Skipping Radiotherapy After Surgery for Prostate Cancer

Radiotherapy (RT) can be withheld after surgery for prostate cancer and given only if there are signs of biochemical recurrence of disease, instead of being given automatically to all patients.

This is the new advice from prostate cancer radiation experts discussing new data presented here at the European Society of Medical Oncology (ESMO) annual meeting. These new data include the first results from the largest trial to compare salvage with adjuvant radiotherapy (the RADICALS-RT trial), and the results of a prospective meta-analysis of three such studies (ARTISTIC).

They show that withholding RT and monitoring men after they have had a radical prostatectomy (RP), and giving early salvage radiotherapy (sRT) when the first signs of biochemical recurrence are seen, produces early outcomes that appear to be slightly better than giving adjuvant RT to all patients.

“Maybe ‘better than’ is not quite the right term to use,” commented discussant Gert de Meerleer, MD, radiation oncology at University Hospital Leuven, Belgium. “They are most probably equal,” he said, “but the advantage of the salvage approach is that you spare many men from undergoing RT, with its adverse effects.”

However, he emphasized that these men must be monitored closely and salvage RT must be given “early” – he said that, for him, this means when the PSA levels reach 0.2 ng/mL “at the very max.”

(Continued on page 6)

Durable Pain Control After Single Radiotherapy to Bone Metastases

New data show that a single fraction of high-dose radiotherapy (RT) leads to better and more durable pain control than standard multifraction (SMF) RT in patients with bone metastases predominantly limited to areas outside the spine.

“Our intent-to-treat analysis revealed that single-fraction stereotactic body RT (SBRT) with either 12 Gy or 16 Gy was not inferior to SMF RT with regard to pain control and time to local progression,” the investigators report. “What was very nice for us to learn is that, by giving a higher dose in a single fraction, we were able to achieve the best of both worlds,” lead investigator Quynh-Nhu Nguyen, MD, from the University of Texas MD Anderson Cancer Center in Houston, told Medscape Medical News.

“We delivered treatment in a single fraction that is convenient for patients, and we gave a higher dose that was safe and, in this instance, more effective in terms of pain response and also duration of response, so it’s a win-win scenario,” she said.

“There are at least 16 randomized controlled trials comparing single-fraction vs. multifraction RT in patients with painful bone metastases, so there is level-one evidence to support giving a high-grade prostate cancer.

(Continued on page 5)
“Landmark” Trial in Prostate Cancer with Mutations

Using genetic testing to target treatment for men with advanced prostate cancer (APCa) has given some “remarkable” results from a phase 3 trial described as a landmark. “Men with PCa should now undergo genetic testing of tumor tissue to identify the 30% or so of patients who can benefit — as is already routinely being done for breast, ovarian and lung cancer,” say researchers.

The results come from the phase 3 PROfound study of the PARP inhibitor olaparib in men who tested positive for DNA repair gene alterations including BRCA1, BRCA2, or ATM mutations. These were men with metastatic castration-resistant PCa (mCRPC) whose disease had progressed after treatment with the newer hormonal agents, such as abiraterone or enzalutamide, and/or with taxane chemotherapy.

In this study, BRCA1 or BRCA2 alterations were seen in 35% to 40% of men, while 18% to 24% had ATM alterations and 34% had other alterations. Between 6.6 and 8.4% of men had more than one alteration.

The new results, presented at the European Society for Medical Oncology (ESMO), show olaparib has significant benefit for men with these gene alterations. The drug delayed cancer progression by about four months compared with new hormonal therapy (NHT), and preliminary data suggest that overall survival was also prolonged, by more than three months. In addition, the response rate was much higher and there was a longer time to pain progression with olaparib.

“To see such a significant effect on disease progression and other clinically-relevant effects such as pain progression and objective response rate is a remarkable achievement in such heavily pre-treated patients with PCa,” said principal investigator Maha Hussain, MD, from the Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Chicago, IL.

“Despite the fact that there was 80% crossover to the olaparib to the control arm, I am delighted to say that PROfound is the first positive biomarker, selected phase 3 clinical study evaluating a molecular targeted therapy in men with metastatic castration-resistant disease,” she commented at a press briefing where the results were highlighted.

Discussant Eleni Efstatiiou, MD, PhD, a medical oncologist at MD Anderson Cancer Center, Houston, TX, described PROfound as a “landmark trial.” She said that the delay in progression seen with olaparib is “impressive because it is considerably higher than the 35% to 40% improvements with which we’ve been very satisfied in previous prostate cancer studies in this more advanced disease setting.”

Although Efstatiiou noted the trend toward improved survival, she emphasized that “we need to wait for the final analysis,” and underlined that “we should not ignore (Continued on page 5)

New Blood Test for Prostate Cancer is Highly Accurate and Avoids Invasive Biopsies

A new and simple blood test has been found to efficiently and accurately detect the presence of aggressive prostate cancer (PCa), according to research by Queen Mary University of London.

In combination with the current PSA test, the new test could help men avoid unnecessary and invasive biopsies, over-diagnosis and overtreatment.

PCa is the most common cancer in Western men, with 1.3 million new cases being diagnosed each year worldwide. It is currently detected using a blood test that measures PSA levels. Although it provides early diagnosis, the PSA blood test has a low specificity (high false positives) with about 75% of all PSA positive results ending up with negative biopsies that do not find cancer.

When a high PSA level in the blood is detected, the patient undergoes a tissue biopsy of the prostate gland, which is invasive and carries a significant risk of bleeding and infection. On biopsy, the majority of patients with elevated PSA levels are found not to have cancer.

Additionally, most diagnosed early-stage PCa are not fatal if left untreated. The current practice of combining PSA testing and biopsy for PCa results in unnecessary biopsies and over-diagnosis and overtreatment of many men. The new prostate cancer test (the Parsortix® system from ANGLE PLC) detects early cancer cells, or circulating tumor cells (CTCs), that have left the original tumour and entered the bloodstream prior to spreading around the body. By measuring intact living cancer cells in the (Continued on page 3)
Doc Moyad’s What Works & What is Worthless Column – Also Known as “No Bogus Science” Column

“Thank You Dr. Chodak for Being You!”

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

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

Thank you Dr. Chodak, for being you. Imagine being 30 years old (aka 25 years ago!!) and having the honor, but simultaneous unimaginable terror, of being a speaker at some of the most notable cancer meetings around the world. Here I was surrounded by some of the top prostate cancer doctors. They were smart, confident and, in some cases, very intimidating. Most of them did not know or give a hoot who I was and that was justifiable. Yet, there were several seasoned doctors that were not just powerful, but also demonstrated grace. They would give me advice, compliment me at times, and always went out of their way not to make me feel inferior, even though I knew I was. One of those doctors was Gerald Chodak.

He was friendly, funny, serious when he needed to be (aka passionate), but most of all just loaded with decorum. I actually looked forward to seeing him at meetings, dinners, or US TOO events, etc. He was a doctor who also practiced personally what he preached professionally. Still, he did something very few health care professionals could say that they have done over an entire career — being unquestionably devoted to patient education and advocacy.

Today, getting some doctors to write for newsletters or to participate in patient meetings/events is a piece of cake because it is so easy to see why everyone wants a slice. The all-around value is clear! In the old days (aka 10-25 years ago), the idea of doctors dedicated to prostate cancer patient education and advocacy seemed strange or odd, which is why many never stuck with it. However, not Chodak. He was there at the beginning, remained at the middle and stayed a part of this amazing patient movement until the end. When I say we lost a patient advocacy giant, well that is the understatement of a lifetime.

Dr. Chodak was remarkable, but his lifelong dedication to advocacy was extra extraordinary! I wish he would have been around a lot longer, but I am so darn grateful that he was around a long time and he helped a lot of patients in his practice. He changed forever the expectation and practice of patient advocacy and education.

I will miss him very much. I am honored and humbled to have known him. Thank you, Dr. Chodak, for being you!

New Blood Test for Prostate Cancer (Continued from page 2)

patient’s blood, rather than the PSA protein which may be present in the blood for reasons other than cancer, it potentially provides a more accurate test for PCa.

The study, published online ahead of print in The Journal of Urology, looked at the use of the CTC test in 98 pre-biopsy patients and 155 newly diagnosed PCa patients enrolled at St. Bartholomew’s Hospital in London.

The research team found that the presence of CTCs in pre-biopsy blood samples were indicative of the presence of aggressive PCa, and efficiently and non-invasively predicted the later outcome of biopsy results. When the CTC tests were used in combination with the current PSA test, it was able to predict the presence of aggressive PCa in subsequent biopsies with over 90% accuracy, better than any previously reported biomarkers.

Additionally, the number and type of CTCs present in the blood was also indicative of the aggressiveness of the cancer. Focusing on more aggressive PCa may reduce over-treatment and unnecessary biopsies for benign and non-aggressive conditions.

Lead researcher Professor Yong-Jie Lu from Queen Mary University of London said: “The current PCa test often leads to unnecessary invasive biopsies and over-diagnosis and overtreatment of many men, causing significant harm to patients and a waste of valuable healthcare resources. There is clearly a need for better selection of patients to undergo the biopsy procedure.

“Testing for CTCs is efficient, non-invasive and potentially accurate, and we’ve now demonstrated its potential to improve the current standard of care. The combination of CTC analysis and PSA detected PCa with the highest level of accuracy ever seen in any biomarker test, which could avoid many unnecessary biopsies. This could lead to a paradigm shift in the way we diagnose PCa.”

As this is a single centre study, the results need to be further validated in other independent research centres before the CTC test is available either privately or on the NHS in the UK, which could take a further three to five years. Clearance by the US Food and Drug Administration could also take three to five years.

Science Daily, 10 September 2019

Men with High-Risk PCa and Low PSA May Benefit More from Surgery than Radiation

Men with high-risk prostate cancer (PCa) accompanied by low PSA levels may survive longer by undergoing radical prostatectomy (RP) rather than radiation therapy (RT), according to a new study.

Using data from the Surveillance, Epidemiology and End Results (SEER) database, investigators identified 9,114 men with Gleason 8 to 10 PCa and PSA levels of 10 ng/mL or less. To date, no uniform treatment standard exists for this group of patients, they noted.

Of these 9,114 men identified using the SEER databases, 4,175 underwent RP, 4,114 received external beam RT (EBRT), and 825 received EBRT plus brachytherapy (EBRT+BT). The (Continued on page 4)
The prostate cancer world has been fractured by the loss of Gerald Chodak, MD, whose larger-than-life presence was a cornerstone of both its research and patient support networks. He passed away on September 28, 2019, at his home in Michigan City, IN, reported due to an aortic aneurysm.

Chodak, 72, stood firm, against much criticism, for his early belief in the conservative management of prostate cancer—a conviction that eventually snowballed into a powerful movement of active surveillance and patient empowerment.

He was also an artist, mingling “vibrant color and abstract shapes” with blown glass, and acrylic paint. He said color always evoked a special reaction in him: “It fills our world, enriching it greatly. I don’t simply see it but rather I react to it emotionally, whether it is the changing colors in the ocean, the birds flying by or the flowers in my garden.”

There are many who would describe Chodak himself as colorful, with an eye for style and a nose for controversy. “He was a pugilist, a contrarian, and that always appealed to me,” said Laurence Klotz, MD, a long-time colleague who admired Chodak’s lonely voice back in the ‘90s.

“Back then around 95% of men with low-grade prostate cancer were treated radically. Gerry recognized this was folly, and that really resonated with me. I ended up kind of running with that,” recalls Klotz, of the University of Toronto, who is known for championing delayed selective intervention, which recommends monitoring alone for men with low-grade prostate cancer that others weren’t,” agreed E. Michael D. Scott, the executive director and president of Prostate Cancer International and the sitemaster for The “New” Prostate Cancer InfoLink. “He was not always the most tactful, but he was also very charming.”

“One of his problems was that people could think he was arrogant, but I didn’t at all,” added Klotz. “He had an electric personality, but in my eyes Gerry was a gentle, caring guy.”

Though Chodak clearly enjoyed courting controversy, he never lost sight of his patients’ struggles. “He really listened to patients, and helped them to come to a decision that worked for them,” said Scott. “He never told them what to do, but he wasn’t afraid to tell them they were talking a load of BS if there was no data to support them.”

“I remember playing golf with him ~20 years ago, and his phone rang,” said Klotz. “It was a patient, and he took the call. That might not sound like much, but most doctors wouldn’t do that. He said all my patients have my phone number.” I mean, this is a guy who was already famous at the time, it’s not like he was scrounging to build a practice.”

That dedication to patients is what inspired Chodak to initiate Us TOO International with support groups that sprouted from a cluster of men who gathered at his office one February day in 1990. “This notion was similar to the nationwide Y-Me National Breast Cancer Organization that was formed for women with breast cancer,” he later explained, in an essay co-authored with two of the founding members.

In recent years, Chodak also became a dedicated contributor of weekly video commentaries for Medscape. “Dr. Chodak was part of the Medscape ‘family’ for 10 years,” recalls Christine Wiebe, senior director for Medscape features, who considered him a friend. “When he first joined us in 2009, I was struck by his earnest concern for patients and his eagerness to inform them about their treatment choices. He was an editor’s dream: professional and dependable, but also provocative.”

Chodak was a surgeon, whose keen hand-eye coordination was also evident outside the operating room. “The guy was an athlete,” recalls Klotz, with a hint of envy. “He was practically a tennis player, and I once saw him dance, I’d never seen anything like it.”

It was on the dance floor that Chodak took possibly some of his most meaningful steps: into the arms of his future wife. “Unlikely things often happen to those who step out of their own way,” Robin Chodak recently wrote, in a moving love story about the couple’s passion to tango.

There’s a painting by Gerry Chodak called “Passing Through”—his depiction of the beauty and resilience of transience. These are the things he leaves behind with his own passing, along with the comfort he provided among those touched by prostate cancer that we “cope through knowledge and hope.”

Medscape Urology
16 October 2019

“Passing Through” – In Memory of Gerald Chodak, MD
by Kate Johnson, Medscape Urology

High-Risk PCa
(Continued from page 3)

study population had a median follow-up of 47 months. “Compared with RP, EBRT and EBRT+BT were significantly associated with an approximately 3.4-fold and 2.1-fold increased risk of death from any cause, respectively, in adjusted analyses,” Yadong Guo, MD, and colleagues at Tongji University in Shanghai, China, reported in Frontiers in Oncology. EBRT was significantly associated with a nearly 2.5-fold increased risk of PCa-specific mortality compared with RP. The risk of PCa-specific mortality did not differ significantly between RP and EBRT+BT. The three-year OS rates were 98.4% for the RP group, 95.1% for the EBRT group, and 96.7% for EBRT+BT group, according to the investigators. The five-year OS rates were 96.8, 87.3, and 92.8%, respectively. At 10 years, the OS rates were 67.5, 58.0, and 61.5%, respectively.

The three-year PCSM rate was 0.5% for the RP group, 1.4% for the EBRT group, and 0.8% for the EBRT+BT group. The five-year PCSM rates were 1.4, 4.8, and 2.3%, respectively. The 10-year PCSM rates were 16.3, 23.7, and 6.5%, respectively.

Commenting on the new study, Amar U. Kishan, MD, Assistant Professor of Radiation Oncology at the University of California, Los Angeles, stated: “While high-grade tumors that produce low amounts of PSA are likely to be more aggressive, there are important limitations in using population databases like the SEER registry in terms of answering questions about comparative effectiveness. For instance, it does not...” (Continued on page 7)
single fraction in this setting,” she explained. “Yet in both Europe and in the U.S., most clinicians still use multifraction RT,” she noted.

“This is probably because there were questions about the durability of response with a single-fraction [approach] given at the lower dose, which meant that men had to undergo retreatment at a rate that was twice as high as those who received multifraction RT,” she added.

The new study was presented at The American Society for Radiation Oncologists (ASTRO) 2019 annual meeting and was published earlier this year in the journal JAMA Oncology.

The trial was conducted in 160 subjects with radiologically confirmed painful bone metastases (mostly non-spine), of whom 81 received SBRT at a dose of 12 Gy if lesions were ≥4 cm or 16 Gy if lesions were <4 cm in size; the other 79 received SMT RT delivered at a dose of 30 Gy in 10 fractions.

“The primary endpoint evaluated was progression of pain defined as worsening pain score (by at least two categories on MD Anderson Symptom Inventory (MDASI), as well as ≥50% increase in dose of opioid medication, reirradiation rate, and pathologic fracture,” investigators note.

At one month, 44% of patients in the SBRT arm achieved either a complete response (CR) or a partial response (PR) compared with 30% in the SMF RT group (P = 0.18, not a statistically significant difference). At three months, 38% of SBRT patients maintained either CR or PR vs. 21% in the SMF group (p = 0.05).

Among evaluable patients who received treatment per protocol, there were a significantly greater number of pain responders at two weeks in the SBRT group, at 62%, than in the SMF RT group, at 36% (P = 0.01), and this held true at both three and nine months.

“Local progression-free survival (PFS) rates were also higher in the stereotactic group than in the multifraction RT group at both one and two years,” investigators stated.

Among patients who were still alive at one year and especially at two years (and most were not) 100% of men in the SBRT group were still free of progression at one year vs. 90.5% of those in the standard RT group. At two years (and in very few patients), 100% of patients in the SBRT group were still free of progression vs. 75.6% in the standard RT group (P = 0.01, a statistically significant difference).

In contrast, no differences in toxic effects were observed between the two groups. Rates of grade 3 nausea and rates of grade 2 and 3 vomiting were low in both.

Asked by Medscape Medical News to comment on the findings, Kenneth Merrell, MD, Mayo Clinic School of Medicine, Rochester, MN, said that it was interesting to see that the use of SBRT in this study led to better pain responses at multiple time points – even within two weeks of treatment – and it also appeared to offer more durable control of the irradiated lesion.

However, despite these investigators using a higher RT dose in the SBRT group than had been used in earlier studies, “the dose spectrum in this study was at the lower end than what is typical for SBRT,” noted Merrell, who was not involved with the study. This raises some questions about what the best dose might really be if SBRT is used for pain relief in men with metastatic disease.

Merrell stressed, “palliation is at the heart of what we do with radiation oncology and it’s always a search to find an optimal palliative treatment that helps relieve pain and suffering while minimizing side effects.”

“For now, the single-fraction SBRT approach is definitely one option for such patients,” Merrell said, and suggested further studies are needed before single-fraction SBRT can be considered standard-of-care in this setting.

Presented at the ASTRO 2019 Annual Meeting, Abstract 100 Medscape Medical News 23 September 2019

“Landmark” Trial in Prostate Cancer with Mutations (Continued from page 2)

that significant adverse events, such as anemia and nausea, were more common with olaparib, as these can have an important effect on a patient’s ability to take the drug.” She added, “in practice, patients will need to be carefully monitored.”

Ignacio Duran, MD, PhD, Hospital Universitario Marques de Valdecilla, Santander, Spain, was equally positive in his praise of the trial. He stated that it offers a “double hit,” as a result of not only the “dramatically superior” efficacy with olaparib but also the proof of a “new concept” that PCa can be treated with targeted therapy.

To find patients with these genes, the team tested prostate tumor tissue with an investigational clinical trial assay developed in conjunction with Foundation Medicine and based on next-generation sequencing.

The men were divided into two groups:

- Cohort A: 245 men with BRCA1, BRCA2, or ATM gene alterations
- Cohort B: 142 men with any of the remaining 12 alterations (BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, PPP2R2A, RAD51B, RADS1C, RADS1D, or RADS4L)

Both cohorts were randomly assigned 2:1 to olaparib 300 mg twice daily or physicians’ choice of either enzalutamide or abiraterone. Men in the NHT group who progressed were allowed to crossover to olaparib.

All men had received previous treatment: both abiraterone and enzalutamide had been given to 17.6 to 19.9% of men and 64.1 to 66.4% had previously received taxanes.

The primary endpoint of this study was radiographic progression-free survival (rPFS) in cohort A, and this showed a significant improvement: median rPFS was 7.4 months with olaparib vs. 3.6 months with NHT (hazard ratio for progression, 0.34; P < 0.0001, a statistically significant difference).

At six months, 60% of olaparib patients were progression-free vs. 23% of those on hormonal therapy, and this fell to 28.0 and 9.4%, respectively, at 12 months. This significant benefit was seen across all subgroups, whether men were stratified by previous taxane use, measurable disease at baseline, site of metastases, baseline performance status, age at randomization, geographic location, and baseline PSA levels.

(Continued on page 8)
IsoPSA Test

(Continued from page 1)

land Diagnostics will work more closely and frequently with the FDA to expedite its review of IsoPSA.

“We are very grateful that the FDA recognizes the potential of IsoPSA, the first test in our pipeline of simple, affordable, and highly accurate cancer tests focused on cancer-relevant changes to protein biomarkers in blood,” said Arnon Chait, PhD, CEO of Cleveland Diagnostics.

“We look forward to working closely with the FDA to expedite the appropriate approvals and get this important new test into the hands of physicians.”

Cleveland Diagnostics has concluded two multicenter clinical trials in top U.S. and international hospitals and clinics, led by Cleveland Clinic, in which the diagnostic accuracy of IsoPSA was compared to that of PSA, the current standard of care in prostate cancer, in men scheduled for prostate biopsy. Results from those studies demonstrated that IsoPSA has superior diagnostic performance to traditional PSA in identifying which men have high-grade disease.

“The clinical utility of PSA is limited by the relatively poor diagnostic accuracy and predictive value of the test,” said Mark Stovisky, MD, CMO at Cleveland Diagnostics and urologist at Cleveland Clinic. “Clinicians today are using an array of diagnostic tests and procedures to inform decisions about a patient’s prostate health and the risk of prostate cancer. We believe that IsoPSA has the potential to fill a major void in this space.”

It is estimated that one in nine men will develop prostate cancer in his lifetime. The results of previous studies have shown that IsoPSA could reduce unnecessary biopsies by at least 45%, saving men from unneeded invasive, potentially risky and expensive procedures that can sometimes lead to serious and lasting side effects.

Business Wire
16 October 2019

Skipping RT After Surgery for Prostate Cancer (Continued from page 1)

Chris Parker, MD, from the Royal Marsden NHS Foundation Trust and the Institute of Cancer Research, London, UK, who presented results from the RADICALS-RT study, said the results have already changed clinical practice at his institution. “This is our new policy – early salvage RT at the first sign of a rise in PSA,” he said.

Commenting on the new data in an ESMO statement, Xavier Maldonado, MD, from the Vall d’Hebron University Hospital, Barcelona, Spain, said, “These are the first results to suggest that postoperative RT for prostate cancer could be omitted or delayed in some patients.

“This will shorten the duration of treatment for these patients and allow better use of resources, since today’s RT is technically sophisticated and therefore expensive,” he said. “However, strict follow-up will be needed to identify patients requiring salvage RT,” he added.

1st Results from RADICALS-RT

“RADICALS-RT is the largest trial so far to compare salvage with adjuvant RT,” Parker noted. It involved 1,396 men with a median follow-up of five years. These men had undergone RP and had post-op PSA ≤0.2 ng/mL, and one or more of the following: pathologic T (pT) 3/4, Gleason score 7 to 10, pre-op PSA ≥10ng/mL, and positive surgical margins.

Meerleer described this patient population as being at intermediate- or low-intermediate-risk of disease recurrence. In his discussion, he commented that “Parker described them as typical patients after surgery, but he pointed out that in other countries men with more advanced disease also undergo surgery.”

These men were randomly assigned to receive adjuvant RT (aRT) or to be followed by observation and to receive salvage RT (Obs+sRT) only if they reached a threshold, which was either two consecutive rises of PSA and PSA levels >1ng/mL, or three consecutive rises in PSA levels.

“After five years, only one third (33%) of this group had received RT. In view of that, it is not surprising that the toxicity reported was less in the salvage RT group,” Parker commented.

Self-reported urinary incontinence was worse at one year in 5.3% of the aRT group vs. 2.7% of the Obs+sRT group (P = 0.008), and grade 3/4 urethral stricture was reported at any time in 8% vs. 5% (P = 0.03, a statistically significant difference).

Parker said it was too early to present results for the primary endpoint of freedom-from-distant metastases (FFDM), as not enough events had taken place. So he presented results for the secondary endpoint of biochemical progression-free survival (bPFS), which was defined as PSA >0.4 ng/mL post-RT, PSA >2.0 ng/mL at any time, clinical progression, initiation of non-protocol hormone therapy, or prostate cancer death. This endpoint of bPFS at five years was seen in 85% of men in the aRT group vs. 88% for Obs+sRT, with a hazard ratio [HR] of 1.10 (95% confidence interval [CI] 0.81 - 1.49, P = 0.56, not a statistically significant difference).

“The results suggest that RT is equally effective whether it is given to all men shortly after surgery or given later to those men with recurrent disease,” Parker said in a statement. “There is a strong case now that observation should be the standard approach after surgery, and RT should only be used if the cancer comes back,” he added.

“The good news is that in [the] future, many men will avoid the side effects of RT,” added Parker. “These include urinary leakage and narrowing of the urethra, which can make urination difficult. Both are potential complications after surgery alone, but the risk is increased if RT is used as well.”

However, Parker also emphasized that longer follow-up is needed, and that the primary endpoint of FFDM is still to be reported. It may be that there is a role for adjuvant RT in some subgroups of this patient population.

ESMO commentator Maldonado agreed, and said some patients may still require adjuvant RT to avoid a very early local relapse and potential subsequent metastases. Future research should focus on identifying such patients, he suggested.

“We need to develop genomic classifiers to help decide the best management strategy for each patient – whether it should include surgery and/or RT, and at which time points,” he said.

Confirmation from Meta-analysis

Confirmation of these results followed in the next presentation, in which Claire Vale, PhD, from the MRC Clinical Trials Unit, University College London, UK, reported results from the ARTISTIC meta-analysis. This combined the results from RADICALS-RT with two other similar studies, RAVES and GETUG-AFU17.

(Continued on page 8)
Men with prostate cancer (PCa) just want to have fun—and play football/soccer instead of doing cancer-specific exercises and preferably wearing spiffy uniforms.

This and other unorthodox clinical pearls come from a first-of-its-kind clinical trial among 214 men with PCa in Denmark. The men, with an average age of 68, were randomized to play football twice a week for six months or to usual care.

“At one-year of follow-up, the football group had significant improvements in mental health and body mass index and fewer hospital admissions compared with controls,” report the investigators, led by Eik Dybboel Bjerre, PhD, postdoctoral scientist, University Hospital of Copenhagen, Denmark.

Also, there was no increased risk of fracture among the footballers despite a 19% incidence of skeletal metastases at baseline. The new one-year data were published online October 1st in *PLOS Medicine*.

At the twice-a-week hourly sessions, which took place at football clubs (FCs), the men divided up and played five vs. five against each other. Two volunteer coaches having minimal PCa education monitored the games. Players at some locations paid for their own uniforms to formalize appearing spiffy uniforms.

“The trial defies conventional wisdom about cancer patients and exercise,” said Bjerre. “The men’s primary motivation is not being healthy,” he explained. “Instead, they were motivated by having fun with peers and being in a structured environment,” he said.

“They don’t talk about PCa or health when they come.”

“Being a footballer,” commented Bjerre, “is the antithesis of being a cancer patient. The men said that playing football means they are not in a passive patient role.”

Bjerre added: “We all know exercise is healthy for you, but don’t really know how to promote this behavior, especially among men.” The trial indicates that team sports may be a good health promotion for cancer patients—and encourage long-term adherence.

Arjun Gupta, MD, oncology fellow, Johns Hopkins University, Baltimore, MD, who highlighted the study on Twitter, agreed. “Sport, especially team-based, is more fun, engaging, and affords the opportunity to build community and be meaningful after that hour is over,” he said in an email. Exercise in the form of prescribed, repetitive activity is uninspiring for many men.

Gupta offered himself as an example: “Having personally been minimally compliant for several years with an exercise and physiotherapy regimen for a torn knee meniscus, I can attest to how boring routine exercise can be.”

For older men, team sports recall their youth and masculinity, several experts told *Medscape Medical News*. “That’s invaluable for men living with prostate cancer,” according to Anna Campbell, MBE, PhD, professor, Clinical Exercise Science, Edinburgh Napier University, UK, who was not involved in the study. She observed that 40% of study participants were on androgen deprivation therapy (ADT) that aims to lower male hormones (androgens) to castration levels.

“A lot of these guys are on ADT, which means their testosterone is lower. They develop breasts, put on weight, get emotional,” she explained. “When they are back playing football, they are doing something manly.”

Campbell said that 50% of cancer patients in the UK opt for conventional cancer-specific exercise programs and the other 50% prefer more idiosyncratic, personalized activity such as joining a local walking group or playing badminton. The men in the Danish study, she suggested, were akin to the latter group.

“In Europe, soccer is the major sport,” said Bjerre. In the FC Prostate Community Trial, 60% of participants had played in their youth. However, only 4% had played football in recent years, so the trial brought many men back to their recreational roots. “If you were going to do the trial in the U.S., you would probably pick another sport,” acknowledged Bjerre.

The new study is the first conducted among cancer patients in local communities or the “real world.” Cost was minimal, with about $1800 expended at each club for balls, cones, etc.

Playing football in the latter decades of life is not without risk. “There were quite a lot of minor sports injuries in the football group—especially muscle strains,” said Bjerre. However, in what amounted to another unorthodox clinical pearl from the trial, the men suggested minor injuries can be a boon to mental health.

Campbell explained: “Even when they got an injury, they would say: ‘Yeah, I got a sports injury!’ They were so proud to have an injury. That’s the truth.”

The primary study outcome was mean change difference in PCa-specific quality of life at 12 weeks. The football group and usual care control group had similar, indicating that sport as a cancer intervention has limitations.

“We can’t give them back their urinary continence,” Bjerre summarized. “But exercise may extend overall survival for men and women living with cancer, according to epidemiological, observational data,” said Campbell.

*Medscape Medical News* 11 October 2019

**High-Risk PCa**

(Continued from page 4)

include data on duration of androgen deprivation therapy given with RT, which we know is critical.”

Bruce Jacobs, MD, MPH, Assistant Professor of Urology at the University of Pittsburgh School of Medicine, said the study is important because a trial with men randomized to these three different treatments is not possible. “So, we have to have other ways to get at the answer,” Dr. Jacobs said. “You have to account for selection bias. RT patients tend to be similar, but when you have surgery vs. RT, then you become concerned that the men are different. With observational studies you must keep that in mind.”

Zachary L. Smith, MD, Assistant Professor of Surgery at Washington University School of Medicine and Barnes-Jewish Hospital in St. Louis, MI, stated: “One reason these high-risk patients tend to fare a little better after RP in many studies is because they can still get RT later if they have recurrence. After RT,” he added, “so few urologists are willing to perform salvage RP that patients often only get ADT. This information is not accounted for in the current study,” he said.
Skipping RT After Surgery for Prostate Cancer (Continued from page 6)

All three trials compared adjuvant RT with salvage RT in men who had undergone RP. “Patient characteristics were balanced within trials and overall,” Vale commented. Median age was 65 and most (77%) had a Gleason sum score of 7. Across the three trials, 1,074 men were randomly assigned to aRT and 1,077 to sRT. To date, 395 men (37%) underwent sRT. Median follow-up was from 47 to 61 months. The meta-analysis reported event-free survival (EFS), and Vale pointed out that the vast majority of first events across all the trials are biochemical failures.

“Based on 245 events, the meta-analysis shows no evidence that EFS is improved with aRT compared to sRT (HR, 1.09; 95% CI, 0.86 - 1.39, P = 0.47),” Vale reported. This translates to a potential absolute difference of 1% at five years in favor of sRT (95% CI, 2% in favor of aRT to 4% in favor of sRT).

Vale concluded that this meta-analysis of data from the three trials suggests that sRT and aRT “offer similar outcomes. However, sRT spares many men from receiving RT, and associated side effects,” she pointed out.

“Results of the ARTISTIC meta-analysis confirm those of RADICALS, and provide greater evidence to support the routine use of observation and early salvage RT,” Vale said in a statement. Presented at the ESMO 2019 Annual Meeting; Abstracts LBA49_PR (RADICALS-RT) and LBA48_PR (ARTISTIC).

Medscape Medical News 28 September 2019

“Landmark” Trial in Prostate Cancer with Mutations (Continued from page 5)

The confirmed objective response rate for olaparib was 33.3% in cohort A vs. just 2.3% in cohort B, at an odds ratio of 20.86 (P <0.0001, a statistically significant difference). Crucially, the time to pain progression, as measured using the Brief Pain Inventory-Short Form, was significantly longer in cohort A vs. B, at a median that was not reached vs. 9.9 months, or a hazard ratio [HR] of 0.44 (P = 0.0192).

In terms of safety, there were more adverse events with olaparib than hormonal therapy, with 50.8% and 37.7%, respectively, experiencing grade 3 or higher adverse events. Dose reductions due to an adverse event were also more common with olaparib, at 22.3 vs. 3.8% of men receiving NHT. Drug discontinuations due to adverse events were more frequent with olaparib at 16.4 vs. 8.5%.

The most common adverse event with olaparib was anemia (21.5%), with fatigue and asthenia seen in just 2.7%. Those two adverse events were also the most commonly seen in hormonal therapy patients but occurred in just 5.4% of cases for both.

Hussain said that the results should encourage the greater use of genetic testing in mCRPC. She noted that oncologists treating breast, ovarian, or lung cancer are already performing genetic testing on tumor tissue.

“To widen the use of testing in PCa,” Hussein said, “we need to begin community education and information sharing regarding the merits of testing.” The results from the current study are “opening up the door for us right now,” she added.

Presented at ESMO 2019; Abstract LBA12_PR
Medscape Medical News 4 October 2019
QUESTION FROM PROSTATE CANCER SURVIVOR:
I had brachytherapy 18½ years ago but about two years ago started having some ED symptoms. My urologist gave me 20mg of Cialis but it did nothing. I found a supplement with Tongkat extract (has heavy B6 and other extracts) that seemed to help for a while but not anymore. Is there anything to the advertisements I hear about supplements?

RESPONSE FROM DR. JEFFREY ALBAUGH:
Thank you for your excellent question and I am often asked about complimentary treatments for erectile dysfunction including herbs. There is not good definitive evidence to support Tongkat extract to treat erectile dysfunction and, even more importantly, many supplements such as the ones you are asking about may contain testosterone, testosterone enhancing products, or other products which may be harmful to you as a prostate cancer survivor. I would not recommend taking this based on the available science. There are many supplements out there that claim to improve erectile function but be very careful with what you put in your body as many of these supplements are not regulated and contain multiple products. Often the claims made for the supplements are not true and some supplements may even be harmful. When I want to learn more about the evidence to support supplements, I turn to my friend and, in my opinion, the leading expert on urology supplements, Mark Moyad, MD, MPH. I carry his book, The Supplement Handbook: A Trusted Expert’s Guide to What Works & What’s Worthless for More than 100 Conditions on my tablet and feel it is an excellent resource on supplements. Single ingredient supplements are lower in cost and have more research evidence to support them, but many supplements lack solid research to support their effects. I have not found any supplement that works as well as the FDA approved treatments for erectile dysfunction. Having said that, there are a few that have some evidence to support a positive effect on erectile function in men with mild to moderate erectile dysfunction. There is some consistent positive data for Korean red ginseng (Panax ginseng) and heart healthy lifestyle changes for erectile dysfunction; and criticism has been proposed of the current erectile dysfunction guidelines for NOT including the evidence for both Panax ginseng and heart-healthy lifestyle changes in clinical guidelines (Moyad & Park, 2012). In terms of complimentary therapies for improving erectile function, I do believe that the greatest complimentary therapy supported by research continues to be a low fat, low cholesterol, plant-based diet, along with exercise and weight control (Collins, et al., 2013; Esposito, et al., 2009; Esposito, et al., 2004). Staying in top physical shape is the most important thing you can do for your heart and your erectile health. In a 2008 systemic review of red ginseng for treating erectile dysfunction, seven randomized controlled trials were examined and the collective evidence supported the effectiveness of red ginseng in the treatment of erectile dysfunction (although the sample size from all trials and methodology quality were too low to draw definitive conclusions and better studies are needed) (Jang, Lee, Shin, Lee, & Ernst, 2008). A 2012 published multicenter, placebo-controlled, double blind study of 119 showed improvement in erectile function, with no side effects (except one case of mild stomach upset) and no safety issues with changes in hormonal or cholesterol markers were noted (Choi, et al., 2012). There is also limited evidence to support L-citrulline. L-citrulline is an amino acid normally made in the body that converts to L-arginine (also an amino acid from the body). L-arginine improves blood flow by creating nitric oxide which helps dilate blood vessels. L-citrulline is taken at lower doses then L-arginine and the high doses needed for L-arginine raise concerns with toxicity. In a small study of only 24 men, half the men with mild to moderate erectile dysfunction had improvement in erection hardness with L-citrulline with no reported adverse effects (Cormio, et al., 2011). The authors conclude it doesn’t work as well as PDE-5 inhibitors (sildenafil, vardenafil, avanafil and tadalafil)
and further research is needed for L-citrulline. If you are considering a supplement, I would recommend looking at the available research to understand further the positive effects it may have, any side effects reported, and also dosing information.

I think it is most important for you to work closely with an erectile dysfunction urologic expert provider to determine the best treatment for your erectile dysfunction. There are multiple evidence-based treatments for erectile dysfunction including oral agents, the vacuum device, intraurethral suppositories, penile injections, and the penile implant. Often men are not taking their medications properly and this can make a difference in response to medications. You need to make sure you have taken it properly to produce maximum effects under the direction of a urologic healthcare provider. If the medication is still not working after multiple attempts of taking the medication properly for maximum effect, it may be time to explore the other evidence-based erectile dysfunction treatments under the supervision of an expert provider. All treatments have pros and cons, but most men who are willing to work with the various treatments are able to find something that works for them.


You can access the new edition of my book or download a free copy of my original book at 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=Hiq0dDEb11O&t=4483s.

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.

Results of the CARD Trial: Benefit for Patients Needing a Third-Line Therapy Option

Metastatic castration-resistant prostate cancer (mCRPC) refers to prostate cancer that has spread outside the prostate and no longer responds to traditional androgen deprivation therapy (ADT). Patients have several different treatment options, including second-generation androgen-signaling-targeted inhibitors (ARTA) like abiraterone or enzalutamide, and chemotherapy drugs (docetaxel, cabazitaxel). However, for patients whose disease progresses after treatment with one ARTA and with docetaxel, questions remain: Should the patient switch to the other ARTA? Should a chemotherapy drug be used?

The results of the CARD trial, an ambitious study presented at the 2019 European Society of Medical Oncology (ESMO) Congress, shed light on what the next step should be. Cabazitaxel, an FDA-approved drug, was shown to be more efficacious with similar toxicity as third-line treatment in patients who had received one ARTA and were progressive on this drug within 12 months, and had also received docetaxel.

At ESMO, researcher Dr. Ronald de Wit, MD, PhD, of Erasmus Medical Center, presented the trial results. Dr. Silke Gillessen, MD, of the University of Manchester, The Christie NHS Foundation Trust, and Kantonsspital St. Gallen, provided additional context during her discussion of the CARD trial, a phase 3 randomized-controlled trial that examined patients with mCRPC who received a third line-treatment after one ARTA and docetaxel, independent of the sequence. The trial included 255 mCRPC patients whose disease had progressed after treatment with two previous regimens: patients must have received and progressed within 12 months on an ARTA (enzalutamide or abiraterone), and must have received at least 3 cycles of docetaxel; the chemotherapy could have been given in the castration-sensitive or the castration-resistant state. Patients were randomized into two groups: 1. receive cabazitaxel OR 2. receive the alternative ARTA (enzalutamide or abiraterone).

Results showed that patients who received cabazitaxel experienced significantly better outcomes, including radiographic progression-free survival (no worsening of disease on scans; median of 8.0 months with cabazitaxel vs. 3.7 months with the ARTA) which was the primary endpoint, reduction in PSA levels by at least 50% (35.7% vs. 13.5% of patients), tumor shrinkage (36.5% vs. 11.5% of patients), and reduced pain than those who received the alternative ARTA (45.0% vs. 19.3% of patients). Additionally, toxicity from cabazitaxel seemed not worse vs. the other study drug, (adverse events of Grade 3 or higher, 56.3% vs. 52.4% of patients).

What does this mean for patients and physicians? The question of what is the optimal next line of treatment for patients fit for chemotherapy who have received docetaxel plus one line of ARTA and were progressing under the first ARTA within 12 months is answered with this trial. Gillessen notes that we need to resist “chemophobia.” Cabazitaxel is a new standard of care for third-line treatment in patients who have progressive disease after docetaxel and progressed within one year or less of abiraterone or enzalutamide and who are fit enough to tolerate chemotherapy.

“Before this trial, we knew from other trials that the response rates and duration of response, if any, to the alternate ARTA were low. This trial has shown very elegantly in a representative patient population, and in a randomized, prospective design, that cabazitaxel is superior in this setting. While only 13% of patients in this trial had docetaxel in the castration-sensitive setting and only one patient had abiraterone in the castration-sensitive setting, we will see these treatments being given in the castration-sensitive setting more frequently,” said Dr. Gillessen. “The question remains how to treat patients with a very good response to the first ARTA of longer than 12 months. One may also raise the question if 20mg/m2 of cabazitaxel would be sufficient (a lower dose than the 25mg/m2 dose given in the trial). So, in summary, the authors have for the first time demonstrated a survival benefit in a third-line setting in a randomized trial, and that is a big step in the right direction, but some questions remain still unanswered.”

For more information visit www.pcf.org, email info@pcf.org, or call 1-800-757-2873.
Us TOO Presents:
Prostate Cancer Pathways
Free Educational Event and Webcast

Saturday, November 9

Robert H. Lurie
Medical Research Center
Baldwin Auditorium
303 E. Superior St.
Chicago, IL 60611

10:00 am - 3:00 pm

Attend this free event in person and enjoy a heart-healthy/prostate-healthy lunch; OR watch the free online webcast providing live audio and video.

To register visit www.ustoo.org/pathwayschicago19 or call (800) 808-7866.

Please note that on-site space is limited. We will attempt to accommodate those registering in person on the day of the event, but we cannot guarantee a seat or a free lunch.

Let Us Help You Plan Your Path Through Every Step of Your Journey...

Prostate Cancer Pathways is a new, dynamic educational event and webcast from Us TOO International for men with prostate cancer and their loved ones. The Pathways event and webcast will include panel discussions featuring medical experts and patients addressing topics that are most important to men with prostate cancer, as determined by survey results from Us TOO support group leaders.

Featuring experts from the Polsky Urologic Cancer Institute of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University at Northwestern Memorial Hospital, topics will include:

- Radiation Oncology - Sean Sachdev, MD
- Medical Oncology - Maha Hussain, MD
- Men’s Sexual Health - Nelson Bennett, Jr., MD
- Clinical Genetics - Carmen Williams, MS, CGC
- Urologic Oncology - Shilajit D. Kundu, MD
- Hematology and Oncology - Alicia Morgans, MD, MPH
- Hematology and Oncology - David J. VanderWeele, MD, PhD

The conversation will be driven by input and questions from you and others in the prostate cancer community. And it’s all free of charge!

All sessions will be webcast live and videotaped.

Hosted by:

In Collaboration with:
Us TOO at Northwestern Support Group at Northwestern Memorial Hospital
Galter Pavillion, 20th Floor, Room 20-250, 675 N. St. Clair St.
Second Wednesday of the Month, 6-7:30pm
Contact: Mary Kate Keeler at mary.fitzgerald@northwestern.edu or (312) 694-6082

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