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**Statins Tied to Better Outcomes in Men With Prostate Cancer Starting Androgen Deprivation**

Statin therapy is associated with improved outcomes in men initiating androgen-deprivation therapy (ADT) for prostate cancer (PCa), new research suggests.

“Interest in statins as a potential chemopreventive agent has grown, and there exist biological rationale, and laboratory and clinical data supporting our findings,” the study team writes in a manuscript published online in *European Urology*.

Observational studies examining statin use and PCa risk have shown a modest but statistically significant overall risk reduction and a more clinically meaningful reduction in advanced or high-grade disease. Whether statin use at the time of primary treatment is associated with improved outcomes is unclear.

To evaluate the association between statin use and outcomes, Dr. Robert Hamilton with Princess Margaret Cancer Center in Toronto, Canada, and colleagues did a post hoc secondary analysis of a randomized controlled trial of men initiating intermittent androgen deprivation (IAD) versus continuous ADT.

The 1,364 men in the trial had PSA levels >3 ng/mL more than one year after primary/salvage radiotherapy (RT). The 585 (43%) statin users were younger than non-statin users (72.7 vs. 73.8 years, P=0.001) and were less likely to have PSA >15 ng/mL (20 vs. 25%, P=0.04, *a statistically significant difference*).

After adjusting for potential confounders, statin therapy was associated with a 36% reduction in risk of death (hazard ratio [HR], 0.64; 95% confidence interval [CI], 0.53-0.78) and a 35% reduction in risk of PCa-specific death (HR, 0.65; 95% CI, 0.48-

(Continued on page 7)

**New AI Tool Analyzes MRI Information to Generate Precision Prostate Cancer Treatment**

A new artificial intelligence (AI) tool that analyzes vast amounts of medical information, including MRI data, earned recent praise for improving prostate cancer (PCa) care, according to the authors of a recent study.

Case Western Reserve researchers and a handful of top medical centers teamed up to develop and validate the platform, known as RadClip. They tested it on MRI scans taken from nearly 200 patients treated across the Cleveland Clinic, Mount Sinai Hospital, University Hospitals, and the Hospital of the University of Pennsylvania.

In addition to accurately predicting the risk of cancer returning, it also spotted subtle differences inside and outside tumor regions on preoperative MRI scans. With further validation, researchers believe RadClip could become a valuable treatment decision tool.

“We’re bringing together and connecting a variety of information, from radiologic scans like MRI to digitized pathology specimen slides and genomic data, for providing a more comprehensive characterization of the disease,” senior author Anant Madabhushi, PhD, director of Case Western’s Center for Computational Imaging and Personalized Diagnostics, said in a statement.

The team also noted their platform outperformed well-known prognostic tools, including Cancer of the Prostate Risk Assessment scoring and the genomic based Decipher Prostate Cancer Test.

(Continued on page 5)
Race Decisional Regret and Prostate Cancer Beliefs: Identifying Targets to Reduce Racial Disparities in Prostate Cancer
DeWitt-Foy ME, Gam K, Modlin C, Kim SP, Abouassaly R

**J Urol** 205: 426-433, 2021

**Purpose:** African American men are more likely to be diagnosed with, die of and experience decisional regret about their prostate cancer (PCa) than non-African American men. Although some clinical discrepancies may be attributed to genetic risk and/or access to care, explanations for racial discrepancies in decisional regret remain largely speculative. We aim to identify sources of PCa decisional regret with a focus on racial disparities.

**Materials and Methods:** A cohort of 1,112 men with localized PCa treated at the Cleveland Clinic from 2010-2016 were matched by race, Gleason score, treatment (external beam radiation, brachytherapy, radical prostatectomy, active surveillance), PSA at diagnosis, age at treatment and time since treatment. All men received 4 surveys, including: the Expanded PCa Index Composite (EPIC) 26, the Decisional Regret Scale, our novel Prostate Cancer Beliefs Questionnaire and a modified EPIC demographics form. Descriptive and comparative statistics and multivariable logistic regression were used to compare survey outcomes by race and treatment.

**Results:** Of 1,048 deliverable surveys 378 (36.1%) were returned. African American men had worse decisional regret than non-African American men, even after adjusting for relevant covariates (Odds Ratio [OR] 2.46, p<0.0001, a statistically significant difference). African American men also had higher PCa Beliefs Questionnaire medical mistrust and masculinity scores, both of which predicted worse decisional regret independent of race (1.42 and 1.35, p=0.0001, respectively, a statistically significant difference).

**Conclusions:** African American men suffer worse decisional regret than non-African American men, which may be partially explained by higher medical mistrust and concerns about masculinity as captured by the PCa Beliefs Questionnaire. This novel survey may facilitate identifying targets to reduce racial disparities in PCa.

A Urine Exosome Gene Expression Panel Distinguishes Between Indolent and Aggressive Prostate Cancers at Biopsy
Kohaar I, Chen Y, Banerjee S, et al.

**J Urol** 205: 420-425, 2021

**Purpose:** Prostate cancer (PCa) is predominantly indolent at diagnosis with a small fraction (15 to 25%) representing aggressive subtype (Gleason score 7-10), which is prone to metastatic progression. It is critical to explore noninvasive assays for the early detection of this aggressive subtype, when it still can be treated effectively. Additionally, there is an emerging need to develop markers that perform equally well across races, as racial differences in the prevalence and mortality of prostate cancer has become evident.

**Materials and Methods:** First catch, non-digital rectal examination urine specimens were collected from patients undergoing diagnostic biopsy. Total RNA was extracted from urinary exosomes and a quantitative expression assay protocol using droplet digital polymerase chain reaction (PCR) was developed for detection of candidate genes in exosomal mRNAs from urine. Clinical performance for the gene expression assay was evaluated to predict high grade cancer (Gleason score 7-10) from low grade cancer (Gleason score 6) and cancer negative cases at biopsy. Assay performance was examined in combination with standard of care (SOC) to determine improvement in model prediction.

**Results:** In a racially diverse patient cohort a 2-gene panel (PCA3, PCGEM1), in combination with SOC variables, significantly improved the prediction of high grade cancer at diagnosis compared to SOC variables alone (area under the curve 0.88 vs. 0.80, respectively, p=0.016, a statistically significant difference). Decision curve analysis showed that there is a benefit of adopting the gene panel for detection of high grade cancer vs. SOC alone.

**Conclusions:** This study highlights the potential for developing broadly applicable PCa diagnostic biomarker panels for aggressive PCa using our novel urine exosome gene expression assay platform.

Check Out the Us TOO Advanced Prostate Cancer Brochure at: www.ustoo.org/AdvancedBrochure
We love our new dog, and we are so grateful he came into our lives recently that we actually named him “Grazie” (Italian for “Thank you,” or “gratitude”). I am not kidding. Apart from the teething (aka “odontiasis” in nerdy medical vernacular) or the chewing of my running shoes, or selectivity biting my big toe when I get out of bed... well, he is adorable. However, I now look at this dog differently thanks to this column and clinical research.

Now when I stare at him, I decided that there is a decent chance that his future is my future, or my future is his future to some degree. Studies conducted over many years suggested that as the owner goes, so does the dog, or vice versa in many cases. What does that mean? Well, it appears, in terms of lifestyle choices, if a dog has an increased risk of a medical condition or is diagnosed with something related to lifestyle, then the owner has an increased risk of that same condition, and vice versa.

For example, this also includes significant weight gain and all the risks that come with that. I find that dogs are now an extension of human health, meaning when many folks get a dog, then they decide to walk more or move more, and it can be healthy, not just for the owner, but also the dog. And, when someone improves their diet, then it appears the diet of their dog also tends to improve. Yet, the antithesis also has merit, suggesting when a person does not want to walk their dog or improve the diet of their pet, then the risk of problems increases in the owner.

A new study looked at over 208,000 dog-owner pairs from Sweden. They simply found that owners of dogs with diabetes were associated with a greater risk of (the owner) developing type 2 diabetes. Dogs can improve mental and/or physical health based on past studies. Perhaps we need to spend a little more time reflecting on the fact that getting a dog to improve our own health, and that of the dog, is not such a bad thing.

So, if your kids do not want to walk the new dog anymore because it robs them of cell or computer time, perhaps that could be part of a bigger problem. If you are trying to get outside more, or move more, and need some motivation, then I ask you, “why not get a dog?”

Now, I am doing my best to walk Grazie at least twice a day because if I do not, then what does this say about my, or Grazie’s future health? Oh, by the way, just in case you were wondering, these same dog researchers from Sweden also looked at over 123,000 cat owners and found no health associations regarding diabetes. It seems cats are more independent (less interdependent) and usually just get their way... probably because they are so “purr-suasive.” Don’t worry, I am keeping my day job!

Reference:

Detection Rate of Prostate Specific Membrane Antigen Tracers for Positron Emission Tomography/Computerized Tomography in Prostate Cancer Biochemical Recurrence: A Systematic Review and Network Meta-Analysis
J Urol 205: 356-369, 2021

Purpose: Restaging of prostate cancer (PCa) in men with biochemical recurrence (BCR) after radical treatment remains challenging since current imaging modalities are suboptimal. To date, prostate specific membrane antigen (PSMA) positron emission tomography (PET)/computerized tomography (CT) seems to represent a very promising diagnostic tool in this setting. We evaluated the detection rate of several PET/CT PSMA based tracers in the restaging of PCa in patients with BCR.

Materials and Methods: According to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement, a systematic search was performed across MEDLINE®, Embase® and Web of Science™. PICOS criteria consisted of: P: patients with BCR after radical prostatectomy (RP) and/or radiation therapy (RT) as primary treatment; I: studies using gallium-68 (Ga)-PSMA-11, Ga-PSMA inhibitor for imaging and therapy, Ga-trishydroxyipridine-GaPSMA, copper-64 (Cu)-PSMA-617, fluorine-18 (18F)-DCFPyL or 11F-PSMA-1007; C: no control group or PET/CT comparative studies; O: patient specific overall detection rate; and S: retrospective/prospective studies. A meta-analysis of proportions and a network meta-analysis were performed. Heterogeneity was assessed using Cochran Q and I2 statistics. Quality was assessed by QUADAS-2. Funnel plots and Egger test were used for publication biases.

Results: A total of 43 studies including 5,832 men were identified and included in the analysis. An overall detection rate of 74.1% (95% Confidence Interval [CI] 69.2-78.5%) was found, with no differences between tracers. The overall detection rates were 33.7, 50.0, 62.8, 73.1 and 91.7% in PSA subgroups of <0.2 ng/mL, 0.2 to 0.49 ng/mL, 0.50 to 0.99 ng/mL, 1.0 to 1.99 ng/mL, and 2.0 ng/mL or greater, respectively. No difference between tracers was found per PSA doubling time or PSA velocity. No tracer proved superior to the others through network meta-analysis. High heterogeneity and inconsistency were found across all analyses. Included studies showed a low risk of bias.

Conclusions: PSMA PET/CT for PCa restaging in men with BCR achieves best detection rates (over 70%) if PSA is <1 ng/mL. At lower levels, the detection rate of PSMA PET/CT is lower (33.7% for PSA <0.2 ng/mL and 50% for PSA 0.2 to 0.49 ng/mL), despite being better than “older” tracers such as choline based PET or CT/bone scintigraphy. Furthermore, no PSMA tracer can be currently considered superior to others. Further studies are needed to better define the diagnostic performance and role of these imaging techniques.
Higher Coffee Intake May Reduce Risk for Prostate Cancer

Increased coffee consumption is associated with a reduced risk for prostate cancer (PCa), according to a review and meta-analysis published online in BMJ Open.

Xiaonan Chen, from Shengjing Hospital of China Medical University, and colleagues conducted a systematic review with a meta-analysis of cohort studies to examine the association between coffee consumption and PCa risk. Data were included from 16 prospective cohort studies with 1,081,586 cohort members and 57,732 cases of PCa.

The researchers observed a significant association between higher coffee consumption and a lower risk for PCa. The pooled relative risk was 0.91 (95% confidence interval [CI], 0.84-0.98) for the highest vs. the lowest category of coffee consumption. A significant linear trend was seen for the association (P =0.006), with a pooled relative risk of 0.988 (95% CI, 0.981-0.995) for each increase of 1 cup of coffee per day. The pooled relative risks were 0.93 (95% CI, 0.87-0.99), 0.88 (95% CI, 0.71-1.09), and 0.84 (95% CI, 0.66 to 1.08) for localized, advanced, and fatal PCa, respectively.

“This study suggests that increased coffee consumption may be associated with a reduced risk of PCa,” the authors write. “If the association is further proved to be a causal effect, men might be encouraged to increase their coffee consumption to potentially decrease the risk of PCa.”

Pan-AKT Inhibitor Capivasertib with Docetaxel and Prednisolone in Metastatic Castration-Resistant Prostate Cancer: A Randomized, Placebo-Controlled Phase II Trial (ProCAID)


Purpose: Capivasertib is a pan-AKT inhibitor. Preclinical data indicate activity in metastatic castration-resistant prostate cancer (mCRPC) and synergism with docetaxel.

Patients and Methods: ProCAID was a placebo-controlled randomized phase II trial in mCRPC. Men received up to ten 21-day cycles of docetaxel (75 mg/m² intravenous, day 1) and prednisolone (5 mg twice daily, oral, day 1-21) and were randomly assigned (1:1) to oral capivasertib (320 mg twice daily, 4 days on/3 days off, or day 2 each cycle), or placebo, until disease progression.

Results: One hundred and fifty men were enrolled. Median cPFS was 7.0 (95% Confidence Interval [CI], 6.3-8.3) and 6.7 months (95% CI, 5.5-7.4) with capivasertib and placebo respectively (hazard ratio [HR], 0.92; 80% CI, 0.73-1.16; one-sided P = 0.32).

Conclusion: Adding capivasertib to chemotherapy did not extend cPFS in mCRPC irrespective of PI3K/AKT/PTEN pathway activation status. Grade III-IV adverse events were equivalent between arms (62.2%). Common capivasertib-related adverse events were diarrhea, rash, fatigue, and nausea.

Risk Prostate Cancer Trial & Whole Pelvis Radiotherapy for High-Risk Prostate Cancer

Irradiating the whole pelvis rather than just the prostate reduces the likelihood of recurrence in men with high-risk locally advanced prostate cancer (PCa), according to a randomized controlled trial. Results from the trial, called POP-RT, were reported at the 2020 European Society for Radiology and Oncology (ESTRO) Online Congress.

“A question that has been plaguing the radiation oncology community for the last 3 or 4 decades is, ‘Should the pelvic nodes be treated prophylactically in men with high-risk PCa?’” said Vedang Murthy, MD, of Tata Memorial Centre in Mumbai, India, who presented the POP-RT trial at the meeting.

“A lot of effort has gone into trying to answer this question,” he added. Unfortunately, the question has remained unanswered, as neither the RTOG 9413 trial nor the French GETUG-01 trial showed clear evidence of benefit.

To gain some insight, Dr. Murthy and colleagues conducted the POP-RT trial (NCT02302105). The study’s final analysis included 222 men with locally advanced PCa who had node-negative disease based on MRI and PSMA PET, but had a high risk for occult pelvic nodal involvement (≥20%) according to the Roach formula. The median nodal risk for the trial population was 37.8%.

The men were randomized to daily image-guided intensity-modulated radiotherapy (IMRT) to the prostate (68 Gy in 25 fractions to the gland and seminal vesicles) or to the whole pelvis (the former plus 50 Gy in 25 fractions to the pelvic nodes as a simultaneous integrated boost, including the bilateral common iliac, internal and external iliac, presacral, and obturator node groups). All men also received at least 2 years of androgen-deprivation therapy (ADT).

Efficacy and Toxicity

At a median follow-up of 68 months, the 5-year rate of biochemical failure (BCF)-free survival, the trial’s primary endpoint, was superior with whole-pelvis RT (WPRT), at 95.0%, vs. prostate-only RT (PORT), at 81.2% (hazard ratio [HR], 0.23; P <0.0001), Dr. Murthy reported.

Disease-free survival (DFS) was better in the WPRT group than in the PORT group (89.5 vs. 77.2%; HR, 0.40; P = 0.002), and the same was true for distant metastasis-free survival (MFS, 95.0 vs. 87.9%; HR, 0.40; P = 0.002).

“Unadjusted DFS was inferior in the WPRT group,” he said. “However, after adjusting for several factors, including the bilateral common iliac, internal and external iliac, presacral, and obturator node groups, all men also received at least 2 years of androgen-deprivation therapy (ADT).”

Conclusion: Adjuvant WPRT reduced BCF, DFS, and MFS compared with PORT. Applying these data to the clinical setting will require extensive validation.
New AI Tool (Continued from page 1)

“Genomic-based tests cost several thousand dollars and involve destructive testing of tissue,” Madabhushi added. “Prognostic predictions from an MRI scan can provide a non-invasive method for making both short-term and long-term treatment decisions.” Among PCa patients undergoing surgery, identifying those who face the highest risk of recurrence and disease-specific mortality is of the utmost importance in determining who may need additional therapy.

The data generated from this AI tool can do just that and help surgeons make important decisions, including how much tissue to remove, while also assisting oncologists in assessing whether a patient will require radiation therapy or chemotherapy.

“This tool can help urologists, oncologists and surgeons create better treatment plans so that their patients can have the most precise treatment,” explained Lin Li, a doctoral student in Case Western Reserve’s Biomedical Engineering Department. The NIH, U.S. Department of Veterans Affairs and Department of Defense all provided funding for this project.

HealthImaging
14 January 2021

Cost Effectiveness of Prostate RT for Men with Newly Diagnosed Low Burden Metastatic Prostate Cancer
JAMA Netw Open 4: e2033787, 2021

Key Points
Question: In men with newly diagnosed, low-volume metastatic PCa, is the addition of prostate RT to ADT cost-effective?

Findings: In this economic evaluation using data from a simulated cohort of 10,000 men with low-volume metastatic PCa, a microsimulation model found that the addition of prostate RT to standard-of-care ADT was associated with reduced net costs and improved quality-adjusted life-years (QALYs) and was, therefore, a dominant cost-effective strategy.

Meaning: These findings support the incorporation of prostate RT as part of initial treatment for men with low-volume metastatic PCa.

Abstract
Importance: Prostate RT (PRT) is a treatment option in men with low-volume metastatic PCa based on the results of the Systemic Therapy in Advancing or Metastatic PCa: Evaluation of Drug Efficacy Arm H (STAMPEDE-H) trial. However, the cost-effectiveness of this treatment remains unaddressed.

Objective: To assess the cost-effectiveness of PRT when added to ADT for men with low-volume metastatic hormone-sensitive PCa (mHSPC).

Design, Setting, and Participants: This economic evaluation used microsimulation modeling to evaluate the cost-effectiveness of adding PRT to ADT. A simulated cohort of 10,000 men with low-volume mHSPC was created. Data from men with low-volume mHSPC were extracted and analyzed from January 18, 2019 through July 4, 2020. Transition probabilities were extracted from the STAMPEDE-H study. Health states included stable disease, progression, second progression, and death. Individual grade 2 or higher genitourinary and gastrointestinal toxic events associated with PRT were tracked. Univariable deterministic and probabilistic sensitivity analyses explored uncertainty with regard to the model assumptions. Health state utility estimates were based on the published literature.

Exposures: The combination of ADT and PRT using regimens of 20 fractions and 6 weekly fractions.

Main Outcomes and Measures: Outcomes included net QALYs, costs in US dollars, and incremental cost-effectiveness ratios. A strategy was classified as dominant if it was associated with higher QALYs at lower costs than the alternative and dominated if associated with fewer QALYs at higher costs than the alternative.

Results: For the base case scenario of men 68 years of age with low-volume mHSPC, the modeled outcomes were similar to the target clinical data for overall survival, failure-free survival, and rates of PRT-related toxic effects. The addition of PRT was a dominant strategy compared with ADT alone, with a gain of 0.16 QALYs (95% Confidence Interval [CI], 0.15-0.17 QALYs) and a reduction in net costs by $19,472 (95% CI, $23,096 to $37,362) at 37 months of follow-up and a gain of 0.81 QALYs (95% CI, 0.73-0.89 QALYs) and savings of $30,229 (95% CI, $23,096 to $37,362) with lifetime follow-up.

Conclusions and Relevance: In the economic evaluation, PRT was a dominant treatment strategy compared with ADT alone. These findings suggest that addition of PRT to ADT is a cost-effective treatment for men with low-volume mHSPC.

POP-RT Trial (Continued from page 4)

0.35; P = 0.01). Overall survival (OS) was 92.5% with WPRT and 90.8% with PORT, a nonsignificant difference (P = 0.83).

At the time of BCF, disease recurred in the regional pelvic nodes (with or without distant metastases) in just 1 patient in the WPRT group, compared with 15 patients in the PORT group. Recurrences at other sites were similar across the groups.

The WPRT group had a significantly higher rate of late genitourinary toxicity (17.7 vs. 7.5%; P = 0.03) but not late gastrointestinal toxicity (6.5 vs. 3.8%; P = 0.4). There were no grade 4 toxicities, and the groups were similar on patient-reported outcomes.

Explaining the Results
Several factors may explain why the POP-RT trial was clearly positive for WPRT, whereas the RTOG 9413 and GETUG-01 trials were not, according to Dr. Murthy. “We had a much higher-risk group,” he elaborated (with 55% of men having a nodal risk exceeding 35%), and PSMA PET was used in the workup in the large majority of patients, improving diagnostic sensitivity.

(Continued on page 8)
Clinical Utility of 4Kscore®, ExosomeDx™ and Magnetic Resonance Imaging for the Early Detection of High-Grade Prostate Cancer

de la Calle CM, Fasulo V, Cowan JE, et al.

*J Urol* **205**: 452-460, 2021

**Purpose:** We aimed to evaluate 4Kscore® and ExosomeDx™ with multiparametric magnetic resonance imaging (mp-MRI) in the detection of high-grade prostate cancer (PCa) and number of biopsies avoided.

**Material and methods:** Patients had 1 liquid biomarker test with or without mp-MRI. High grade PCa was defined as Gleason grade (GG) group 2 or greater. The overall number of avoided biopsies (with GG 1 or less), and number of missed GG ≥2 cancer among the biopsied patients, were determined.

**Results:** Of the 783 men in the overall cohort 419 (53.5%) underwent biopsy. 4Kscore and ExosomeDx scores higher than the manufacturers’ cut point were associated with PI-RADS™ scores 3 to 5 and GG ≥2 PCa. Limiting biopsy to the men with liquid biomarker scores above the manufacturers’ cut point would have resulted avoiding 29.5 to 39.9% unnecessary biopsies overall, while missing 4.0 to 4.8% ≥GG 2 PCa in the biopsy group. Screening algorithms with up-front liquid biomarker testing followed by mp-MRI if the biomarker was above the manufacturers’ cut point, then followed by biopsy if the mp-MRI was positive or if 4Kscore ≥20 or ExosomeDx ≥19 would have missed 4.8% to 5.6% of ≥GG 2 PCa in the biopsy group while avoiding 39.4 to 43.0% biopsies and 29.5 to 39.9% mp-MRI overall. Similar algorithms with up-front mp-MRI followed by liquid biomarker testing for negative mp-MRI would have missed 2.4% of GG ≥2 PCa in the biopsy group but only avoided 17.2 to 19.3% biopsies overall.

**Conclusions:** Screening algorithms with up-front liquid biomarker testing followed by mp-MRI and biopsy at certain biomarker thresholds could reduce unnecessary biopsies, mp-MRI and overdetection of GG 1 PCa.

Greater Subcutaneous Fat Improves mCRPC Treatment Response

Greater subcutaneous adiposity is associated with improved response to chemotherapy combined with androgen deprivation therapy (ADT) among men with metastatic castration-resistant prostate cancer (mCRPC), according to data presented at the European Society for Medical Oncology (ESMO) Virtual Congress 2020.¹

In a study of 58 men with mCRPC, Andrew E. Hahn, MD, of The University of Texas MD Anderson Cancer Center in Houston, TX and colleagues found men who had an objective response to chemotherapy plus ADT had a significantly higher subcutaneous adipose tissue (SAT) index than those who had no response (87.9 vs. 62.7 cm²/m², P = 0.01). Visceral adipose tissue, body mass index, and skeletal muscle mass were not significantly associated with response.

All men had participated in a clinical trial in which they had received a combination of abiraterone, apalutamide, cabazitaxel, and cabazitaxel. Investigators assessed body composition at the level of L3.

(Continued on page 8)

Circulating Tumor Cells May Predict Response to Radium-223 in Metastatic CRPC

Circulating tumor cells (CTCs) may be useful as biomarkers of response to radium-223 treatment for metastatic castration-resistant prostate cancer (mCRPC), according to study findings presented at the American Society for Radiation Oncology (ASTRO) 2020 Virtual Annual Meeting.

The study enrolled 22 men with mCRPC who had a median age of 71 years. Of these, 8 men (36%) had fewer than 6 metastases, 7 (32%) had 6-20 metastases, and 7 (32%) had >20 metastases. All progressed to mCRPC on androgen deprivation therapy (ADT), and 5 men (23%) previously received docetaxel.

The median overall survival was 18.4 months, according to Keisuke Otani, MD, PhD, of Massachusetts General Hospital in Boston, MA, who presented study findings.

Investigators measured CTCs using 2 methods: CellSearch® to enumerate CTCs and a prostate CTC expression assay based on polymerase chain reaction to perform RNA expression analyses. They used the assay to arrive at a CTC RNA score.

Pretreatment CTC counts of 5 CTCs or more per 7.5 mL of blood correlated with worse survival compared with less than 5 CTCs per 7.5 mL (median 10.0 vs. 29.2 months), Dr. Otani and colleagues found. An elevated pretreatment digital CTC RNA score of 20 or higher calculated using the CTC RNA expression assay also was associated with worse survival compared with a score of less than 20 (median 11.6 vs. 29.2 months). The pretreatment digital CTC RNA score was significantly higher among men who had demonstrated disease progression on bone scans at 6 months compared with those with stable or decreased disease burden.

Presented at the 2020 ASTRO Virtual Annual Meeting, Abstract 3222

*Renal & Urology News* 27 October 2020

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>
Prostate Radiotherapy with Adjuvant Androgen Deprivation Therapy (ADT) Improves Metastasis-Free Survival Compared to Neoadjuvant ADT: An Individual Patient Meta-Analysis


*J Clin Oncol* 39: 136-144, 2021

**Purpose:** Influence of sequencing androgen deprivation therapy (ADT) and radiotherapy (RT) on outcomes in prostate cancer (PCa) remains unclear. Here we evaluate the optimal sequencing of ADT with prostate-directed RT in localized PCa.

**Methods:** MEDLINE (1966-2018), Embase (1982-2018), ClinicalTrials.gov, and conference proceedings (1990-2018) were searched to identify randomized trials evaluating the sequencing, but not duration, of ADT with RT. Two randomized phase III trials were identified, and individual patient data were obtained: Ottawa 0101 and NRG Oncology’s Radiation Therapy Oncology Group (RTOG) 9413. Ottawa 0101 randomly assigned men to neoadjuvant or concurrent vs. concurrent or adjuvant short-term ADT. RTOG 9413, a 2 × 2 factorial trial, included a random assignment of neoadjuvant or concurrent vs. adjuvant short-term ADT. The neoadjuvant or concurrent ADT arms of both trials were combined into the neoadjuvant group, and arms receiving concurrent or adjuvant ADT were combined into the adjuvant group. The primary end point of this meta-analysis was progression-free survival (PFS). Statins and ADT

(Continued from page 1)

0.87, P=0.004, a statistically significant difference). As an exploratory endpoint, the researchers examined whether statin use was associated with time off ADT among 681 men in the IAD group. They found that statin users in the IAD group had longer time off treatment (P=0.06, not a statistically significant difference). The authors say limitations of their study include the potential for residual confounding between statin users and nonusers, and confounding by indication. They conclude, “This study supports the benefit of statins in men on ADT. A prospective trial is warranted.”

*Reuters Health* 11 January 2021

**Results:** The median follow-up was 14.9 years. Overall, 1,065 men were included (531 neoadjuvant and 534 adjuvant). PFS was significantly improved in the adjuvant group (15-year PFS, 29 vs. 36%, hazard ratio [HR], 1.25 [95% Confidence Interval [CI], 1.07 to 1.47], P = 0.01, a statistically significant difference). Biochemical failure (subdistribution HR [sHR], 1.37 [95% CI, 1.12 to 1.68], P = 0.002), distant metastasis (sHR, 1.40 [95% CI, 1.00 to 1.95], P = 0.04), and metastasis-free survival (HR, 1.17 [95% CI, 1.00 to 1.37], P = 0.050) were all significantly improved in the adjuvant group. There were no differences in late grade ≥ 3 gastrointestinal (2 vs. 3%, P = 0.33) or genitourinary toxicity (5 vs. 5%, P = 0.76) between groups.

**Conclusion:** The sequencing of ADT with prostate-directed RT has significant association with long-term PFS and MFS in localized PCa. Our findings favor use of an adjuvant over a neoadjuvant approach, without any increase in long-term toxicity.
Subcutaneous Fat
(Continued from page 6)

on baseline computed tomography (CT) scans at trial registration. Of the 58 men, 12 had an objective response to treatment and 46 did not.

Dr. Hahn and his coauthors cited previous studies suggesting that adiposity may improve clinical outcomes in men with CRPC. These include a study by Jong Soo Lee, MD, and colleagues published in The Journal of Urology in 2018. Their evaluation of data from 282 men found that a SAT index of 39.9 cm²/m² or greater at CRPC diagnosis had higher progression-free and cancerspecific survival rates than those with a subcutaneous fat index <39.9 cm²/m².

References
1. Presented at the ESMO Virtual Congress 2020, Abstract 669P.

Renal & Urology News
24 September 2020

POP-RT Trial & Whole-Pelvis Radiotherapy (Continued from page 5)

In delivering RT, “we made sure to include the common iliac nodes and to go up to L4 and L5 and the common iliac junction,” Dr. Murthy further noted. Also, the POP-RT trial had a higher prostate dose (biological equivalent dose of 129.6 Gy), used image-guided IMRT, and administered ADT for much longer than the other trial (2 years vs. 4-8 months).

“Prophylactic RT in this trial improved BCF-free survival and DFS in high-risk PCa patients. The improvement in outcomes was seen in spite of giving long-term ADT and in spite of doing dose escalation,” Dr. Murthy summarized. “There is no OS difference as of yet, but that remains to be seen.

“Based on these results, it would be fair to say that whole-pelvis RT should be considered for these men with high-risk and very-high-risk PCa,” he concluded.

Practice-Changing Findings
“Overall, I’m very impressed with this study,” commented Colleen A. Lawton, MD, of Medical College of Wisconsin, Milwaukee. “The primary endpoint of BCF-free survival is not a great one, but fortunately, the distant MFSl, a secondary endpoint, was statistically improved also. The POP-RT results are not surprising given other lines of evidence,” she noted. For example, early results of a trial among postprostatectomy patients (RTOG 0534) suggest a benefit of pelvic lymph node RT, and findings from studies in other adenocarcinomas, such as breast and rectal, show that treating the lymph nodes improves outcomes.

“I think the data are practice changing ... mostly because there is so much retrospective data suggesting a benefit from lymph node RT for PCa, especially with adequate doses, but this is the first prospective randomized trial to use proper dosing to the primary and lymph nodes, and adequate ADT,” Dr. Lawton said. "The use of PSMA PET is also important from a selection perspective in identifying patients more likely to have microscopic versus gross lymph node involvement, and in follow-up to identify which patients fail in the lymph nodes.

“I agree with the authors’ conclusions and definitely recommend lymph node RT for high- and very-high-risk patients in addition to the ADT,” she concluded. “The dose to the lymph nodes at 50 Gy in 25 fractions is a bit higher than has been used in all of the RTOG trials (45 Gy in 25 fractions), and I do believe that adequate doses are critical in seeing a benefit to treatment.”

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QUESTION FROM PROSTATE CANCER SURVIVOR:
My wife has decided that due to COVID, we can no longer kiss or do anything sexual. I know I’m on borrowed
time because I had radiation therapy and they told me that my erections would get weaker over the 2 years after
treatment. It’s been 17 months since the radiation and that means that I have only 7 months left. Is she right?

RESPONSE FROM DR. ANNE KATZ:
It must be difficult to be watching the calendar and counting down the days and months … but there is no
promise that you will lose all erectile function by a certain date. It could happen sooner (I hope not) or later,
so try and live in the present and don’t be pressured by a random date. While we generally say that erectile
functioning does decline with time, there are other factors involved such as age, other diseases and, of course,
your level of anxiety.

In terms of COVID, if you and your wife are following public health recommendations (limiting social contacts,
practicing social distancing when out, wearing a mask outside your home) there is no reason to think that you are
at risk from sexual contact with your spouse. Perhaps there is something else going on in her life that is prompting
her concern about COVID; I suggest it’s time for a heart-to-heart talk with her!

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:
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.

**Promising Target to Inhibit Prostate Cancer Growth**

*Early studies find that molecule “CCS1477” slows tumor growth*

Research published recently in *Cancer Discovery* (https://cancerdiscovery.aacrjournals.org/content/early/2021/01/06/2159-8290.CD-20-0751) describes a new therapy with promising preclinical activity that is now being tested in clinical trials for very advanced prostate cancer patients. Early studies suggest this treatment has promising activity for the significant proportion of patients with advanced prostate cancer whose tumors remain driven by the AR (androgen receptor), but no longer respond to the newer AR-targeted therapies.

Why is this so important for patients? Advanced prostate cancer that has developed resistance to hormone therapy has no cure. It’s like a car engine that continues to run when the “fuel supply” (testosterone) is cut off by ADT, or even by newer androgen directed therapies. Although treatments are available, the disease often continues to progress, and more options are urgently needed for such patients.

A PCF-funded team led by Dr. Johann de Bono (Institute of Cancer Research, London and Royal Marsden NHS Foundation Trust) and Dr. Karen Knudsen (Thomas Jefferson University) has identified a promising new therapeutic target in prostate cancer (called p300/CBP), and is credentialing this target biologically and in clinical trials. p300/CBP is critical to the activity of the AR, the primary driver of prostate cancer growth.

For the first time, researchers were able to show that blocking p300/CBP with a new experimental treatment causes a decrease in AR signaling and slows tumor growth. This inhibitor molecule – referred to as CCS1477 – is currently in a phase 1 clinical trial (https://clinicaltrials.gov/ct2/show/NCT03568656) of patients with advanced prostate cancer. To confirm that CCS1477 is able to block AR activity in patients, the team also looked at markers of AR activity in the blood and biopsy tissues of patients in the trial. Results from the trial on the optimal dosage, safety, and preliminary efficacy of CCS1477 are not yet available.

Taken together, the results show that CCS1477 merits further study as a possible treatment for castration-sensitive and castration-resistant prostate cancer, both alone and in combination with existing medications.

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