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Androgen Cycling Shows Promise in Castration Resistant Prostate Cancer

Androgen Annihilation Strategy Prolongs Radiographic Progression-Free Survival in Metastatic Castration Resistant Prostate Cancer

An androgen annihilation strategy using apalutamide significantly slows progression in men with chemotherapy-naive metastatic castration-resistant prostate cancer (mCRPC), say results from the phase 3 ACIS trial.

Adding the androgen receptor antagonist to standard care – abiraterone acetate and prednisone – prolonged radiographic progression-free survival (rPFS) by 6.0 months at the trial’s primary analysis and by 7.4 months at final analysis. Adverse events were consistent with the drug’s known safety profile.

Investigator Dana E. Rathkopf, MD, of Memorial Sloan Kettering Cancer Center, New York said “mCRPC is frequently driven by activated androgen receptors and elevated intratumoral androgens. Therefore, androgen annihilation using agents with distinct mechanisms that target both pathways is attractive.”

With this in mind, investigators conducted the ACIS trial, enrolling 982 men having mCRPC that had progressed on androgen deprivation therapy (ADT) but who had not received chemotherapy or androgen receptor signaling inhibitors (ARSIs) for castration-resistant disease. Subjects were randomized evenly to apalutamide or placebo, each given with abiraterone plus prednisone. All patients continued ADT.

(Continued on page 4)

Medications for Benign Prostatic Hyperplasia Linked to Risk for Heart Failure

Widely used medications for benign prostatic hyperplasia (BPH) – also known as enlarged prostate – may be associated with a small, but significant increase in the probability of developing heart failure, suggests a Journal of Urology study.

Risk is highest in men taking an alpha-blocker (ABs) medication for BPH rather than a different type called 5-alpha reductase inhibitors (5-ARIs), according to a new research study by D. Robert Siemens, MD, and colleagues of Queen’s University, Kingston, Ontario, Canada.

“While no one should stop taking their BPH medications based on these results, our study contributes new evidence for understanding the complex interaction of factors affecting heart disease risk in men with BPH,” Dr. Siemens comments.

BP is a quite common condition in men, especially at older ages. It occurs when the prostate gland becomes enlarged, causing symptoms such as frequent and difficult urination. Millions of men take medications to reduce BPH symptoms – most commonly ABs, 5-ARIs, or a combination of the two.

Both BPH and cardiovascular disease are common in older men, which may reflect shared risk factors or causes. Clinical trials have suggested that men taking ABs or 5-ARIs might be more likely to develop heart failure: a chronic condition where the heart can’t pump enough blood to keep up with demand. However, other studies have found no such link.

To clarify the association between BPH medications...
Prostate Radiofrequency Focal Ablation (ProRAFT) Trial: A Prospective Development Study Evaluating a Bipolar Radiofrequency Device to Treat Prostate Cancer


Purpose: We determined the early efficacy of bipolar radiofrequency ablation with a coil design for focal ablation of clinically significant localized prostate cancer (PCA) visible at multiparametric (mp) magnetic resonance imaging (MRI).

Materials and Methods: A prospective IDEAL phase 2 development study (Focal Prostate Radiofrequency Ablation, NCT02294903) recruited treatment-naïve patients with a single focus of significant localized PCAs (Gleason 7 or 4 mm or more of Gleason 6) concordant with a lesion visible on mp-MRI. Intervention was a focal ablation with a bipolar radiofrequency system (Encage™) encompassing the lesion and a predefined margin using nonrigid MRI-ultrasound fusion. Primary outcome was the proportion of men with absence of significant localized disease on biopsy at 6 months. Trial follow-up consisted of serum PSA, mp-MRI at 1 week, and 6 and 12 months post-ablation. Validated patient reported outcome measures for urinary, erectile and bowel functions, and adverse events monitoring system were used. Analyses were done on a per-protocol basis.

Results: Of 21 men recruited, 20 received the intervention. Baseline characteristics were median age 66 years (interquartile range [IQR] 63-69) and preoperative median PSA of 7.9 ng/ml (5.3-9.6). A total of 18 patients (90%) had Gleason 7 disease with median maximum cancer 7 mm (IQR 5-10), for a median of 2.8 cc mp-MRI lesions (IQR 1.4-4.8). Targeted biopsy of the treated area (median number of cores 6, IQR 5-8) showed absence of significant localized PCAs in 16/20 men (80%), concurrent with mp-MRI. There was a low profile of side effects at patient reported outcome measures analysis and no serious adverse events.

Conclusions: Focal therapy of significant localized prostate cancer associated with an MRI lesion using bipolar radiofrequency showed early efficacy to ablate cancer with low rates of genitourinary and rectal side effects.

Final Results from TITAN Study Confirm Apalutamide Benefit in Metastatic Castration Sensitive Prostate Cancer

The survival benefit of adding apalutamide to standard care for metastatic castration-sensitive prostate cancer (mCSPC) persisted at nearly 4 years of follow-up, according to the final analysis of the phase 3 TITAN trial. At a median follow-up of 44 months, the median overall survival (OS) was not reached in men who received apalutamide plus standard androgen deprivation therapy (ADT), but the median OS was 52.2 months in men who received placebo plus ADT.

“In the final analysis, the risk of death with apalutamide was reduced by 35% (Hazard Ratio [HR] 0.65, P < 0.0001). This was similar to the hazard ratio of 0.67 in the primary analysis of TITAN, despite an almost 40% crossover rate from the placebo to the apalutamide group,” said Kim N. Chi, MD, a medical oncologist at BC Cancer Vancouver Prostate Centre. Dr. Chi reported these results at the 2021 Genitourinary Cancer Symposium (GuCS).

The international, double-blind TITAN trial compared apalutamide (240 mg daily) with placebo, both added to standard ADT, in 1,052 men with mCSPC, including those with high- and low-volume disease, prior docetaxel use, prior treatment for localized disease, and prior ADT for no more than 6 months.

At the primary analysis, reported in the New England Journal of Medicine in 2019, the dual primary endpoints of radiographic progression-free survival (rPFS) and OS met statistical significance at a median follow up of 22.7 months. At the final analysis, the median treatment duration was 39.3 months for the apalutamide arm, 20.2 months for the placebo arm, and 15.4 months for men who crossed over from placebo to apalutamide.

“After adjusting for crossover, the effect of apalutamide on OS increased (HR, 0.52), indicating a reduction in the risk of death by 48% vs. placebo,” Dr. Chi said. He (Continued on page 6)
**Doc Moyad’s What Works & What is Worthless Column – Also Known as “No Bogus Science” Column**

**“Viva Artichoke Season?!”**

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.

Do you know why the early part of the year through May (aka RIGHT NOW, folks) is my favorite time of the year? Is it because I honestly believe Michigan can win the NCAA football and basketball championships? Is it because Us TOO does not require you to work so hard for them during the post-holiday season? You probably guessed from the title of this column that I get so excited during this time of year because it is PRIME ARTICHOKE SEASON!

Man, I love artichokes because they are the Rodney Dangerfield of the diet world... they just do not get enough respect, so this is where I can be of assistance. Artichokes are a cornerstone of the Mediterranean diet despite other far more expensive products from this region getting more attention and health credit, such as olive oil or wine (gee I wonder why they get more credit? Sarcasm alert). Italy, Spain, France, and California (where it is the official state vegetable, no kidding) are just some of the many producers of artichokes.

Artichokes, to me, should be the paradigm of a super food, even though I dislike that term because every healthy food should be classified as SUPER! First, they taste amazing, especially since they have tremendous latitude in preparation or presentation (like the tofu of the cooking world), and they have a wonderful surprise when you get to the center of them... kind of like your old favorite sugary box of cereal, but without all the calories, sugar, and cost. You know what I am talking about... right? The artichoke heart, baby! Oh my, does that thing taste amazing or what?! Is anything more salubrious (I love that word), or hale (I love that word too), than a single artichoke? It is only 50-75 calories with virtually no sodium and loaded with heart-healthy dietary potassium (about 500 mg), and magnesium (25% of daily need), and countless other nutrients such as calcium (yes calcium!). Another surprise is that the artichoke also carries a small, but respectable amount of protein (about 4-5 grams), or about as much as any other leaf-like true veggie out there. Yet, one of the greatest secrets of the artichoke lies in the fact that it helps keep YOUR train on time (so to speak). It ensures that YOUR “train” runs on time so your train is not put under too much stress or strain. What am I talking about? I am talking about 7-10 GRAMS of DIETARY FIBER per artichoke, my locomotive analogy loving friends! Find me a single pill that contains everything I mentioned, including such a high amount of fiber for such a low amount of calories and cost, and I will show you a NOBEL PRIZE!

The only major catch? If you love to eat more than 1 artichoke in 1 sitting (I eat 2-3 at a time) then, even though it is not a massive source of vitamin K (15-20% of daily needs), it could become a larger source if you are obsessed with eating them. Let your doctor and nutritionist know about your dietary intake if you are on the blood thinning drug warfarin (aka Coumadin). Of course, do not eat the hairy inside part of

(Continued on page 4)

**CCR Score Can Guide Treatment After Radiation in Prostate Cancer**

The combined clinical cycle risk (CCR) score – derived from both clinical and genetic factors – can identify men with intermediate- and high-risk localized prostate cancer (PCa) who could potentially forgo androgen deprivation therapy (ADT), a retrospective study suggests.

“Whether you have RT alone, RT plus any duration of ADT, insufficient duration ADT, or sufficient ADT duration by guideline standard, the risk of metastasis never exceeds 5% at 10 years even in high- and very-high-risk men,” Tward said.

He and his team found that half the men in their study with unfavorable intermediate risk disease, 20% with high-risk disease, and 5% with very-high-risk disease scored below the CCR threshold. This implies that, for many men, ADT after radiation “adds unnecessary morbidity for an extremely small absolute risk reduction in metastasis-free survival,” Tward explained, “but I had a hunch this off-the-shelf test would be very good at helping with ADT decisions after RT.”

“Yet, one of the greatest secrets of the artichoke lies in the fact that it helps keep YOUR train on time (so to speak). It ensures that YOUR “train” runs on time so your train is not put under too much stress or strain. The CCR score is a validated prognosticator of metastasis and death in localized PCa. The test is available commercially as Prolaris. It is used mostly to make the call between active surveillance and treatment,” Tward explained, “but it has in their own mind what that risk reduction is that works for them,” he added. “For some men, a 1-2% drop in absolute risk is worth it,” he said, “but most men would not be willing to endure ADT side effects if the absolute benefit is <5%.”

In the validation study Tward presented at GUCS 2021, 70% of men had intermediate-risk disease, and 30% had high- or very-high-risk disease according to National Comprehensive Cancer Network criteria. All 741 men received RT equivalent to at least 75.6 Gy at 1.8 Gy per... (Continued on page 8)
The new product, a radio-labeled small molecule, lutetium-177 [177Lu] Lu-PSMA-6170, is under development by Endocyte/Novartis. It binds to prostate-specific membrane antigen (PSMA) and delivers high doses of beta radiation (RT). The short mean path length of the beta particles with 177Lu-PSMA (0.7 mm), limits damage to surrounding tissues. The unblinded trial was conducted at 11 centers in Australia. Participants were men with mCRPC (median age, 72 years) whose disease progression while receiving docetaxel and androgen receptor-directed therapy.

To be eligible for the trial, men had to have metastases that expressed PSMA (detected after screening with 2 PET-CT scans). About one quarter of the men that were screened were not eligible to take part.

Men were randomly assigned to receive cabazitaxel 20 mg/m² every 3 weeks IV for up to 10 cycles or [177Lu] Lu-PSMA 6.0–8.5 GBq IV every 6 weeks for up to 6 cycles.

The primary outcome was a ≥ 50% reduction in PSA level from baseline. On intention-to-treat analysis, this was achieved by 66 and 37% of patients.

Androgen Annihilation Strategy Prolongs rPFS in mCRPC (Continued from page 1)

“The trial met its primary endpoint,” Rathkopf reported. In the primary analysis, conducted at a median follow-up of 25.7 months, the median investigator-assessed rPFS was 22.6 months with apalutamide and 16.6 months with placebo (Hazard Ratio [HR], 0.69; P < 0.0001, a statistically significant difference).

Results held up at final analysis at a median 54.8 months of follow-up. The median overall survival was 36.2 months and 33.7 months, respectively, a nonsignificant difference.

For both rPFS and overall survival, there were trends toward benefit in two clinical subgroups typically having poorer prognosis – men with visceral metastases and men aged 75 years and older. In analyses of biomarkers, benefit was greater in men whose tumor cells were luminal subtype and in men who had average or high androgen receptor activity.

The apalutamide and placebo groups did not differ significantly on time to second PFS, initiation of cytotoxic chemotherapy, chronic opioid use, and pain progression. However, apalutamide therapy increased the percentage of men who achieved a confirmed PSA decline of at least 50% (79.5 vs. 72.9%) and an undetectable PSA at any time during treatment (24.6 vs. 19.2%).

Apalutamide was associated with a higher rate of grade 3/4 treatment-emergent adverse events (63.3 vs. 56.2%), including fatigue, hypertension, rash, cardiac disorders, and fracture/osteoporosis. Health-related quality of life declined over time in both treatment groups, although not to a clinically meaningful extent.

“Clinical and biomarker subgroups identified in this analysis will need further exploration to better delineate who might benefit most from the addition of apalutamide to abiraterone and prednisone in mCRPC,” Rathkopf said, noting that she currently looks at the whole picture when deciding whether to use the combination.

“It’s not just luminal subtype or Gleason grade or age. You have to look at all of these variables together. There are definitely men that are more suited to a more aggressive approach early on,” she elaborated. “And some patients want to be more aggressive. A progression-free survival gain of 6–7 months up front is meaningful to them. A longer time to progression and a more profound decline in PSA will allow them to possibly enjoy their life more during this treatment period, balanced against whatever toxicities we may see with the combination.”

“To its merit, the ACIS trial was large, used an active, standard-of-care comparator, and had a blinded design,” said invited discussant Joshi J. Alumkal, MD, of the Rogel Cancer Center at the University of Michigan, Ann Arbor, who was not involved in the study.

“However, due to increased toxicity, cost, similar rPFS, and the lack of overall survival benefit, and in light of the clinical insights from other studies with combined or sequential ARSI treatment, I do not believe results from ACIS change practice at this time,” he said.

“Additional research into the varied molecular pathways driving this disease will be essential for tailoring therapy to improve clinical outcomes for various patient subsets,” Alumkal maintained.

“To move the needle in CRPC, it is important to understand the biology in those patients who derive the least benefit from ARSI treatment,” he elaborated. “Understanding the key drivers in these tumors may provide a roadmap for how to address the most aggressive subsets of CRPC tumors that appear to do quite poorly, even with ARSI escalation as done in SPARTAN or ACIS.”

Reported at the 2021 GuCS, abstract 9.

Medscape Medical News
12 February 2021

Doc Moyad’s Column (Continued from page 3)

this veggie, which is known as the “choke” (no kidding).

Finally, what about the research Moyad? What about it? Prostate cancer and artichokes... good luck finding a single major study on your next search, BUT “Mediterranean diet and prostate cancer” gets a ton of positive research almost daily”, and yet, does anyone focus on this poor old lower calorie nutrient dense artichoke?

Nope! I get all CHOKED UP when I think about the health benefits of a small, medium, or large artichoke. Is there a more perfect, whole, unprocessed, healthier food on the planet? BTW – What do you call a conversation between 2 artichokes? A serious HEART to HEART discussion.

Reference:
TheraP Beats Cabazitaxel in Metastatic Castrate Resistant Prostate Cancer (Continued from page 4)

and heart failure, Dr. Siemens and colleagues used Ontario health data to identify more than 175,000 men diagnosed with BPH. About 55,000 men were being treated with ABs alone, 8,000 with 5-ARIs alone, and 41,000 with a combination of ABs and 5-ARIs. The rest were not taking either type of BPH medication.

On analysis of follow-up data, men treated with ABs and/or 5-ARIs were more likely to be diagnosed with heart failure. The risk of developing heart failure was increased by 22 percent in men taking ABs alone, 16 percent for those taking combination therapy, and 9 percent for those taking 5-ARIs alone, compared to the control group of men not taking BPH medications. The associations were significant after adjusting for other characteristics, including heart disease risk factors.

Heart failure risk was higher with older "nonselective" ABs vs. newer "selective" ABs. Risk was higher in men taking ABs for a prolonged time: 14 months or longer.

Dr. Siemens and coauthors emphasize that while the increased probability of developing heart failure was statistically high, the absolute risk was relatively low. Risk factors such as previous heart disease, high blood pressure and diabetes had a much greater impact on heart failure risk compared to BPH medications. “Our study suggests men taking ABs and/or 5-ARIs are more likely to be diagnosed with heart failure,” Dr. Siemens said. “This is an important finding, given that BPH is common among older men, and that these medications are so widely used.”

Dr. Siemens adds, “Since men with BPH may continue these medications for several years, it is important physicians be aware of this risk, including both primary care physicians and urologists, especially in patients with previous heart disease or cardiovascular risk factors.”

Newswire
08 March 2021
No Benefit of Dose Intensified Salvage RT for Prostate Cancer Recurrence

Dose-intensified salvage radiotherapy (SRT) is not superior to conventional dose SRT and is associated with increased late rectal toxicity in men with biochemical progression (BCP) of prostate cancer (PCa) after radical prostatectomy (RP), according to new findings.

“The results tell us more is not always better,” Dr. Neeraj Agarwal of Huntsman Cancer Institute, in Salt Lake City said in a statement from the American Society of Clinical Oncology (ASCO) 2021 Genitourinary Cancers Symposium (GuCS), where the research was presented.

“In this study of men with recurrence of PCa after surgery, standard dose of RT was as effective as the higher dose of RT in controlling the disease, and was less toxic,” said Dr. Agarwal, who was not involved in the study.

“RP is the standard primary treatment for localized PCa. However, up to 40% of men will experience BCP post-RP. For these patients, SRT to the prostate bed is the only available curative treatment option,” study presenter Dr. Pirus Ghadjar, with Charité Hospital, Berlin, Germany, explained in his presentation.

“An important question is the optimal SRT dose. Retrospective comparisons have suggested that the biochemical progression-free survival (bPFS) is improved around 2.5% per grade dose intensification. But the results of well-conducted randomized trials were lacking until now,” he said.

The Swiss Association for Clinical Cancer Research (SAKK) 09/10 trial was an open-label, multicenter, randomized superiority trial comparing dose-intensified (70 Gy in 35 fractions) vs. conventional dose (64 Gy in 32 fractions) SRT to the prostate bed in 350 men with BCP after RP. BCP was defined as 2 consecutive PSA rises with the final PSA > 0.1 ng/mL or 3 consecutive rises. The primary endpoint was freedom from BCP, based on a PSA ≥0.4 ng/mL and rising or clinical progression.

At randomization, the median PSA level was 0.3 ng/mL. At the time of data cutoff (July 3, 2020), the median follow-up was 6.2 years and 138 BCP events had occurred. The estimated freedom from BCP rate at 6 years was 62.3% in the conventional 64-Gy dose group and 61.3% in the dose-intensified 70-Gy group.

After adjusting for stratification factors, no between-group difference was seen in freedom from BCP (hazard ratio [HR], 1.14; log-rank P=0.44, not a statistically significant difference). The finding was consistent across subgroups. There were also no significant differences regarding secondary efficacy endpoints of clinical progression-free survival, time to hormonal treatment, and overall survival.

Rates of late grade-2 and -3 genitourinary toxicity did not differ significantly between the 2 RT dose groups, but late grade-2 and -3 gastrointestinal toxicity was more common with dose-intensified RT.

Discussant for the study Dr. Richard Valicenti of the University of California Davis School of Medicine said, “The results are in line with those from another phase-3 trial conducted at Peking University that showed dose escalation to 72 Gy had no improvement in 4-year biochemical freedom from control vs. a 66 Gy regimen.”

“These data from SAKK and Peking University contrast with the outcomes of phase-3 trials for dose intensification for intact prostate. Unlike the SAKK and Peking University study, these trials had a radiographically identifiable target so it just might be that an intensified post-RP RT dose is better with a personalized target than not,” Dr. Valicenti commented.

Presented at the ASCO 2021 GuCS, 11 February 2021.

Join a Virtual Prostate Cancer Support Group

While we all must remain safe and socially distant due to COVID-19 restrictions, it is important for everyone to continue to monitor and address their health concerns, and stay connected to others. Us TOO has virtual prostate cancer support groups that continue to meet regularly and host guest speakers. These meetings can be accessed by phone or by internet, and can be attended from any location. For a list of groups, please visit:

www.ustoo.org/virtual-ustoo-support-groups

Final Result of TITAN
(Continued from page 2)

noted that the treatment effect on OS favored apalutamide in men with both high- and low-volume disease.

“Treatment with apalutamide also significantly prolonged second PFS on subsequent therapy and delayed onset of castration resistance,” Dr. Chi said. Median second PFS was 44.0 months with placebo and was not reached with apalutamide. Median time to castration resistance was 11.4 months in the placebo arm and was not reached in the apalutamide arm.

Health-related quality of life was also maintained with apalutamide throughout the study and did not differ from the placebo group. Safety was consistent with previous reports. “Importantly, the cumulative incidence of treatment-related falls, fracture, and fatigue was similar between groups, as was the cumulative incidence of treatment-related adverse events and serious adverse events,” Dr. Chi said.

An increased incidence of any-grade rash that was seen in the apalutamide group was expected but plateaued after about 6 months. “These results confirm the favorable risk-benefit profile of apalutamide,” Dr. Chi concluded.

Presented at the 2021 GuCS, Abstract 11

M.Dedge Hematology and Oncology
13 February 2021

Check Out the
Us TOO
Advanced Prostate Cancer Brochure at:
www.ustoo.org/AdvancedBrochure
Androgen Cycling Shows Promise in Castration Resistant Prostate Cancer
Results Comparable to Enzalutamide in Post-Abiraterone Setting

A treatment strategy based on the manipulation of testosterone levels was shown to be a potential aid for managing castration-resistant prostate cancer (CRPC), according to a randomized proof-of-principle trial.

“Following disease progression with abiraterone, treatment with bipolar androgen therapy (BAT) or enzalutamide led to a median progression-free survival (PFS) of 5.7 months (clinical or radiographic progression). A similar proportion of men in each treatment arm had at least a 50% reduction in baseline PSA level (PSA50 response), and overall survival (OS) did not differ significantly between the groups,” reported Samuel R. Denmeade, MD, of Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins in Baltimore, and colleagues.

“The median time to PSA progression (PSA-PFS) with enzalutamide increased from 3.8 months after abiraterone to 10.9 months after crossover from BAT (P=0.008). The results suggested BAT might have a role in altering the adaptive process that transforms hormone-sensitive prostate cancers (PCa) into CRPC,” they stated in the Journal of Clinical Oncology published online ahead of print in October 2020.

“I think the key result of this study is that sequencing testosterone and then anti-testosterone therapy, in this case enzalutamide, seems to be the ideal way to modify the adaptive process,” Denmeade told MedPage Today.

“A tumor seems to be sensitive and then adapts and becomes insensitive, so you switch treatments. As a therapeutic concept, BAT evolved from the long-recognized conversion of PCa from hormone-sensitive to hormone (castration)-resistant disease during prolonged androgen deprivation therapy (ADT). Therapeutic resistance to ADT is almost universal,” Denmeade told colleagues. Newer androgen-receptor (AR) inhibitors have become standard second-line therapy, but resistance increases with each line of AR-directed treatment.

“In response to low-androgen conditions created by antiandrogen therapy, PCa cells can develop resistance by means of adaptive upregulation of AR, the authors continued. Preclinical studies showed that the adaptive process can make PCa cells vulnerable to supraphysiologic testosterone levels. Episodic exposure to supraphysiologic can induce downregulation of AR and potential re-sensitization of cancer cells to androgen- ablative treatment. Preliminary clinical investigations demonstrated the feasibility and safety of BAT or rapid cycling between supraphysiologic and near-castrate serum levels of testosterone. The work formed the basis for the multicenter randomized phase II TRANSFORMER trial to compare BAT and enzalutamide in metastatic CRPC that had progressed on abiraterone but remained asymptomatic.

The study involved 195 men who received intramuscular testosterone once every 28 days or daily enzalutamide. Men in both arms were concurrently managed with testosterone suppression by surgical or medical methods. The primary endpoint was clinical or radiographic PFS. Crossover was allowed at disease progression. Secondary endpoints included OS, PSA50 and objective response rates, PFS from randomization through crossover (PFS2), safety, and quality of life (QoL). All analyses were based on the intention-to-treat principle and included all randomized patients.

Primary analysis showed a median PFS of 5.6 months with BAT and 5.7 months with enzalutamide (HR 1.13, 95% CI 0.82-1.57). At data cutoff a year later, median PFS was identical in the 2 arms (5.7 months, HR 1.4, 95% CI 0.83-1.55). A prespecified analysis showed PFS did not differ by duration of response to prior abiraterone (<6 months vs. ≥6 months) but that a shorter response numerically favored BAT and a longer response favored enzalutamide.

Median OS did not differ significantly but favored BAT (32.9 vs. 29.0 months). Consistent with the PFS data, shorter PFS with abiraterone favored BAT and longer PFS with prior abiraterone favored enzalutamide.

PSA50 response rate was similar in the two treatment arms (28.2% with BAT, 25.5% with enzalutamide). The time to first PSA progression was short in both groups but favored enzalutamide (3.8 vs. 2.8 months, HR 1.51, 95% CI 1.06-2.16, P=0.02).

At clinical or radiographic progression, men could cross over to the opposite therapy, after a 28-day washout period. Crossover was limited to patients who remained asymptomatic but excluded patients who had pain-related clinical progression. The authors reported that 37 (39.3%) men in the BAT arm crossed over to enzalutamide and 48 (47.6%) crossed over from enzalutamide to BAT. Crossover was done in 90% of cases due to radiographic progression. In general, patients who crossed over from enzalutamide to BAT fared better as compared with the opposite crossover:

- OS: 37.1 vs. 30.2 months
- Objective response: 28.6% vs. 7.3% (P=0.03)
- PSA50 (unverified): 77.8% vs. 21.3%
- PSA-PFS: 10.9 vs. 1.1 months (P=0.0001)
- PFS2: 28.2 vs. 19.6 months (P=0.015)

Adverse event (AE) rates were similar in both treatment arms and most were grade 1/2. Rates of grade 3/4 AEs were 28.1% with BAT and 35.1% with enzalutamide. Serious AEs occurred in 19.1% of the BAT arm and 20.6% of the enzalutamide group. More men discontinued BAT because of AEs as compared with enzalutamide (9.0% vs. 5.2%).

Enrollment has already begun for a follow-up trial to evaluate multiple cycles of alternating testosterone extremes (supraphysiologic and castrate or near-castrate levels). BAT might also have a role in conjunction with immunotherapy as preliminary data have suggested a potential priming effect of BAT to make PCa cells more responsive to immunotherapy.

“We’re at a point where we’re trying to understand the best way to use this treatment,” said Denmeade. “We’re still working on how to incorporate testosterone into the treatment paradigm. We think it has the potential to augment and extend the response.” MedPage Today 23 February 2021
CCR Score After RT (Continued from page 3)

fraction, with 84% getting or exceeding 79.2 Gy. About half the men (53%) had ADT after RT.

Genetic testing was done on stored biopsy samples years after men were treated. Half of them were below the CCR threshold of 2.112. For those above it, the 10-year risk of metastasis was 25.3%. CCR outperformed CCP alone, CAPRA alone, and NCCN risk groupings for predicting metastasis risk after RT.

“People are going to be very uncomfortable with these findings because it’s been ingrained in our heads for the past 20-30 years that you must use hormone therapy with high-risk PCs, and you should use hormone therapy with intermediate risk,” Tward said. “It took me a while to believe my own data, but we have used this test for several years to help men decide if they would like to have hormone therapy after RT. Patients clearly benefit from this information,” he stated.

“Though this validation study was ‘successful,’ additional research is needed,” according to study discussant Richard Valicenti, MD, of the University of California, Davis.

“Widespread acceptance for routine use faces challenges since no biomarker has been prospectively tested or shown to improve long-term outcome,” Valicenti said.

“Clearly, the CCR score may provide highly precise, personalized estimates and justifies testing in tiered and appropriately powered noninferiority studies according to NCCN risk groups. We eagerly await the completion and reporting of such trials so that we have a more personalized approach to treating men with PCs.”

Presented at the 2021 GuCS, Abstract 195.

Medscape Medical News 15 February 2021

UK Dogs with a Nose for PCa (Continued from page 1)

Furthermore, the trained ANN identified regions of interest in the GC-MS data, informed by the canine diagnoses.

Dr. Claire Guest, co-founder, and Chief Scientific Officer of Medical Detection Dogs, described the findings as “hugely exciting.”

“This additional information could support the PSA and would provide earlier, non-invasive, sensitive detection of clinically aggressive prostate cancers that would most benefit from early diagnosis, simply from a urine sample. This has enormous potential and, in time, the ability of the dogs’ nose could be translated to an electronic device.”

Professor Karol Sikora, CMO Rutherford Health, who comments on oncology issues for Medscape UK, tweeted: “Really exciting findings out from @MedDetectDogs which show their dogs can detect the most aggressive forms of PCs with high specificity & sensitivity. It’s significant as early diagnosis is so important. The dogs Midas and Florin deserve a treat!”

Reference


This article was adapted from Univadis, part of the Medscape Professional Network.

Medscape News UK
19 February 2021

Video is available of the first webinar in our 2021 series, What is Right for Me in My Prostate Cancer Treatment?, a discussion on the topic of Bone Health and Nutrition, recorded on February 25th.

Access the Video at:

www.ustoo.org/ustoo-video

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QUESTION FROM PROSTATE CANCER SURVIVOR:
My urologist has recommended that I use an injection in my penis to get erections because nothing else has worked. I am really not keen to do this – please help!

RESPONSE FROM DR. ANNE KATZ:
I have yet to meet a man who is excited about penile injections ... but they WORK! What I have found is that with good education, a demonstration, and test dose, most men find that (a) the injection itself is not terribly painful, and (b) the proof is in the pudding, so to speak, and with evidence of reward, using the injection gets easier over time.

Many men have no idea what this entails. I have been asked if the needle goes into the head of the penis (no, it goes into the side of the shaft) or into the opening of the urethra (once again no). There are videos available on the internet that show how this is done and this can be helpful, but I think that a good education session with a knowledgeable health care provider, who can answer questions and calm the nerves, is important. I also like the partner of the man to be present for the education session and test dose because they often find themselves involved, especially if the man has a big abdomen and can’t see the “target!”

The important thing is not to feel pressured to do this, either by a medical practitioner or a partner. You have to get used to the idea and it may or may not be right for YOU.

Watch Dr. Katz’s 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 at: 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:
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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.

**Current Challenges in Treatment of Patients with Metastatic Prostate Cancer**

*Presentation by Himisha Beltran, MD, Dana-Farber Cancer Institute*

At PCF’s 27th Annual Scientific Retreat, held virtually in late 2020, Dr. Himisha Beltran presented an update on research into treatments for metastatic prostate cancer.

Despite years of research, many recent advances, and reports of “exceptional responders,” metastatic prostate cancer kills more than 30,000 men in the US each year, and many more globally. Dr. Beltran described one unique approach to researching the problem: the PCF N=1 Natural History Study. This is a highly collaborative, multi-institutional study that will facilitate data collection on patients with specific mutations in their tumors treated with investigational cancer therapies or who exhibit “exceptional” (read: exceptionally good or exceptionally bad) responses to standard of care treatments. With enough data, researchers may be able to uncover patterns that they would not see by looking at just a few patients, and use this information to design new precision medicine clinical trials and treatments.

Also crucial to attacking metastatic prostate cancer are biomarkers: characteristics of cancer that can be measured and used to describe the extent and severity of the cancer, predict patient response and/or to guide choice of therapy. Such is the crux of precision medicine: identifying the right patient (using biomarkers) for the right drug at the right time. One important and promising biomarker is prostate-specific membrane antigen (PSMA), found on the surface of prostate cancer cells. Many emerging therapies targeting PSMA, using a variety of approaches, are working their way through clinical trials. (Note: since Dr. Beltran’s talk, [https://www.pcf.org/blog/highly-sensitive-new-type-of-prostate-cancer-scan-gains-fda-approval](https://www.pcf.org/blog/highly-sensitive-new-type-of-prostate-cancer-scan-gains-fda-approval) PSMA PET imaging was approved by the FDA).

Finally, resistance to androgen therapy is a hallmark of many metastatic tumors. Researchers are working to identify the underlying mechanisms of this and to design new treatments (or combinations of treatments). As just one example, early phase clinical trials of drugs targeting a specific molecule on the surface of neuroendocrine prostate cancer (a highly aggressive form) are underway. In the next 5 to 10 years, Dr. Beltran envisions that we will know how to better use existing biomarkers to assess patients, and we will also have new biomarkers. New targets for drugs, and new drugs with novel mechanisms, will get us that much closer to the goal of zero deaths from prostate cancer.

*For more information visit [www.pcf.org](http://www.pcf.org), email info@pcf.org, or call 1-800-757-2873.*