BRCA2 Mutations Have Stronger Link to Cancer in Men Than Do BRCA1 Mutations

Compared with men with germline BRCA1 pathogenic variants (PVs), those with BRCA2 PVs are more likely to be affected by cancer, according to a new study.

The research “fills a knowledge gap on cancer phenotypes in men with germline BRCA1 and BRCA2 pathogenic variants,” Dr. Laura Ottini of Sapienza University of Rome told Reuters Health by email.

“Our results, derived from analyses of the largest available male BRCA1/2 PV carrier data set, show that being affected by any cancer and developing multiple cancers, particularly breast, prostate, and pancreatic cancers, is associated with a higher probability of being a BRCA2, rather than a BRCA1, PV carrier,” she said.

Dr. Ottini and colleagues examined data on more than 6,900 men, of whom 3,651 were BRCA1 and 3,251 BRCA2 PV carriers. They were recruited by study groups worldwide from cancer genetic clinics between 1966 and 2017, and their median age was 51.6 years.

Nearly 20% had at least one cancer diagnosis, the researchers report online ahead of print in JAMA Oncology. BRCA2 PV carriers were significantly more likely to be affected by any cancer (odds ratio, 3.23) and to have more than one primary tumor. BRCA2 PV carriers were at greater risk of developing breast cancer (OR, 5.47) prostate cancer (OR, 1.39), and pancreatic cancer (OR, 3.00). However, they had a significantly lower probability of colorectal cancer (OR, 0.47).

(Continued on page 8)

Benefits of PSA Test for Prostate Cancer Substantially Greater Than Generally Recognized

The benefits of the prostate-specific antigen (PSA) test to screen men for prostate cancer (PCa) may be greater than the harm, say investigators at Weill Cornell Medicine, New York- Presbyterian, University of Washington School of Medicine and the Fred Hutchinson Cancer Research Center.

While organizations such as the U.S. Preventative Services Task Force (USPSTF) and the American Academy of Family Physicians have been lukewarm or opposed to the routine use of the PSA test, in a commentary published June 17 in the New England Journal of Medicine, the investigators demonstrate that these recommendations are based on problematic estimates of the benefits and harms of screening. They argue the evidence suggests more widespread screening will reduce deaths and help men avoid debilitating metastatic disease.

“The overarching message for the last eight years has been against PSA testing, and its use has declined significantly as a result,” said senior author Dr. Jim Hu, the Ronald P. Lynch Professor of Urologic Oncology at Weill Cornell Medicine and director of the LeFrak Center for Robotic Surgery at New York- Presbyterian/Weill Cornell Medical Center. “At the same time, metastatic PCs in older men has been rising after reaching an all-time low in 2011, as we have document-
Enzalutamide and Survival in Nonmetastatic Castration Resistant Prostate Cancer

Sternberg CN, Fizaz K, Saad F, et al., for the PROSPER Investigators


Background: Preliminary trial results showed that enzalutamide significantly improved metastasis-free survival among men who had nonmetastatic, castration-resistant prostate cancer (nmCRPC) and rapidly increasing prostate-specific antigen (PSA) levels while taking androgen-deprivation therapy (ADT). Results from the final analysis of overall survival have not yet been reported.

Methods: In this double-blind, phase 3 trial, men with nmCRPC (defined on the basis of conventional imaging and a PSA doubling time of ≤10 months) who were continuing to receive ADT were randomly assigned (in a 2:1 ratio) to receive enzalutamide at a dose of 160 mg or placebo once daily. Overall survival was assessed with a group sequential testing procedure and an O’Brien-Fleming-type alpha-spending function.

Results: As of October 15, 2019, a total of 288 of 933 men (31%) in the enzalutamide group and 178 of 468 (38%) in the placebo group had died. Median overall survival was 67.0 months (95% confidence interval [CI], 64.0 to not reached) in the enzalutamide group and 56.3 months (95% CI, 54.4 to 63.0) in the placebo group (hazard ratio for death, 0.73; 95% CI, 0.61 to 0.89; P=0.001, a statistically significant difference). The exposure-adjusted rate of adverse events of grade 3 or higher was 17 per 100 patient-years in the enzalutamide group and 20 per 100 patient-years in the placebo group. Adverse events in the enzalutamide group were consistent with those previously reported for enzalutamide; those most frequently reported were fatigue and musculoskeletal events.

Conclusions: Enzalutamide plus ADT resulted in longer median overall survival than placebo plus ADT among men with nmCRPC and a rapidly rising PSA level. The risk of death associated with enzalutamide was 27% lower than with placebo. Adverse events were consistent with the established safety profile of enzalutamide.

(Funded by Pfizer and Astellas Pharma; PROSPER ClinicalTrials.gov number, NCT02003924)

Use of degarelix, a gonadotropin-releasing hormone (GnRH) antagonist, is associated with lower short-term risks for death and cardiovascular events than GnRH agonists in patients with metastatic prostate cancer, according to investigators.

Shahrokh F. Shariat, MD, of Vienna General Hospital in Vienna, Austria, and colleagues conducted a systematic review and meta-analysis of eight randomized clinical trials published during 2008 to 2019 and comprising 1,646 men treated with degarelix and 986 with a GnRH agonist (leuprolrelin or goserelin). (Concomitant administration of bicalutamide with a GnRH agonist for flare suppression was given in six studies.)

“GnRH antagonist use was associated with a significant 52% and 48% lower risk for all-cause mortality and cardiovascular events, respectively, compared with agonist use over approximately three to 12 months,” the investigators reported in European Urology. The team found no significant differences in the risks for PSA progression or serious adverse events (AEs), such as liver enzyme elevation, hepatic failure, and urine retention, between groups. Low rates of musculoskeletal events and fracture precluded rigorous analysis of these AEs.

GnRH agonist use, in contrast, was associated with lower risks for injection site reactions (4.8 vs. 38%). The study revealed no significant difference in fatigue rate between the GnRH antagonist and GnRH agonists. Overall, treatment-emerging AEs occurred significantly more frequently in the GnRH antagonist than agonist recipients (73% vs. 68%), but the rate of serious AEs were non-significantly similar between the groups (9.8 vs. 11%). A total of 6.5% of GnRH antagonist users and 5.9% of GnRH agonist users discontinued androgen deprivation therapy due to AEs.

This meta-analysis was limited by the short follow-up time of the trials that prevented definitive conclusions. “These findings should be interpreted with caution owing to the short follow-up duration and assessment of cardiovascular events as secondary endpoints in the included trials,” Dr. Shariat’s team stated. They noted that their data do provide clinicians with useful information for patient counseling about the potential benefits and risks of a GnRH antagonist and agonist.

Cancer Therapy Advisor 7 July 2020
Benefits of PSA Test for PCa Substantially Greater Than Generally Recognized (Continued from page 1)

I love many things about research, including the fact that if you look hard enough you find studies that you would have never dreamed of, had it not been for the sensitivity (different perspective) of a particular research team to address a unique issue. My guess is this new study on parking fees at National Cancer Institute (NCI)-Designated Cancer Treatment Centers will get minimal attention, but at least it should raise some awareness and even get a nice shout out or yell. Ahhhhhhh!

Researchers from Memorial Sloan Kettering Cancer Center and NYU School of Medicine in New York City looked at the parking fees from 63 cancer centers and found a lot of space (pun intended) for improvement. First, the good news—approximately 32% of the cancer centers offered free parking. However, here comes some bad news — approximately 40% of them had no specific online information about parking costs, which would not allow for adequate fiscal planning for longer treatment courses, which of course would include fiscal planning for friends and family visitation or accompaniment. Parking costs were generally correlated with the cost of living in the city where the cancer center was located, which is not a surprise. The range of hourly parking fees was $0-19, and per day were $0-40. Expensive cities have expensive costs, but also have profound fundraising potential, more on this in a moment.

The estimated parking costs for a basic course of treatment lasting weeks to months with some common cancers were $0 to almost $1,000! Transportation is one of the highest out-of-pocket costs for patients receiving multiple treatments (chemotherapy, radiation...). This is strange to me because I have never thought about parking fees, including costs of parking at a cancer center, patient conference or event. Look, I am not trying to start some kind of free parking revolution here, but all of this stuff seems so strange. Many of these cancer centers have received massive amounts of money from donors, which is fabulous and remarkable and part of the reason they offer state-of-the-art research and treatment—arguably some of the best on this planet! However, I have never personally observed a campaign to raise millions of dollars to place in some type of endowment to allow free parking to all cancer patients while undergoing treatment. Why? I have no idea and I had no idea this was even an issue until this paper was published.

So, what are we waiting for? The Free Parking for All endowment? Who is with me?! Seriously, whether you run a support group, or are part of a support group, or are a health care professional, we should utilize whatever power we all have to encourage minimal-to-no parking fees when receiving education or treatment at the local cancer center. Cancer patients have enough to worry about, and even more than ever now because of this pandemic. Parking fees? There is plenty of space for improvement!

Reference:
New Focus on ADT in Prostate Cancer Guideline
AUA, SUO, ASTRO Offer 38 Recommendations Across Categories of Advanced Disease

For the first time in its long and storied history, hormonal therapy for advanced prostate cancer (PCa) has received broad and detailed attention in a clinical practice guideline.

The new American Urological Association (AUA) guideline provides direction for the use of hormonal therapy (or androgen-deprivation therapy, ADT) for men with multiple categories of advanced and metastatic PCa.

“[ADT] is a mainstay of management that we’ve known about since the Nobel Prize-winning work in the 1940s,” said guideline co-chair Michael Cookson, MD, of the University of Oklahoma Health Sciences Center in Oklahoma City. “It’s taken a long time to get there, and that’s partly due to the fact that a lot of what we did was empirical. There weren’t many trials designed to show the true benefit.”

Another guideline first reflects the growing recognition of the different stages of disease evolution before the emergence of metastatic castration-resistant PCa (mCRPC).

“There’s a lot of excitement in the field about newly diagnosed metastatic disease,” Cookson told MedPage Today. “Most of the early trials were in men who failed hormonal therapy. Now the trials have moved back to earlier in the disease, looking at conventional hormonal therapy, plus. That ‘plus’ initially included chemotherapy, which showed survival advantages of 12 to 18 months. That was big.

“Then additional androgen-active therapies, such as abiraterone and then oral agents such as enzalutamide and now apalutamide. That translated into a year or more of additional cancer control and survival when PCa was treated earlier with the combination,” he said.

“The guideline also addressed the evolutionary period before emergence of radiographically confirmed mCRPC, often associated with a rapid rise in prostate-specific antigen (PSA). Now known as nonmetastatic CRPC, the disease state has three FDA-approved options in the androgen receptor antagonist drug class: darolutamide, in addition to enzalutamide and apalutamide. The drugs’ approval was based primarily on the newly recognized endpoint of metastasis-free survival and relatively limited overall survival data,” said Cookson. Subsequently, a survival advantage was reported for enzalutamide.

“That’s been a real area of controversy,” he continued. “Many clinicians were hesitant to fully embrace the therapy because they didn’t really understand the true benefit of this new endpoint called metastasis-free survival. The ‘purists’ among oncologists, and maybe just the purists in general, want an overall survival benefit. Now we’re starting to see that happen. There are three studies in that category, and as the data mature, I think we’ll see more of that, since the drugs are pretty similar.”

Frontline standard of care for mCRPC remains docetaxel for men with no prior exposure to the drug. Cabazitaxel or a novel anti-androgen agent is appropriate in the setting of docetaxel failure.

New to guideline history — and to many clinicians who treat PCa — is genetic testing. “About a fourth of CRPC harbors germline or somatic mutations,” said Cookson. New drugs that target the mutations continue to emerge on a regular basis, affording opportunities for precision-medicine approaches to treatment of CRPC. The most common mutation is BRCA2, and the FDA has already approved two drugs to treat CRPC harboring BRCA2 mutations, the PARP inhibitors olaparib and rucaparib.

“There are instances in which men have been on conventional therapy — chemotherapy or hormonal therapy — and they’ve also failed the newer antiandrogens, such as abiraterone and enzalutamide,” said Cookson. “In the past, we didn’t have much hope for them. Now there is a class of drugs that, if they have the right genetic makeup in their tumor, they’re going to have a better chance to respond to the therapy.”

Immunotherapy may also have a role for some men with CRPC. The PD-1 inhibitor pembrolizumab (Keytruda) has tumor-agnostic approval for treatment of heavily mutated solid tumors (microsatellite instability-high). The field of PCa is “still in its infancy” with regard to use of drugs that target genetic alterations in tumors.

“The key message in the guideline is for PCa specialists to be aware of recommendations for genetic testing, particularly for men with aggressive disease that progresses rapidly through conventional therapies,” Cookson added. “Moreover, testing for germline mutations has implications for genetic counseling, including family members who might be at increased risk for several types of cancer.”

The guideline was developed in collaboration with the Society of Urologic Oncology (SUO) and the American Society for Radiation Oncology (ASTRO). The guideline panel made a total of 38 recommendations pertaining to the PCa continuum of care:

- Early evaluation and counseling
- Nonmetastatic biochemical recurrence after exhaustion of local treatment options
- Metastatic hormone-sensitive PCa
- Nonmetastatic CRPC
- mCRPC
- Bone health

The complete guideline is available on the AUA website. Cookson and the other guideline co-chair, William Lowrance, MD, of the University of Utah School of Medicine and the Huntsman Cancer Institute in Salt Lake City, summarized the key points of the guideline during the AUA virtual meeting.

“For the past several years, the PCa landscape has been rapidly evolving due to changes in PSA screening standards, as well as the approval of new classes of treatment options for use in various PCa disease states,” Lowrance said in a statement. “This guideline is comprised of clinical recommendations based on this new evidence and aims to further support the medical community and patients as they navigate through the various stages of this disease.”

MedPage Today
30 June 2020
increased risk of PCSM, respectively, in adjusted analyses," Dr. Fletcher’s team reported in JAMA Network Open.1
Among men with Gleason grade 2 to 5 disease in these areas, black men had a 1.9-, 1.3-, 1.3-, and 1.5-fold increased risk of PCSM compared with white men.
“The most striking finding was that there are specific ‘hot spots’ in which racial differences in PCa mortality are most pronounced,” said Dr. Fletcher, who conducted the study while at Brigham and Women’s Hospital in Boston but is now at the James Buchanan Brady Urological Institute at The Johns Hopkins Medical Institutions in Baltimore.

**Contributing Factors**
Although the study was not designed to determine definitively the underlying causes of the geographic variability in the racial disparity in PCa survival, “we are inclined to attribute a large part of this variability to differences in access to care,” Dr. Fletcher told Renal & Urology News. “Prostate cancer, especially of a low-risk nature, requires continual surveillance and communication with the healthcare system to monitor for disease progression. We believe that areas with worse mortality for black men may also have more pronounced disparities in care access and follow-up for minority populations. However, the possibility of men in these areas having higher genetic predisposition to more aggressive disease cannot be definitively ruled out.”

Dr. Fletcher said his team’s data reinforce work from prior studies showing that racial differences in PCSM are more marked in men initially presenting with low-risk disease, with black men experiencing worse survival compared with white men. “This may be mediated by differences in patterns of management and definitive treatment for men in this risk group,” Dr. Fletcher said.

The new findings enable targeted investigation of particular geographic areas to determine what factors (such as access to care, treatment patterns, and disease biology) contribute most to these race-based mortality differences, he said. “More granular qualitative analyses of care processes in these areas may further elucidate the mechanisms of our findings.”

In an accompanying editorial, Willie Underwood III, MD, MSc, MPH, of the Buffalo New York Community Center for Health Equity, commented that the new study “contributes to the literature that non-biological factors are likely associated with the significant disparity in PCSM among black vs. white men, thus contributing to the discussion that increased PCSM among black men compared with white men is unnecessary and preventable.”

An earlier study showing regional variation in PCSM led investigators to conclude that the variation may be related to differences in access to care. Among white men aged 40 years or older, the age-adjusted death rate (per 100,000 men per year) from PCa ranged from 60.8 in Alaska to 86.4 in Wyoming. The incidence rate for all PCa stages combined ranged from 294.8 in Arizona to 427.8 in New Jersey. The incidence rate of distant-stage disease ranged from 10.4 in Atlanta to 28.6 in Hawaii.

“Among black men aged 40 years or older, the age-adjusted death rates ranged from 129.2 in Rhode Island to 196.7 in North Carolina. The rates for overall incidence ranged from 374 in Hawaii to 692.6 in Michigan; the rates for distant-stage disease ranged from 33.3 in Arizona to 76.9 in West Virginia. Nonmetropolitan areas generally had higher death rates (74.9 vs. 71.7) and incidence of late-stage disease (19.3 vs. 17.1) and lower prevalence of PSA screening (53% vs. 58%) compared with metropolitan areas,” the investigators reported.

“Our principal findings are that the geographic variation in PCa death rates is positively associated with incidence of late-stage disease and with residence in non-metro areas and that the incidence of late-stage disease is inversely associated with the utilization of PSA testing,” the authors wrote. “All of these factors suggest that lower access to medical care may contribute to a higher death rate from PCa in certain regions of the U.S.”

**Conservative Management**
Other studies have revealed substantial differences in how PCa is managed across the nation. In a recent report published in European Urology, Stacy Loeb, MD, of the Manhattan Veterans Affairs Medical Center and New York University, and colleagues described a study of 20,597 men receiving PCa care in the VA healthcare system showing that men receiving care at facilities in the Midwest and West had 23% and 36% increased odds, respectively, of undergoing conservative management such as active surveillance (AS) and watchful waiting (WW) compared with those receiving care at Northeast facilities.2

“Even after adjusting for multiple patient and non-patient factors, we observed persistent regional variation in conservative management use among veterans,” Dr. Loeb told Renal & Urology News. “It is unclear whether these differences relate to regional differences in patient preferences, availability of other treatment options for PCa, or other factors.”

**Initial Treatments Compared**
Another study, published in 2019 in Advances in Radiation Oncology, found geographic variation in the use of RP, radiation therapy (RT), and AS among 462,811 men treated for localized PCa from 2010 to 2014.4

Nationwide, as a first-line management strategy, researchers found that approximately 63.5% of men underwent RP, 31% received RT, and 5% underwent AS. RP, however, was used most commonly in the Midwest (Minnesota, South Dakota, Iowa, and Wisconsin; 75% of cases) and High Plains (Nebraska, Kansas, Missouri, Oklahoma, and Texas; 73.4%) regions, whereas RP was least used in the South Atlantic (Delaware, Maryland, District of Columbia, Virginia, West Virginia, North Carolina, South Carolina, and Georgia; 59%) regions. RT was most commonly used in the South Atlantic (41%) and New England (Maine, Vermont, New Hampshire, Massachusetts, Rhode Island, and Connecticut; 39%) regions. RT was used least in the Midwest (25%) region. AS was used most commonly in the New England (7.3%) and Midwest (6.8%) regions and least used in the High Plains (2.6%) and Mid-South (Kentucky, Tennessee, Arkansas, Louisiana, Mississippi, and Alabama; 2.8%) regions.

(Continued on page 7)
**Evaluation of Use of Shorter Radiation Regimens for Breast and Prostate Cancer in the US, 2015-2017**

Gillespie EF, Tringale KR, Bach PB, Bekelman JE

JAMA Netw Open 3: e2010519, 2020

**Introduction:** For breast and prostate cancer, shorter radiation treatment (RT) regimens lasting three to five weeks are evidence-based practices that are similarly effective and safe, and substantially less costly for payers and patients, compared with extended regimens lasting six to nine weeks. National guidelines endorsed shorter radiation regimens for breast cancer in 2011 and for prostate cancer (PCa) in 2018. In July 2019, the Centers for Medicare & Medicaid Services proposed a mandatory episode-based payment model for RT services, partly motivated by an interest in accelerating uptake of shorter RT regimens, and publicly released Medicare data on US RT episodes during the period from 2015 to 2017. During this period prior to guideline endorsement of shorter regimens for PCa, we hypothesized that growth in uptake of shorter regimens would be greater in breast cancer than in PCa.

**Methods:** The data set contains RT-episodes covering 84% of Medicare beneficiaries. In this cross-sectional study, we included beneficiaries with breast cancer and PCa treated with external RT (conventional, intensity-modulated, or proton RT). We classified episodes into two groups: shorter regimens (11 to 20 daily treatments for breast cancer or 11 to 30 for PCa) and extended regimens (>20 or >30 daily treatments, respectively). The study was approved as exempt for the need for informed consent by the Memorial Sloan Kettering Cancer Center institutional review board because publicly available anonymized data were used. The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.

We calculated compound annual growth rates and used multivariable linear regression to compare rates of change in the use of shorter regimens between breast cancer and PCa. We compared RT-related spending for shorter vs. extended RT from the amount reimbursed by Medicare for facility and professional services over the 90-day episode, adjusted for inflation to 2017. Statistical significance was set at two-sided P < 0.025, applying a Bonferroni correction for two main analyses. Data analysis was performed from September to December 2019 using SAS Enterprise Guide statistical software version 9.1 (SAS Institute).

**Results:** From 2015 to 2017, among 85,570 RT episodes for women with breast cancer aged 65 to 74 years (67%), 75 to 84 years (28%), and 85 years or older (19%), shorter RT regimens increased from 33.1% (95% confidence interval [CI], 32.5-33.6%) to 42.4% (95% CI, 41.9-43.0%) (P < 0.001, a statistically significant difference) at a compound annual growth rate of 13.2%. Among 71,720 episodes for men with PCa aged 65 to 74 years (63%), 75 to 84 years (33%), and 85 years or older (4%), shorter regimens increased from 13.4% (95% CI, 13.0-13.9%) to 16.7% (95% CI, 16.2-17.2%) (P < 0.001) at a compound annual growth rate of 11.6%. Rates of change in use of shorter regimens did not differ significantly between the two cancers (compound annual growth rate, 13.2% vs. 11.6%; difference, 1.6%).

Mean 90-day RT-related spending was 33% lower for beneficiaries with breast cancer treated with shorter vs. extended regimens and 34% lower for PCa treated with the shorter vs. lower RT regimens (Table).

**Discussion:** Among Medicare beneficiaries receiving RT between 2015 and 2017, the rate of uptake of shorter RT regimens was modest and did not differ meaningfully between breast cancer and PCa. We also found that shorter RT regimens for PCa, like breast cancer, reduce radiation-related spending by approximately one-third. During the study period, guidelines had endorsed shorter regimens for breast cancer but not PCa; comparable uptake underscores the challenge of implementing less costly evidence-based practices in cancer care.

Today, accelerating uptake of shorter RT regimens is an urgent priority to enhance evidence-based, patient-centered cancer care. Development, testing, and scaling of strategies to achieve this goal (default options, audit and feedback, and patient engagement) is warranted. This study has limitations.

**Table:**

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**References:**
Postdiagnosis Body Mass Index, Weight Change, and Mortality from Prostate Cancer, Cardiovascular Disease, and All Causes among Survivors of Nonmetastatic Prostate Cancer

Treveschel AN, Hartman TJ, Jacobs EJ, et al.

**Purpose:** To investigate the association of postdiagnosis body mass index (BMI) and weight change with prostate cancer–specific mortality (PCSM), cardiovascular disease-related mortality (CVDM), and all-cause mortality among survivors of nonmetastatic prostate cancer (PCa).

**Methods:** Men in the Cancer Prevention Study II Nutrition Cohort diagnosed with nonmetastatic PCa between 1992 and 2013 were followed for mortality through December 2016. Current weight was self-reported on follow-up questionnaires approximately every two years. Postdiagnosis BMI was obtained from the first survey completed 1 to <6 years after diagnosis. Weight change was the difference in weight between the first and second postdiagnosis survey. Deaths occurring within four years of the follow-up were excluded to reduce bias from reverse causation. Analyses of BMI and weight change included 8,330 and 6,942 participants, respectively.

**Results:** Postdiagnosis BMI analyses included 3,855 deaths from all causes (PCSM, N=500; CVDM, N=1,155). Using Cox proportional hazards models, hazard ratios (HRs) associated with postdiagnosis obesity (BMI ≥30 kg/m²) compared with healthy weight (BMI 18.5 to <25.0 kg/m²) were 1.28 for PCSM (95% CI, 0.96 to 1.67), 1.24 for CVDM (95% CI, 1.03 to 1.49), and 1.23 for all-cause mortality (95% CI, 1.11 to 1.35). Weight gain analyses included 2,973 deaths (PCSM, N=375; CVDM, N=881). Postdiagnosis weight gain (>5% of body weight), compared with stable weight (± <3%), was associated with a higher risk of PCSM (HR, 1.65; 95% CI, 1.21 to 2.25) and all-cause mortality (HR, 1.27; 95% CI, 1.12 to 1.45) but not CVDM.

**Conclusion:** Results suggest that among survivors of nonmetastatic PCa with largely localized disease, postdiagnosis obesity is associated with higher CVDM and all-cause mortality, and possibly higher PCSM, and that postdiagnosis weight gain may be associated with a higher mortality as a result of all causes and PCa.

**Benefits of PSA Test for PCa Greater Than Recognized (Continued from page 3)**

Weigh the benefits and harms of screening.

“We hope organizations reconsider the value of the PSA test in light of our estimates and revise their recommendations,” Dr. Shoag said. “More men should have the opportunity to get the benefits of screening. In my opinion, these outweigh the potential harms over a longer, more realistic time horizon for most healthy men.”

“This benefit is compounded in the modern era, as physicians now know that not every PCa needs to be treated,” the authors write. Almost half of American men diagnosed with low-risk PCa are followed with close monitoring, called active surveillance (AS), rather than receiving immediate treatment. Recently, the advent of an increasing number of non-invasive tests to assess PCa risk, including the 4K score test, free PSA, PCA3, the Prostate Health Index (PHI) and prostate magnetic resonance imaging (MRI) are providing physicians with more information to improve decision-making after abnormal PSA test results.

“Together with these advances, we hope that a better understanding of the benefits of the PSA test will help more men receive the right treatment at the right time and reduce the burden of metastatic PCa,” Dr. Hu said. “Finally, most men diagnosed with low-risk PCa choose AS: there is less overtreatment and side effects, and they are monitored with curative intent. Biomarkers may be able to mitigate the harms of over-detection, and use of AS to mitigate the harms of over-treatment.”

The study was supported by the Wallace Fund, the Damon Runyon Cancer Research Foundation Physician Scientist Training Award at Weill Cornell Medicine, and the US Department of Defense CDMRP W81XWH1910577 and National Institutes of Health awards R50 CA221836 and U01 CA199338 at the Fred Hutchinson Cancer Center.

**Reference:**

Weill-Cornell Medicine
17 June 2020

**PCa Mortality and Treatment (Continued from page 5)**

**Systemic Therapy**

Systemic treatment of advanced PCa also varies by region. For example, in a real-world study of 4,275 patients using a large national insurer’s claims database, Megan E. V. Caram, MD, of the University of Michigan in Ann Arbor and colleagues, showed that 61.9% of men in a region that included Alaska, California, Hawaii, Oregon, and Washington received abiraterone as first-line treatment in 2014 compared with only 26.7% in a region comprising Iowa, Kansas, Minnesota, Missouri, Nebraska, North Dakota, and South Dakota. The investigators published their findings in *BMC Cancer*, where they explained that “geographic variation in treatment patterns may be a result of other factors associated with geography, such as rural/urban differences, patient income, race, and health system factors.”

**References:**

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UCLA Researchers Find Cryotherapy to Be an Effective Treatment Option for Men with Intermediate-Risk Prostate Cancer

UCLA researchers have found that hemi-gland cryoablation, or cryotherapy, is an effective, primary treatment for men with clinically-significant, or grade 2, prostate cancer (PCa).

In a group of 61 men with intermediate-risk PCa, researchers found 80% had no signs of cancer at six and 18 months after cryotherapy. In 10% of cases, there was minor residual cancer and 10% didn’t respond to treatment.

**Background:** According to the American Cancer Society, PCa is the most common cancer diagnosed in men in the U.S. Common treatments of low or intermediate-risk PCa include radical prostatectomy (RP), radiotherapy (RT) or brachytherapy. Each has side effects, fueling efforts to find if cryotherapy could be a better option.

UCLA began offering cryotherapy treatment option in 2008. It is used to treat only cancerous areas of the prostate and minimizes damage to vital areas. Cryotherapy is used to treat intermediate-risk PCa, defined as tumors that can be observed for a while, but could progress if not treated. Men who select cryoablation opt for preservation of quality of life and are watched and checked for recurrence of cancer.

**Method:** For this research, a team of clinical scientists used MRI-guided biopsy – an accurate method of collecting tissue samples from the prostate gland – uniformly across men before and after treatment. Partial prostate cryoablation was performed on 61 men diagnosed with intermediate-risk PCa. Men all underwent MRI-guided biopsy before and after the procedure and had follow-up up to 18 months.

**Impact:** A less invasive option than traditional surgical approaches, prostate cryotherapy offers men the potential for cure without common side effects including erectile dysfunction, incontinence, or other problems that are a result of a traditional surgery or radiation therapy. There is also a shorter recovery period, shorter hospital stay, less blood loss and less pain.

While these results are very encouraging, physician-scientists note that research on the use of cryotherapy treatment for prostate cancer is still very preliminary considering the long history of prostate cancer, and more research on its effectiveness must be done.

**UCLA Health**
30 June 2020

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**BRCA2 Mutations Have Stronger Link to Cancer (Continued from page 1)**

“These data will help to optimize medical care in male BRCA1 and BRCA2 PV carriers,” Dr. Ottini said. “In particular, screening and surveillance programs in men with BRCA1 and BRCA2 PVs should be tailored in light of these gene-specific cancer phenotype differences.”

“Overall,” she concluded, “this study will help oncologists to sensitize men with BRCA PVs in the perception of their personal cancer risk, and no longer only of their female relatives. Furthermore, these data will guide further studies, which we are working on, in order to develop increasing personalized and gender-specific guidelines to guarantee a better clinical management for all patients.”

_Reuters Health Information_
16 July 2020

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PROSTATE CANCER EDUCATION & SUPPORT NETWORK
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Us TOO INTERNATIONAL, 2720 S. RIVER ROAD, SUITE 112, DES PLAINES, IL 60018
QUESTION FROM PROSTATE CANCER SURVIVOR:
I am starting something called SBRT (I’m not 100% sure what that is!) later this month and I’m afraid to have sex with my girlfriend (we recently got together after I was widowed a year ago) in case I pass on the radiation to her. I have had difficulty finding any information about this.

RESPONSE FROM DR. ANNE KATZ:
SBRT stands for stereotactic body radiation therapy and it is a newer form of external beam radiation that takes place over a shorter period of time, for example five treatments in five weeks (one treatment each week). Higher doses of radiation are given at each treatment and this method has been tested in men with low- and intermediate-risk prostate cancer (Gleason 6 or 7). The treatment is highly effective; a recent study of over 2,000 men with low- and intermediate-risk prostate cancer showed 85 to 90% had no rise in PSA seven years after treatment with SBRT (Kishan et al., 2019).

Radiation kills cancer cells by damaging their DNA so that the cancer cells can no longer divide, and so they die. The cancer cells are then broken down by the body and removed. The cells do not die immediately; it takes days or weeks of treatment for the DNA to be damaged and this is why the side effects of radiation are felt for weeks or months after treatment is over.

There is no risk that you can “pass on” the radiation to your girlfriend. SBRT is just a new way of radiating the prostate and instructions for patients are essentially the same as for those who have “regular” external beam radiation. You are not “radioactive” and you cannot harm others during or after treatment.

Sexual side effects for men treated with SBRT are very similar to those men experience after “regular” external beam radiation, with about half of men experiencing erectile difficulties after five years. This is dependent on age and erectile function before treatment.


Watch Dr. Katz’ presentation on sexual health and intimacy from the Prostate Cancer Pathways for Patients and Caregivers event recorded at Englewood Health in Englewood, NJ on September 29, 2018.
https://www.youtube.com/watch?v=A2ZdDHw2WGY&t=8542s

Read previous issues of Between the Sheets at 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
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).

The PCF is the world’s leading philanthropic organization funding and accelerating prostate cancer research. Founded in 1993, the PCF has raised more than $745 million and provided funding to more than 2,000 research programs at nearly 200 cancer centers and universities.

Prostate Cancer and COVID-19: What’s the Connection?
Cases of COVID-19 and deaths are rising rapidly across the US and in many countries globally. Thousands of scientists around the world are working on vaccines and cures. Some of those scientists were full-time prostate cancer researchers just a few months ago. What happened? One reason is that many labs not doing COVID-19 research have been temporarily shuttered. But there’s some fascinating biology connecting COVID-19 and prostate cancer that may yield a cure.

Some data suggest that men are more likely to die of COVID-19 than women. There may be many reasons for this, including biological mechanisms, underlying health status, and social/behavioral exposures. One biological piece may lie in a protein called TMPRSS2. In early 2020 in Germany, it was discovered that one of the ways that COVID-19 fatally infects is by entering lung cells using a “door handle” protein called TMPRSS2. TMPRSS2 is a receptor protein that is regulated by androgen, that is, testosterone. The TMPRSS2 and ACE-2 proteins are required for the coronavirus to enter lung cells.

Now we need to ask the question “Do male hormones drive TMPRSS2 in the lungs?” essentially creating more “door handles” to help the virus enter lung cells? Early data suggests that this is true. Based on what we know about TMPRSS2, this begs another question: “If we block male hormones (to decrease the number of ‘door handles’ on each lung cell), or if we stop the ‘door handle’ from turning with a drug, can we potentially block the virus from entering the lungs?”

Over the last 20 years, PCF has funded research into TMPRSS2 and prostate cancer. Thus, we know that in about half of all prostate cancer patients, TMPRSS2 is a key factor that drives prostate cancer, and TMPRSS2 is a key drug target in prostate cancer bone metastasis. Thanks to this foundational research, we also know TMPRSS2 could potentially be a drug target for COVID-19. Real-world evidence of the potential prostate cancer-hormone-COVID-19 connection was initially demonstrated by a PCF-funded study of men with prostate cancer in Italy that reported that men with prostate cancer who were taking ADT were four times less likely to be infected with the coronavirus than men who were not on ADT, and five times less likely to die. (Of note, at this time there are no recommendations to give ADT to men with prostate cancer solely for COVID-19 protection).

Because TMPRSS2 is a longstanding prostate cancer drug research target, very quickly, multiple prostate cancer researchers in the PCF research enterprise began collaborating with infectious disease experts, pulmonologists, and other experts to test their anti-TMPRSS2 drug approaches against COVID-19. Clinical trials around the world are investigating hormone therapy (eg. ADT, enzalutamide) and the TMPRSS2-blocking agents camostat or nafamostat in both hospitalized and outpatient populations.

For more information visit www.pcf.org, email info@pcf.org, or call 1-800-757-2873.