t focus on these things, so pay attention to changeable behaviors. Stop smoking. Control your blood pressure. Control your diabetes. Lose weight. “We men think we are invulnerable, but this is one battle you can win by being afraid, not by being brave,” Tewari concluded.

Medscape Medical News
7 August 2020
Can Grape Seed Extract Slow Prostate Cancer Spread?

A recently completed study at two UC Health locations suggests that a commonly used, relatively inexpensive product, grape seed extract, could benefit some men with prostate cancer (PCa).

Grape seed extract is readily available in pill, capsule and liquid form on the aisles of health food and grocery stores. Many people take it as a dietary supplement – it contains antioxidants and may help to reduce inflammation and lower blood pressure, although studies of those benefits are sparse.

By contrast, grape seed extract has been the subject of National Institutes of Health-funded studies for well over a decade at the Skaggs School of Pharmacy and Pharmaceutical Sciences on the University of Colorado Anschutz Medical Campus. There, Drs. Chapla Agarwal and Rajesh Agarwal and their research colleagues isolated a specific compound in grape seed extract that, not only inhibits the growth of PCa tumors, but also kills the cells that drive PCa growth.

A study published in 2014 followed many years of lab work by the Agarwals that established the cancer-fighting properties of grape seed extract in cell cultures and in mice. In 2009, they published a study summarizing evidence from their own studies and others that grape seed extract administered to mice was effective in slowing the growth of, not only PCa, but also skin, colorectal and breast cancers.

From bench to bedside:
Grape seed extract for PCa

This and other work provided the foundation for the current study, led by Dr. Paul Maroni, associate professor of Surgery-Urology at the University of Colorado School of Medicine. Maroni met with Rajesh Agarwal about the feasibility of a clinical trial that would test the effectiveness of grape seed extract in treating human patients with PCa. They put together a trial protocol, based not on hope, but on the years of evidence the Agarwals had developed.

“The basic science suggested that grape seed extract might slow down PCa progression,” Maroni said.

In a relatively speedy seven-month period, the trial recruited 20 men from UC Health University of Colorado Hospital on the Anschutz Medical Campus and UCHealth Cancer Care and Hematology Clinic – Harmony Campus in Fort Collins. The subjects were men who had previously completed surgery, radiation treatment or both for their PCa. They also had to have slowly increasing PSA numbers – a key marker for PCa growth – despite lacking evidence through imaging or other tests that the cancer had metastasized, or spread.

Slowing the next treatment step for PCa

The idea was to see if taking 150 milligrams of grape seed extract twice a day for a year could slow the progression of the disease, as measured by the time it took for the patient’s PSA level to double. The longer that period, the longer providers could hold off androgen deprivation therapy (ADT) to suppress the hormones that drive PCa.

“ADT can blunt the cancer’s spread, but it also comes with a host of serious side effects, including hot flashes, fatigue, weight gain, weakened bones and increased risk for metabolic problems, heart disease and fractures,” Maroni said.

“Some men need that therapy to slow the spread of cancer to other parts of the body,” he stressed.

“We don’t mind if a treatment gives patients side effects if there is a lot of value for them in terms of a longer life or a decreased burden of treatment later,” he said. “But if the PSA is rising slowly, years may go by before there are symptoms or detectable metastasis.”

In that case, the strategy is to watch and wait, and if grape seed extract lengthens that period, that’s a plus. “The study suggests that the supplement treatment achieved at least partial success and deserves further study,” Maroni said.

Using grape seed extract: posting the results

The study was accepted for poster presentation at the American Association for Cancer Research (AACR), and was given by Maroni in a recorded address at a June 22 virtual meeting of AACR. As the authors noted in the poster presentation, the “observation period” for patients with non-metastatic PCa “presents an opportunity to treat men with compounds having a favorable side effect profile that hopefully delay disease progression” and the need for ADT.

The primary objective of the trial was for the PSA doubling time (PSADT) to increase by 30% or more. Nine of the 20 enrollees met that goal. PSA levels declined in three men. Overall, PSADT rose from 5.4 to 6.4 months — slightly less than 20% — suggesting the grape seed extract helped to slow cancer cell growth.

Eight men failed treatment due to a PSADT of less than three months, requiring more aggressive therapy.

Adverse events included hypertension and dehydration, but the researchers added that men generally tolerated grape seed extract well.

More research needed for using grape seed extract to slow cancer growth

The team concluded with a call for more research into the potential benefits of the supplement for men with non-metastatic PCa who have otherwise exhausted their treatment options.

“That’s now in the works,” Maroni said, and aims to recruit another 20 men.

“We want to see if we can replicate this study data,” Maroni said, stating he is reasonably optimistic that the new patient recruitment phase will begin in August.

Rajesh Agarwal emphasized that, regardless of the trial’s findings, grape seed extract is not a stand-alone treatment for cancer of any kind and is never a substitute for standard medical care. The same applies to other natural substances with potential cancer-fighting properties that he has researched.

“If you are on any kind of treatment regimen, don’t do anything else without first consulting with your physician,” he added. But he is hopeful that the recent study leads to more options for clinicians treating PCa.

Maroni said men with slowly progressing prostate cancer may be able to avoid therapies with challenging side effects for longer periods of time, a boon for their quality of life.

University of Colorado UC Health
10 August 2020
Introduction & Objectives: While active surveillance (AS) is an established standard of care for low-risk (LR) prostate cancer (PCa), its utility for favorable intermediate risk (fIR) PCa is less evident. Growing evidence from prospective studies suggests worse outcomes on AS. Prior retrospective studies have been limited by inability to differentiate between AS or watchful waiting (WW).

Herein, using a recent update in the Surveillance, Epidemiology and End Results (SEER) Database, we provide the first population-level analysis of AS, WW and AT (first line surgery or radiation therapy) for LR and fIR PCa.

Materials & Methods: Men diagnosed with cT1N0M0 localized Gleason Grade Group (GG) 1-2 PCa between 2010-2015 were identified. Patients were stratified by GG and initial treatment into six cohorts; initial treatment was defined as AS, WW, or AT utilizing the new “Watchful waiting recode (2010+)” variable. The Kaplan-Meier method and log-rank test were used to compare cancer-specific (CSS) and overall survival (OS). All statistical tests were performed using SPSS®, version 23.0.

Results: 162,804 men were diagnosed with cT1-4N0M0 localized GG1 or GG2 PCa between 2010-2015. GG2 patients on AS have worse CSS and OS than GG2 patients who received AT and GG1 patients treated with AS or AT (log rank tests p<0.05). WW patients (GG1 and GG2) have the worst survival outcomes of any cohort (log rank tests p<0.05).

Conclusions: With improved distinction between WW and AS in the SEER dataset, it is evident that GG2 patients placed on AS have worse CSS and OS than comparable cohorts. In conjunction with increasing data from prospective cohorts, AS should not be the preferred treatment modality for GG2 PCa.

Development and Validation of a Deep Learning Algorithm for Gleason Grading of Prostate Cancer from Biopsy Specimens


JAMA Oncol. 23 July 2020; Published online

Key Points

Question: How does a deep learning system (DLS) for assessing prostate biopsy specimens compare with interpretations done by specialists in urologic pathology and by general pathologists?

Findings: In a validation data set of 752 biopsy specimens obtained from two independent medical laboratories and a tertiary teaching hospital, this study found that rate of agreement with subspecialists was significantly higher for the DLS than it was for a cohort of general pathologists.

Objective: To evaluate the ability of a DLS to grade diagnostic prostate biopsy specimens.

Design, Setting and Participants: The DLS was evaluated using 752 de-identified digitized images of formalin-fixed paraffin-embedded prostate needle core biopsy specimens obtained from three institutions in the United States, including one institution not used for DLS development. To obtain the Gleason grade group (GG), each specimen was first reviewed by two expert urologic subspecialists from a multi-institutional panel of six individuals (years of experience: mean, 25 years; range, 18-34 years). A third subspecialist reviewed discordant cases to arrive at a majority opinion. To reduce diagnostic uncertainty, all subspecialists had access to an immunohistochemical-stained section and three histologic sections for every biopsied specimen. Review was conducted from December 2018 to June 2019.

Main Outcomes and Measures: The frequency of the exact agreement of the DLS with the majority opinion of the subspecialists in categorizing each tumor-containing specimen as one of five categories: non-tumor, GG1, GG2, GG3, or GG4-5. For comparison, the rate of agreement of 19 general pathologists’ opinions with subspecialists’ majority opinions was also evaluated.

Results: For grading tumor-containing biopsy specimens in the validation set (N=498), the rate of agreement with subspecialists was significantly higher for the DLS (71.7%; 95% Confidence Interval [CI], 67.9-75.3%) than for general pathologists (58.0%; 95% CI, 54.5-61.4%, P <0.001). In subanalyses of biopsy specimens from an external validation set (N=322), the Gleason grading performance of the DLS remained similar. For distinguishing non-tumor from tumor-containing biopsy specimens (N=752), the rate of agreement with subspecialists was 94.3% (95% CI, 92.4-95.9%) for the DLS and similar at 94.7% (95% CI, 92.8-96.3%) for general pathologists (P=0.58).

Conclusions and Relevance: In this study, the DLS showed higher proficiency than general pathologists at Gleason grading prostate needle core biopsy specimens and generalized to an independent institution. Future research is necessary to evaluate the potential utility of using the DLS as a decision support tool in clinical workflows and improve the quality of PCa grading for therapy decisions.
Vaccine Shows Promise in Advanced Prostate Cancer According to Proof-of-Concept Study

YourVaccx a new type of cancer vaccine developed by ImmunSYS, is safe according to a proof-of-concept study, and shows promising effectiveness in patients with metastatic prostate cancer (PCa) and other difficult-to-treat advanced solid tumors. Study findings were presented in a poster titled, “Regression of metastatic cancer and abscopal effects following in situ vaccination by cryosurgical tumor cell lysis and intratumoral immunotherapy: A case series,” at the American Society of Cancer Research (AACR) 2020 Virtual Meeting II, June 22-24, 2020.

YourVaccx uses a proprietary procedure developed by ImmunSYS that is designed to boost the activity of the immune system to fight cancer. Therapy comprises two steps. First, a portion of the tumor is destroyed by a technique called local cryosurgical tumor cell lysis (disintegration), so that molecules found within the tumor are released to the exterior. These molecules activate and instruct patients’ immune cells to attack the tumor.

A combination of three immunotherapy agents are then injected into the disrupted tumor, which is intended to block inhibitory signals from cancer cells that prevent the immune system from acting and to promote the proliferation of immune cells and their migration into cancer sites. The combination of both techniques is expected to create a local, self-directed vaccine that triggers an abscopal effect – a phenomenon in which shrinkage of a tumor treated with local therapy results in the shrinkage of tumors found elsewhere in the body. The company now has announced data from a proof-of-concept study (NCT03695835), where YourVaccx was used to treat 27 patients with metastatic cancers. Most patients (21 of the 27 enrolled) had metastatic PCa, while the remaining six had other types of equally advanced cancers, including bladder, colon, and pancreatic cancer.

All patients completed at least one treatment cycle that consisted of cryosurgical lysis of the tumor, followed by a local injection of a triple combination of immunotherapy medications - Yervoy (ipilimumab), Keytruda (pembrolizumab) or Opdivo (nivolumab), and Leukine (sargramostim) – into the disrupted tumor.

Nivolumab, ipilimumab, and pembrolizumab are immune checkpoint inhibitors that target proteins involved in the processes used by cancer cells to escape the immune system. Nivolumab and pembrolizumab target the PD-1 protein on T-cells – immune cells capable of fighting tumors – and prevent its interaction with PD-L1 in tumors, boosting anti-cancer responses. Ipilimumab targets the CTLA-4 protein also on T-cells, causing them to expand and become activated. Sargramostim is also designed to boost immune system activity. It acts by stimulating the bone marrow to produce more white blood cells – the main cell type of the immune system – and typically is given to patients to restore cell numbers following chemotherapy. The triple combo treatment was followed by a 30-day period in which men received under-the-skin (subcutaneous) injections of sargramostim.

All men were assessed after completing the therapy, which varied from one to three cycles of treatment, spaced by intervals of at least one month. Three PCa patients were excluded from the analysis due to lack of follow-up imaging data. From the 24 eligible men, 10 (42%) achieved significant reductions in tumor volume, including nine (38%) attaining a complete response (complete tumor elimination). Among the 18 metastatic PCa patients eligible for treatment efficacy analyses, nine (50%) achieved a complete response. Six additional men (33%) experienced disease stabilization after receiving the treatment.

Most responses were durable, with five of the nine men who responded to treatment maintaining responses that lasted from one to more than 4.5 years. Treatment also was found to lower the levels of PSA, a marker of PCa, by at least 50% in more than half (62%) of the men who participated in the study.

The therapy was generally safe and well-tolerated. Three men with PCa experienced six severe or life-threatening adverse events (side effects). No treatment-related deaths were reported during the study.

“We are pleased to present these encouraging findings at the AACR virtual annual meeting II,” Eamonn Hobbs, chairman and CEO of ImmunSYS, said in a press release.

“These results demonstrate long-term, durable responses, ranging from 1 to 4.5 years, and a favorable tolerability profile in tough-to-treat patient populations. There is an unmet need for effective treatment options for men with metastatic cancers and these data demonstrate the potential that YourVaccx has to significantly improve the lives of patients,” Hobbs said.

Immune Checkpoint Blockade for Prostate Cancer: Niche Role or Next Breakthrough?

de Almeida DVP, Fong L, Rettig MB, Autio KA

A number of trials have evaluated the use of single-agent immune checkpoint inhibitors for the treatment of metastatic castration-resistant prostate cancer (mCRPC). The benefit appears to be limited to a small subset of patients, such as those with tumors with microsatellite instability, highlighting the importance of biomarkers to identify which patients may be more likely to respond. Given the lack of efficacy for most patients with mCRPC, our understanding of the mechanisms of primary resistance to checkpoint inhibitors and of the tumor immune microenvironment in prostate cancer is critical. Knowledge gained in these key areas will allow for the identification of novel combination therapies that will circumvent resistance mechanisms and should be tested in clinical trials. Improving our understanding of the effects of androgen deprivation therapy on immune cells and of the most favorable disease setting (e.g., biochemically recurrent vs. CRPC) may aid in the optimal use of checkpoint inhibitors in combination with other agents. If successful, this may move immune checkpoint inhibitors into the treatment armamentarium of prostate cancer management.

ASCO Reading Room
9 July 2020
Purpose: Radical prostatectomy (RP) alone is often inadequate in curing men with clinically localized, high-risk prostate cancer (PC). We hypothesized that chemohormonal therapy (CHT) with androgen-deprivation therapy (ADT) plus docetaxel before RP would improve biochemical progression-free survival (BPFS) over RP alone.

Patients and Methods: Men with clinically localized, high-risk PC were assigned to RP alone or neoadjuvant CHT with ADT plus docetaxel (75 mg/m² body surface area every three weeks for six cycles) and RP. The primary end point was three-year BPFS, overall survival (OS), and specific mortality, and overall survival (OS).

Results: In total, 788 men were randomly assigned. Median follow-up time was 6.1 years. The overall rates of grade 3 and 4 adverse events during chemotherapy were 26% and 19%, respectively. No difference was seen in three-year BPFS between neoadjuvant CHT plus RP and RP alone (0.89 vs. 0.84, respectively; 95% Confidence Interval [CI] for the difference, −0.01 to 0.11; P=0.11). Neoadjuvant CHT was associated with improved overall BPFS (hazard ratio [HR], 0.69; 95% CI, 0.48 to 0.99), improved MFS (HR, 0.70; 95% CI, 0.51 to 0.95), and improved OS (HR, 0.61; 95% CI, 0.40 to 0.94) vs. RP alone.

Conclusion: The primary study end point, three-year BPFS, was not met. Although secondary end points improved, any potential benefit must be weighed against toxicity. Our data do not support the routine use of neoadjuvant CHT and RP in men with clinically localized, high-risk PC at this time.

Beyond PSA New Prostate Cancer Screening Options (Continued from page 2)

misses 8% of ≥GG2 cancers, whereas mpMRI misses 9%. The PHI strategy reduces “mpMRI and biopsies without compromising detection of significant PCas, and also reduces costs,” Nicholas Boxall, MB ChB, from Cambridge University Hospitals NHS Foundation Trust in the United Kingdom, explained (EAU abstracts 303 and 306).

“Instead of screening everyone, we’re risk-adapting who needs to be screened, identifying the right population and defaulting to MRI as an alternative to invasive biopsy, and doing secondary tests to look at biomarkers,” said Gerald Andriole, MD, from the Washington University School of Medicine in St. Louis, Missouri.

“We don’t have to auto-tottle to aggressive treatment,” he reported. “We’re getting better than we were 10 years ago, but we need slightly better tests, and we also need better biopsies; urologists must be more careful.”

Medscape Medical News 7 August 2020

Hot SHEET—SEPTEMBER 2020

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US TOO INTERNATIONAL PROSTATE CANCER EDUCATION & SUPPORT
Between the Sheets...

This column provides 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.

This column was compiled with the help of Dr. Jeffrey Albaugh, Director of Sexual Health at NorthShore University HealthSystem and at Jesse Brown VA Medical Center in Chicago, IL. Dr. Albaugh is a funded researcher, a board certified advanced practice urology clinical nurse specialist, and a board certified sexuality counselor. In addition to his many publications in peer reviewed journals and chapters in books on sexual dysfunction, Dr. Albaugh published *Reclaiming Sex and Intimacy After Prostate Cancer Treatment*. He has been quoted in media and publications as an expert in the treatment of sexual dysfunction, and is a member of the Us TOO Board of Directors.

**QUESTION FROM PROSTATE CANCER SURVIVOR:**
I feel very fortunate to be free from cancer after my surgery. I hate to admit it, but the erectile dysfunction really messes with my mind. I didn’t think it would bother me as much as it does, but I don’t feel like the man I was anymore. Do you have any advice for me?

**RESPONSE FROM DR. JEFFREY ALBAUGH:**
You are not alone in your feelings or struggles. I have seen and spoken to literally thousands of men after prostate cancer treatment who have many mixed feelings about dealing with erectile dysfunction. It is wonderful to be cancer free and that is good news for you. Erectile dysfunction is still frustrating and it can impact your psychological well-being. It is not unusual to feel depression, anxiety, frustration, irritability and struggles in your relationship. It can be helpful to talk to a mental healthcare professional and I often give a list of local providers in my area who have expertise in relationship and sexual issues to my patients (I, myself, am a certified sexuality counselor with training in couples therapy, in addition to being board certified in urology). There is information and resources on anxiety and depression with prostate cancer on the Us TOO website at [www.ustoo.org/anxiety-and-depression](http://www.ustoo.org/anxiety-and-depression). After prostate cancer treatment, the changes in sexual function may negatively impact your self-image and your psychological well-being.

There are many resources for men struggling with various psychological problems like depression, anxiety and/or relationship issues. It can be helpful to talk to your urology healthcare provider to see if they have mental health colleagues that might help you, or information on mental healthcare professionals in the area. It can really help to work with a trained healthcare professional. If you are struggling with relationship, intimacy or sexual issues you can go to [www.aasect.org/referral-directory](http://www.aasect.org/referral-directory) to find expert counselors and therapists across the country. You can also participate in a prostate cancer support group to talk to other men struggling with similar problems, and virtual support is available through [www.ustoo.org/pdfs/Virtual_Support_Group_List.pdf](http://www.ustoo.org/pdfs/Virtual_Support_Group_List.pdf), [www.inspire.com/groups/us-too-prostate-cancer](http://www.inspire.com/groups/us-too-prostate-cancer), or [www.ancan.org/prostate-cancer](http://www.ancan.org/prostate-cancer). Your partner can participate in a support group through [www.ustoo.org/oforumforher](http://www.ustoo.org/oforumforher).

Erectile dysfunction can be frustrating and upsetting. It can help to talk to other people as you continue to navigate your way through erectile dysfunction. It can also help to work with your urology healthcare team to design the best erectile dysfunction treatment plan for you.

All erectile dysfunction treatments have pros and cons and these are laid out for you in the book I wrote for men with prostate cancer and their partners “Reclaiming Sex & Intimacy After Prostate Cancer, 2nd Edition,” which can be downloaded for free at my website: [www.drjeffalbaugh.com](http://www.drjeffalbaugh.com).

Watch Dr. Albaugh’s presentation on sexual health and intimacy from the *Prostate Cancer Pathways for Patients and Caregivers* event recorded at NorthShore University HealthSystem in Skokie, IL on November 3, 2018 at [https://www.youtube.com/watch?v=HiqOdDEb1l0&t=4483s](https://www.youtube.com/watch?v=HiqOdDEb1l0&t=4483s).

**Read previous issues of Between the Sheets at [www.ustoo.org/BTS](http://www.ustoo.org/BTS).**

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
Progress on Prostate Cancer Research

September 2020

Advancements in prostate cancer research provide hope for finding a cure and lead to the discovery of new treatments to minimize the impact of a man’s prostate cancer and maximize his quality of life. This regular Hot SHEET supplement includes some of the latest research from the Prostate Cancer Foundation (www.pcf.org).

Stress and Prostate Cancer
By Janet Farrar Worthington

Does prostate cancer make stress worse? For many men dealing with prostate cancer, the answer is a definite yes. Treatment, side effects, insurance hassles, the next PSA test – all this uncertainty breeds stress.

But here’s a question that may be even more significant:
Does stress make prostate cancer worse? This one’s not so easy to answer. “Everybody has an individual response to stress,” says medical oncologist Suzanne Conzen, M.D., Prostate Cancer Foundation (PCF)-funded investigator and Chief of Hematology and Oncology at the University of Texas Southwestern Medical Center in Dallas. “And that’s the key,” she adds: “it’s not so much the stress itself but the physiological response that can take a toll, and that may hinder our ability to fight cancer.”

The body responds to stress with a surge of corticosteroids; primarily cortisol. “We are hard-wired to respond to stress with this ‘fight or flight’ response.” Unfortunately, many of us react to everyday troubles with the same surge of stress hormone as if we were under attack. Our hypothalamus, located in the most primitive part of the brain, tells our adrenal glands, “This is the big one! Go to Defcon 3.” And cortisol, revving up in its effort to save us, can cause harm instead, affecting normal functions including the immune system, and even changing genes that are expressed in cancer cells.

Some people have a higher stress response than others. It could be an inherited tendency; or they haven’t necessarily developed effective ways of coping with exposure to stressors,” says Conzen. “However, not all people who have a high stress response get cancer; and a lot of people are under stress and don’t get cancer. But that’s the complexity: not everybody who smokes gets lung cancer, but smoking is a risk factor. What you want to do is reduce your risk factors,” and your response to stress – like a bad diet, or smoking, or being overweight – is a risk factor for prostate cancer that can be changed.

“We think high cortisol levels are probably not a good thing in men who have prostate cancer. At least a subset of those men may have tumors that respond to high levels of stress because the prostate cancer expresses a protein, the glucocorticoid receptor, that is activated by cortisol,” and although Conzen is working on how to determine who these men are, right now, there’s no way to know for sure.

Cortisol, a hormone, attaches to a protein called the glucocorticoid receptor (GR) in cells throughout your body, and this is like flipping a switch that activates stress in all those cells, including cancer cells. In prostate cancer, Conzen has found that the GR “is more highly expressed in cancer that is resistant to androgen deprivation therapy (ADT).”

But it’s complicated, she adds: “We think it’s not only how much GR your tumor has, it’s how active it is.” With a PCF Challenge Award, Conzen and colleagues in her lab are working to find a way to measure how active cortisol and GR are in a prostate tumor, “whether it’s turning on and off a lot of genes, or just a few genes. The amount of GR does not necessarily correlate with the activity of the protein.”

So, how to fix it – if a man has aggressive prostate cancer, and high cortisol/GR activity? “One hypothesis would be, deprive that tumor of your body’s stress hormone receptor activity by keeping the stress hormones relatively low.” This could happen with some type of medication – or, it could happen with stress reduction. What is that, exactly? It could mean making changes in your life, so there are fewer stressful factors in it. It also could mean making changes in you – with the help of such things as exercise, yoga, meditation, and counseling. For more on Dr. Conzen’s research, go to www.pcf.org/c/stress-and-prostate-cancer.

Interested in more ways to improve your wellness? This Prostate Cancer Awareness Month, show your support by taking a simple challenge to eat 30 healthy foods in 30 days. While eating healthy and exercising can’t stop you from getting cancer, it can lower your risk. Whether you or someone you love had been affected by prostate cancer – or if you just want to learn the principles of a healthy lifestyle – you can join in the challenge this September. Go to www.pcf.org/eat to learn more and sign up!

For more information visit www.pcf.org, email info@pcf.org, or call 1-800-757-2873.
The SEA Blue 2020 Prostate Cancer Walk/Run is On!
Us TOO and UroPartners present SEA Blue 2020. For 16 years, SEA Blue has been the largest prostate cancer walk/run event in Chicago. This year, due to COVID-19 restrictions, the event will be virtual and open to participants anywhere in the world. Join us for a virtual SEA Blue that will feel as close as possible to our in-person events.

Activities will Include:
• Team Challenge
• Walk/Run on Your Own
• Prostate Cancer Education
• Entertainment

We have all felt the effects of COVID-19 in a variety of ways. With that in mind, the registration fee for SEA Blue 2020 is PAY WHAT YOU CAN! (or if you need a suggestion, how about $30 in honor of the 30th anniversary of Us TOO?).

SEA Blue is the main fundraising event for Us TOO International. Please help us raise money to help those affected by prostate cancer with Support, Education, Advocacy and Awareness at no charge.

Register or Donate at:
www.seablueprostatewalk.org

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