Informed Prostate Cancer Support Group Inc.
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JULY 2021 NEWSLETTER

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Sunday, July 11, 2021

Volume 14 Issue 07

- **Saturday, July 17, 2021 IPCSG - Live-Stream Event, 12:00pm PT**

Dr. Justin Houman - Men's Health, Pre and Post Prostate Cancer Treatment

- Dr. Justin Houman is a urologist and fellowship-trained Male Reproductive Medicine and Surgery specialist, whose practice is focused on men's health, include male hormone management, sexual and ejaculatory dysfunction, male fertility, male incontinence, and Peyronie's disease. Dr. Houman will be discussing men's health with respect to pre and post prostate cancer treatments.
- Erectile Dysfunction and Prostate Cancer I Justin Houman MD https://youtu.be/qbYPa438QD8
- Due to COVID-19, no in-person meetings at the Sanford Burnham Prebys Medical Discovery Institute will take place until further notice. This meeting will be live-streamed and will also be available on DVD.
- **For further Reading: https://ipcsg.blogspot.com/**
- **For Comments, Ideas and Questions,** email to Newsletter@ipcsg.org

June 2021 Informed Prostate Cancer Support Group Meeting

Summary by Bill Lewis

PSMA PET Scans and Theranostics

Jeremie Calais, MD, MSc – Director, Clinical Research Program, Ahmanson Translational Theranostics Division; Assistant Professor, Nuclear Medicine and Theranostics, Dept. of Molecular and Medical Pharmacology, UCLA.

Theranostics combines a diagnostic ability with a therapeutic capability, using the same molecular target in the body. In the case of prostate cancer, the target is a protein called PSMA, which is present on prostate cancer cell membranes, and which is "overexpressed" by up to a thousand-fold on prostate cancer cells – wherever they may be in the body. Other cells in the body do not have PSMA protein, with few exceptions – most notably, the salivary glands in the jaw, and the kidney.

A radioactive drug is injected, and the organic part of the drug molecule finds and binds to the PSMA protein selectively. Gallium-68 is a radioactive isotope commonly used for imaging, attached to a PSMA-binding organic group, as its emitted gamma rays can be detected by a CT machine, allowing for a computed 3D image of "hot spots" in the body. Other radioactive isotopes, similarly attached to a PSMA-binding organic group, emit higher-energy, tumor-killing radiation. This is called molecular radiotherapy, radioligand therapy, or radionuclide therapy. Lutetium-177 emits beta particles that only travel 1 mm, so is very suitable for selectively damaging the cell to

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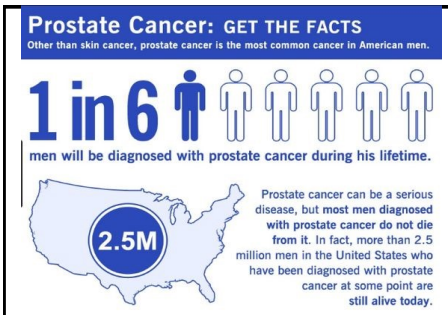

Organization

a 501c3 non-profit organization - all positions are performed gratis

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Stephen Pendergast ..... Editor

NEWSLETTER

Table of Contents

Section.....Page

Future Meetings 1

Last Speaker Summary.....1,3-6

What We Are About 2

Video DVD's.....2

Editorial.....2

Lighter Side 6

Articles of interest..... 6-9[13]

Networking, Finance..... 10

Directions and Map to Meet.. 10

PROSTATE CANCER—*2 WORDS, NOT A SENTENCE*

What We Are About

Our Group offers the complete spectrum of information on prevention and treatment. We provide a forum where you can get all your questions answered in one place by men that have lived through the experience. Prostate cancer is very personal. Our goal is to make you more aware of your options before you begin a treatment that has serious side effects that were not properly explained. Impotence, incontinence, and a high rate of recurrence are very common side effects and may be for life. Men who are newly diagnosed with PCa are often overwhelmed by the frightening magnitude of their condition. Networking with our members will help identify what options are best suited for your life style.

Meeting Video DVD's

DVD's of our meetings are available for purchase on our website at https://ipcsg.org/purchase-dvds and are generally available by the next meeting date.

Join the IPCSG TEAM

If you consider the IPCSG to be valuable in your cancer journey, realize that we need people to step up and HELP. Call **President** Bill Lewis @ (619) 591-8670 ; or **Director** Gene Van Vleet @ 619-890-8447.

From the Editor

Due to COVID-19, no in-person meetings will be held until further notice. We will continue to post and distribute the newsletter in the interim. Our speaker this month will be broadcast via the IPCSG website at https://ipcsg.org/live-stream and can be watched by scrolling down and clicking on the "WATCH THE PRESENTATION" button. The broadcast will begin approximately 10 minutes before to the listed start time.

In this issue:

First, we have Bill Lewis's great summary of the Theranostics talk, followed by Articles of Interest

- Support for MRI-Targeted Biopsy in Prostate Cancer Screening
- AI tool analyzes CT scans to spot prostate cancer in seconds –
- Positive Predictive Value and Correct Detection Rate of 18F-rhPSMA-7 PET in Biochemically Recurrent Prostate Cancer Validated by Composite Reference Standard -
- Biochemical Persistence of Prostate-Specific Antigen After Robot-Assisted Laparoscopic Radical Prostatectomy: Tumor Localizations Using PSMA PET/CT Imaging
- Progression on active surveillance for prostate cancer in Black men: a systematic review and meta-analysis
- Letter regarding "18F-Fluciclovine PET/CT performance in biochemical recurrence of prostate cancer: a systematic review"
- Anti-androgen therapy can fuel spread of bone tumors in advanced prostate cancer: Miniature 3D bone-like tissue models show effects of anti-androgens
- Could Docetaxel Have Role in Unfavorable-Risk Prostate Cancer? | MedPage Today
- Machine learning algorithms can more efficiently predict biochemical recurrence after robot-assisted radical prostatectomy
- Cardiovascular toxicities associated with abiraterone compared to enzalutamide–A pharmacovigilance study
- Outcomes of metastasis-directed therapy of bone oligometastatic prostate cancer | Radiation Oncology | Full

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(Continued from page 1)

which it becomes attached.

[Sidebar: Positron emission tomography/computed tomography (PET/CT) with 68Ga-PSMA is a non-invasive diagnostic technique to image prostate cancer with increased prostate-specific membrane antigen (PSMA) expression. PSMA is a transmembrane protein present in all prostatic tissues. Increased PSMA expression is seen in several malignancies, although prostate cancer is the tumor where it presents higher concentrations. Almost all prostate adenocarcinomas show PSMA expression in most of lesions, primary and metastatic. Immunohistochemistry has demonstrated that the expression of PSMA increases in patients with de-differentiated, metastatic or hormone-refractory tumors. Moreover, the expression level of PSMA has a prognostic value for disease outcome. PET measures the three-dimensional distribution of 68Ga-PSMA, producing semi-quantitative images that allow for non-invasive assessment of PSMA expression. From DOI: 10.1016/j.remn.2017.07.004]

A Gallium-68 PSMA PET/CT scan (the drug is called Ga 68 PSMA-11) may be scheduled at UCLA, with a referring physician's request. Ask your medical team to contact 310-794-1005 or see https://www.uclahealth.org/psma

It is uncommon to get insurance reimbursements for the $3,300.00 cost at this time, but UCLA is working to get such approvals. For now, it is up to the patient to appeal to his insurance provider.

Two clinical trials with PSMA PET/CT scans free-of-charge are open:

1. a randomized trial (50/50 chance) for patients scheduled for definitive radiation therapy (https://clinicaltrials.gov/ct2/show/NCT04457245)

2. a multiple serial imaging trial (x3) for patients scheduled to receive a novel androgen receptor axis inhibitor (e.g, Zytiga, Xtandi, etc.) (https://clinicaltrials.gov/ct2/show/NCT04279561)

PSMA as a target for Nuclear Theranostics: Lutetium177-PSMA theranostics has sometimes (roughly 50% of patients respond) provided dramatic reductions in PSA values, and caused disappearance of metastatic lesions. There are some side effects which are frequent, reversible and moderate: fatigue; dry mouth or dry eyes; nausea/vomiting; or diarrhea or constipation. Rare: kidney damage. If bone metastases: blood counts may drop (anemia, platelets, or white blood cells – but less drop than is common with chemo), or "flare effect" (pain increases for up to a week, then decreases). Generally the side effects are considered tolerable by patients.

The VISION trial results were just reported in the ASCO meeting in June, with metastatic castrate-resistant prostate cancer (mCRPC) patients randomized to continued treatment with ADT (Lupron or the like) plus Zytiga, Xtandi or Erleada, with or without Lutetium177-PSMA treatments. In these advanced-disease patients, overall survival was extended from 11.3 to 15.3 months.

The Lutetium177-PSMA drug was just (June 2021) given FDA breakthrough designation, meaning an accelerated path to approval. Dr. Calais expects the drug to be approved in late 2021 or early 2022.

Meanwhile, there is an "expanded access" program at UCLA that will be open soon (waitlisting is now available), for patients with mCRPC who have failed chemotherapy. A PSMA PET scan is required for eligibility. Up to 6 cycles of Lu177-PSMA may be given, at 6-8 week intervals. See https://clinicaltrials.gov/ct2/show/NCT04825652

Questions:

Is ADT required as an adjunct to Lu177-PSMA therapy? No. Is it preferable – we don't know yet.

Is PSMA PET more sensitive than Axumin? Definitely, though it is still not perfect. Pathology exams of removed tissue are the "gold standard," followed by PSMA PET, Axumin, CT and bone scans, in order of decreasing sensitivity.

How does 18 F-DCFpyl (PYLARIFY; piflufolastat F 18; also known as PyL) compare with Ga 68 PSMA-11? They

(Continued on page 4)

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are very similar in sensitivity and specificity, with PyL a tiny bit better – but with no practical difference for clinical recommendations.

What will be the participant cost for the new Lu177-PSMA trials? Past research trials cost about $10K per cycle (as does treatment in Germany or Australia). With the expanded access program, Novartis is expected to provide the drug at no cost, but about $1500 incidentals cost (including hospital/nursing/administration) per cycle will still be charged to the patient.

How much whole-body radiation comes from Lu177-PSMA therapy compared to IMRT (i.e., standard X-ray therapy)? It's very hard to estimate the dose, part of which is excreted, but the amount can range from 3 to 150 Grey in different cases, depending on the number and size of metastases.

We recommend that you watch the video online for more definitive information about the talk and slides: https://www.youtube.com/watch?v=2gp10-9k0HA

A dvd of the talk and Dr. Calais' slides will be available for purchase from the IPCSG about one month after the meeting.

On the Lighter Side

"If you're gonna complain, you can cut it yourself."

Golfer's Recurring Nightmare

Trojan Pizza

Welcome to Chemistry 101, where we study elements and their interactions

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Articles of Interest

Support for MRI-Targeted Biopsy in Prostate Cancer Screening

by Mike Bassett, Staff Writer, MedPage Today July 9, 2021

— Large Swedish study showed the approach cut overdiagnosis, unnecessary biopsies

A prostate cancer screening strategy using MRI with targeted and standard biopsy reduced the detection of clinically insignificant cancers as well as unnecessary biopsies, researchers reported.

Such an approach was also as effective as a standard biopsy strategy in detecting clinically significant cancers, said Tobias Nordstrom, MD, PhD, of the Karolinska Institutet in Stockholm, in a presentation at the virtual European Association of Urology Congress.

The results were published simultaneously in the *New England Journal of Medicine (NEJM)*.

Nordstrom and colleagues found that the detection of clinically insignificant tumors and benign findings on biopsy were lower by 64% and 74%, respectively, among men with elevated prostate-specific antigen (PSA) levels, when biopsy was performed when MRI results were positive rather than using a standard strategy.

"Overdiagnosis is a critical barrier to any screening implementation of prostate cancer," Nordstrom said. "We all know from studies performed before that MRI with targeted biopsies reduces overdiagnosis in men referred to prostate biopsy in clinical cohorts. But there is a lack of evidence on how MRI performs in a screening population."

The prospective, randomized, population-based STHLM3-MRI trial included men ages 50 to 74 and was designed to evaluate different screening strategies for prostate cancer. In this analysis, Nordstrom reported findings from a strategy that combined MRI-targeted and standard biopsy in men with positive results on MRI compared with use of a standard biopsy strategy.

The study included 12,750 men, 1,532 of whom had a PSA level of ≥3 ng/mL. Of these, 603 were randomized to undergo standard biopsy, and 929 to MRI, with targeted and standard biopsy if the MRI results indicated prostate cancer.

The primary outcome was the probability of detection of clinically significant prostate cancer (the percentage of patients with a Gleason score of 3+4 or greater). Key secondary outcomes included the detection of clinically insignificant cancers and biopsies with benign findings.

"We found that the MRI-targeted strategy was non-inferior for the detection of significant cancers," Nordstrom reported. "However, we could not deem the MRI-targeted strategy as superior."

The team did find, however, that the MRI-targeted strategy detected fewer clinically insignificant cancers (Gleason score 6). Specifically, 4% of the cancers detected with MRI-targeted biopsy were Gleason score 6 compared with 12% in the standard-biopsy arm, for a difference of -8% (95% CI -11% to -5%).

When Nordstrom and co-authors normalized the findings to 10,000 men (ages 50 to 74 with elevated PSA levels of 3 ng/mL or more) the targeted biopsy approach in men with a positive MRI resulted in:

- 409 fewer men undergoing biopsy
- 366 fewer biopsies with benign findings
- 88 fewer clinically insignificant cancers

Those numbers represented 48%, 78%, and 62% lower incidences, respectively, with the use of MRI and the combined biopsy approach, Nordstrom reported.

In the *NEJM* article, the researchers explained that an important question was whether men with positive MRI results should undergo a standard biopsy in addition to targeted biopsy. The findings showed that the addi-

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tion of standard biopsy resulted in the discovery of 30 more clinically significant cancers among the men in the experimental biopsy group and the detection of 18 fewer insignificant cancers.

"Thus, detection of 1.7 clinically significant cancers would be delayed for each clinically insignificant cancer avoided," the investigators calculated. "Our results therefore support the use of standard biopsy in addition to targeted biopsy for men who have positive MRI results, an observation that is in line with previous findings."

In addition, the team said, a reduced biopsy rate and potential downstream savings from reducing overtreatment could result in costs savings that would offset the additional costs of MRI.

AI tool analyzes CT scans to spot prostate cancer in seconds

AI tool analyzes CT scans to spot prostate cancer in seconds

newatlas.com

By Nick Lavars

Continuous advances in artificial intelligence promise to shake up medical care in all kinds of exciting ways, with the ability to rapidly scan medical images and spot signs of disease far more efficiently than humans can. Scientists in Australia have now adapted this technology for the early detection of prostate cancer, with their software outperforming trained radiologists to detect cancerous growths in seconds.

For many medical ailments, an early diagnosis can greatly improve the treatments available and therefore the chances of overcoming them. Improvements in machine learning and computing power have led to highly capable forms of artificial intelligence that could be invaluable in this regard. We've seen AI tools that can improve an ECG's ability to reveal heart dysfunction, more accurately predict survival rates of ovarian cancer and just this week, calculate diabetes risk by measuring fat around the heart.

The latest example of this comes from researchers at Melbourne's RMIT University and St Vincent's Hospital, who started with CT scans of asymptomatic patients both with and without prostate cancer. The scientists note that, generally speaking, CT scans are useful for detecting ailments like bone and joint problems, but it is difficult for radiologists to use them to detect prostate cancers.

Using the CT scans, the AI software was trained to search for irregularities that could be indicative of the disease. The tool improved with each scan, refining its abilities and adapting to analyze scans from different machines, eventually spotting the smallest features of the disease. In time, it was able to outperform radiologists and detect cancerous growths in seconds, even before patients exhibited any symptoms.

“We’ve trained our software to see what the human eye can’t, with the aim of spotting prostate cancer through incidental detection,” says study author Dr Ruwan Tennakoon, from RMIT. “It’s like training a sniffer dog – we can teach the AI to see things that we can't with our own eyes, in the same way a dog can smell things human noses can’t.”

The scientists say the technology could be adapted to a variety of diagnostic equipment, such as MRI machines. The hope is that it can be used as a type of integrated screening tool for CT scans, which involve high doses of radiation and therefore aren't suitable for regular cancer screening. But if a patient is having a CT scan for some other reason, the AI tool could be used to screen them for cancer at the same time.

“Australia doesn’t have a screening program for prostate cancer but armed with this technology, we hope to catch cases early in patients who are scanned for other reasons,” says Dr Mark Page, Head of CT in Diagnostic Imaging at St Vincent’s Hospital Melbourne. “For example, emergency patients who have CT scans could be simultaneously screened for prostate cancer. If we can detect it earlier and refer them to specialist care faster, this could make a significant difference to their prognosis.”

The research was published in the journal *Scientific Reports*.

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Positive Predictive Value and Correct Detection Rate of 18F-rhPSMA-7 PET in Biochemically Recurrent Prostate Cancer Validated by Composite Reference Standard

Maythinee Chantadisai, Gabriel Buschner, Markus Krönke, Isabel Rauscher, Thomas Langbein, Stephan G. Nekolla, Kilian Schiller, Matthias M. Heck, Tobias Maurer, Alexander Wurzer, Hans-Juergen Wester, Calogero D'Alessandria, Wolfgang Weber and Matthias Eiber

Journal of Nuclear Medicine July 2021, 62 (7) 968-974; DOI: https://doi.org/10.2967/jnumed.120.255661

Abstract

The objective of this retrospective study was to assess the detection rate (DR), positive predictive value (PPV), and correct detection rate (CDR) of ^{18}F-rhPSMA-7 PET/CT in biochemical recurrence (BCR) of prostate cancer (PCa) after radical prostatectomy (RP) using composite validation.

Methods: ^{18}F-rhPSMA-7 PET/CT scans of patients with BCR between July 2017 and June 2018 were retrospectively reviewed. All suspicious lesions were recorded. The reference standard was histopathology or combinations of histopathology, imaging, or prostate-specific antigen (PSA) follow up, defined as composite reference standard. DR was calculated as the proportion of PSMA PET–positive patients to all patients independent of the reference standard, whereas the CDR was the percentage of patients who had at least 1 true-positive PSMA PET lesion localized that corresponded with the reference standard. The PPV was defined as the proportion of patients who had true-positive to all positive findings. The correlation between DR and patient characteristics was evaluated.

Results: A total of 532 patients with a median PSA level of 0.97 ng/mL (interquartile range: 0.41–2.46 ng/mL) were included. Of these, 162 patients had composite follow-up at a median duration of 5.6 mo (range: 1.1–14.2 mo). The proportion of patients who had no lesion visualized on PET/CT, localized disease, and any distant metastases (M1) were 20%, 43%, and 37%, respectively. PET DR among all patients was 80%. On a per-patient basis, the PPV of ^{18}F-rhPSMA-7 PET/CT in the composite cohort was 88%, and the CDR was 70%. The PPV in the histopathology-proven cohort was 91%, and the CDR in this subgroup was 73%. In patients with PSA levels ≥ 1 ng/mL the DR and PPV were 90% and 91%, respectively, resulting in a CDR of 82%. In patients with PSA levels < 1 ng/mL, the DR and PPV were 69% and 85%, respectively, resulting in a CDR of 59%. There was a significant positive correlation between ^{18}F-rhPSMA-7 PET/CT detection efficacy and stratified PSA levels (P = 0.005), as well as PSA nadir after prostatectomy (P < 0.001).

Conclusion: ^{18}F-rhPSMA-7 PET/CT offers high PPV in BCR after RP. Its CDR is dependent on the prescan PSA value with excellent CDR in patients with PSA ≥ 1 ng/mL.

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Biochemical Persistence of Prostate-Specific Antigen After Robot-Assisted Laparoscopic Radical Prostatectomy: Tumor Localizations Using PSMA PET/CT Imaging

Dennie Meijer, Maarten L. Donswijk, Yves J.L. Bodar, Pim J. van Leeuwen, Henk G. van der Poel, Wouter V. Vogel, Jakko A. Nieuwenhuijzen, N. Harry Hendrikse, Daniela E. Oprea-Lager and André N. Vis

Journal of Nuclear Medicine July 2021, 62 (7) 961-967; DOI: https://doi.org/10.2967/jnumed.120.252528

Abstract

Since the introduction of radiolabeled prostate-specific membrane antigen (PSMA) PET/CT, the ability to visualize recurrent prostate cancer has improved substantially. However, diagnostic accuracy is largely lacking for

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radiolabeled PSMA PET/CT in patients with biochemical persistence (BCP; that is, persistently measurable prostate-specific antigen [PSA] values after robot-assisted laparoscopic radical prostatectomy [RARP]). Therefore, the aim of this study was to determine the role of PSMA (i.e., ^{18}F-DCFPyL or ^{68}Ga-PSMA-11) PET/CT imaging in patients who experience BCP after RARP and to evaluate the sites of persistent disease on PSMA PET/CT.

Methods: In total, 150 consecutive patients with BCP after RARP who underwent radiolabeled PSMA PET/CT imaging were retrospectively evaluated. BCP was defined as any detectable first serum PSA value after RARP (≥0.1 ng/mL) at least 6 wk after surgery, in the absence of an undetectable PSA value after RARP. A multivariable logistic regression analysis was performed to identify predictors for the detection of metastases outside the prostatic fossa (≥miN1) on PSMA PET/CT.

Results: PSMA PET/CT was performed at a median PSA value of 0.60 ng/mL (interquartile range, 0.3–2.4) after a median of 6 mo (interquartile range, 4–10) after RARP. In total, 101 of 150 patients (67%) had lesions with PSMA expression on PET/CT, and 89 of 150 (59%) had lesions with increased PSMA expression sites outside the prostatic fossa. Moreover, 39 of 150 patients (26%) had PSMA-positive lesions outside the pelvis. On multivariable analysis, higher PSA values after RARP (P = 0.004) and positive pathologic lymph node status (P = 0.006) were independent predictors for ≥miN1.

Conclusion: In the presence of BCP, a high proportion of patients already had disease metastatic to the pelvic lymph nodes or showed evidence of distant metastases, as indicated by PSMA PET/CT. Higher PSA levels after RARP and positive pathologic lymph node status were significantly associated with metastases outside the prostatic fossa. In patients with BCP, PSMA PET/CT imaging is warranted to guide salvage treatment strategies.

Progression on active surveillance for prostate cancer in Black men: a systematic review and meta-analysis

Progression on active surveillance for prostate cancer in Black men: a systematic review and meta-analysis | Prostate Cancer and Prostatic Diseases

nature.com

Michael R. Abern

Abstract

Background

Several studies evaluated prostate cancer (PCa) outcomes in Black men on active surveillance (AS); most studies contained few Black men and results were conflicting. We performed a systematic review and meta-analyze of race and outcomes on AS.

Methods

A systematic search was performed for articles of men with Grade Group 1 or 2 (GG1 or GG2) PCa on AS. All studies required race-specific comparative progression data. Progression to treatment, PSA, or biopsy progression were considered and relative risk (RR) estimates of Black men progressing were extracted and pooled using random-effects models. Differences by study-level characteristics were evaluated using subgroup and a cumulative meta-analysis by time.

Results

In total, 12 studies were included (3137 Black and 12,206 non-Black men); eight prospective (27%, n = 4210) and four retrospectives (73%, n = 11,133) cohorts. The overall RR of progression for Black men was 1.62 (95%CI, 1.21–2.17), I^2 = 64% (95% CI, 32–80%), (χ^2 = 30.23; P = 0.001; τ^2 = 0.16). Black men with GG1 PCa alone had a higher pooled progression: RR = 1.81 (95% CI, 1.23–2.68). Including only studies with clinical progression (excluding progression to treatment), potentiated results: RR = 1.82 (95%CI, 1.27–2.60). However, a cumulative meta-analysis demonstrated decreasing pooled effect over time, with contemporary studies after 2019 showing a tempered effect

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(RR: 1.29, 95% CI: 1.20–1.39).

Conclusions

Many studies attribute racial disparity in PCa to delayed presentation of disease, however, AS is unique since all AS eligible men have a low grade and stage PCa. Our findings suggest Black men may have an increased risk of progression during AS, but the association is not so strong that Black men should be discouraged from undergoing AS. Indeed, contemporary evidence suggests stricter inclusion, better confirmatory testing or better access to care may temper these findings. Importantly, these results utilize self-reported race, a social construct that has many limitations.

Letter regarding "^{18}F-Fluciclovine PET/CT performance in biochemical recurrence of prostate cancer: a systematic review"

Editorial
Published: 08 July 2021
Ephraim E. Parent
Prostate Cancer and Prostatic Diseases (2021)Cite this article

Rais-Bahrami and colleagues have provided an informative overview of the applications of ^{18}F-fluciclovine (FACBC, Axumin®, Blue Earth Diagnostics Ltd) positron emission tomography (PET) for detection and localization of disease in men with biochemically evidence of recurrent prostate cancer [1]. The authors found that the detection rate of metastatic lesions with ^{18}F-fluciclovine PET was overall correlative to prostate-specific antigen (PSA) levels, but that even at low PSA levels of <0.5 ng/mL, ^{18}F-fluciclovine was able to detect a majority of lesions. Additionally, Rais-Bahrami et al importantly found that ^{18}F-fluciclovine PET affected patient management and targeted ^{18}F-fluciclovine radiotherapy planning resulted in improved outcomes. It should be noted that, as with most PET radiopharmaceuticals, the literature regarding use of ^{18}F-fluciclovine in the setting of prostate cancer is limited by small sample sizes and a large heterogeneity of study design, limiting the ability to generalize the findings of specific studies to the disease spectrum as a whole.

To this point, the authors of this review evaluated 315 articles, but limited inclusion for data analysis to prospective studies of ≥25 patients with biochemical recurrent prostate cancer. This effort to avoid variability from small sample design, resulted in a review of only 6 relevant articles and 3 conference presentations. Thus, while this review may avoid some bias, the resulting small sample size has remarkable heterogeneity and does not allow for an in-depth analysis of many of the more unanswered questions regarding the utility of ^{18}F-fluciclovine PET in the setting of prostate cancer. For example, within this small data set, there was inconsistent inclusion of: use of a reference standard, androgen deprivation therapy (ADT) status [2, 3], radical prostatectomy [4, 5], radiation therapy [2, 4], Gleason score, and initial nodal status [6, 7]. Additionally, there was heterogeneity in the actual imaging amongst the studies, with included studies starting PET scanning immediately after injection of ^{18}F-fluciclovine [7], 2 minutes [6] after, and with the reminder following the standard 3-5 minute delay post injection. All of these variables have been shown to affect diagnostic outcomes in the literature.

Given their self-imposed constraints, the authors made an attempt to correct for the aforementioned variables. Ultimately, however, the disparate nature of each study leads to wildly variable conclusions, such as patient-level detection rates which varied from 26% [6] to 83% [5]. The overall value of ^{18}F-fluciclovine in the setting of biochemical recurrent prostate cancer is well established, but there are many unresolved questions regarding the diagnostic accuracy of ^{18}F-fluciclovine PET that a more targeted review and thoughtful approach to the literature inclusion may reveal. Some areas of uncertain utility for ^{18}F-fluciclovine include: PET-MRI in the setting of prostate-intact prostate cancer [8], ^{18}F-fluciclovine PET for osseous metastatic disease [9], and the continuing applicability of ^{18}F-fluciclovine in the United States with the recent FDA approval of ^{68}Ga PSMA-11 [10]. This last point is particularly pertinent given that the two studies that the review article included that compared ^{68}Ga PSMA-11 to ^{18}F-fluciclovine [6, 7] came to vastly different conclusions regarding the comparative accuracy of ^{18}F-fluciclovine PET. For ^{18}F-fluciclovine to maintain its role in the United States as the de facto molecular imaging agent for biochemical prostate cancer, more targeted analysis must be performed to assure the molecular imager and ordering physicians of its relevancy.

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NETWORKING

Please help us in our outreach efforts. Our speakers bureau consisting of Gene Van Vleet is available to speak to organizations of which you might be a member. Contact Gene 619-890-8447 or gene@ipcsg.org to coordinate.

Member John Tassi is the webmaster of our website and welcomes any suggestions to make our website simple and easy to navigate. Check out the Personal Experiences page and send us your story. Go to: https://ipcsg.org/personal-experience

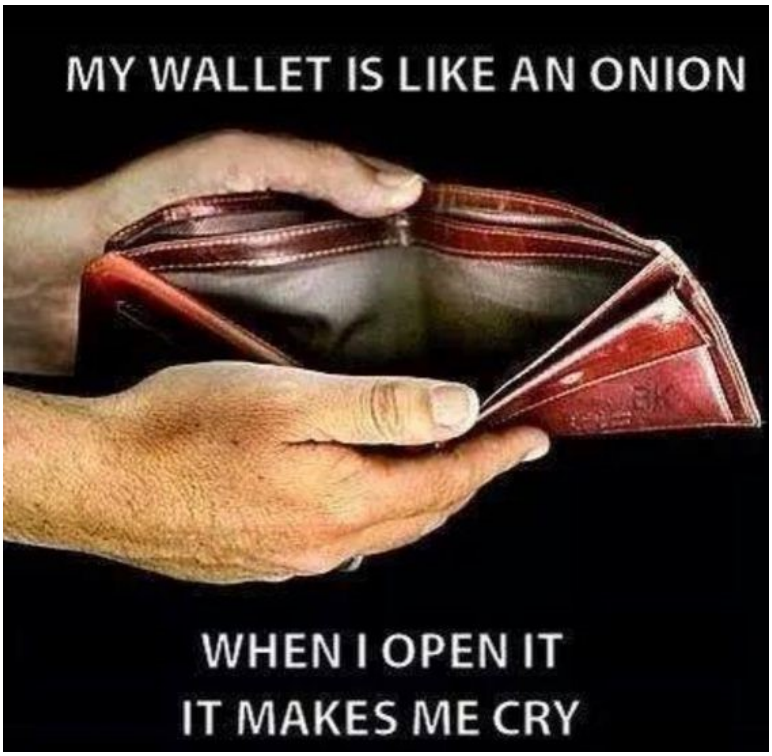
Our brochure provides the group philosophy and explains our goals. Copies may be obtained by mail or email on request. Please pass them along to friends and contacts.

Ads about our Group may be in the Union Tribune the week prior to a meeting. Watch for them.

FINANCES

We want to thank those of you who have made special donations to IPCSG. Remember that your gifts are tax deductible because we are a 501(c)(3) non-profit organization.

We again are reminding our members and friends to consider giving a large financial contribution to the IPCSG. This can include estate giving as well as giving in memory of a loved one. You can also have a distribution from your IRA made to our account. We need your support. We will, in turn, make contributions from our group to Prostate Cancer researchers and other groups as appropriate for a non-profit organization. Our group ID number is 54-2141691. Corporate donors are welcome!



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Anti-androgen therapy can fuel spread of bone tumors in advanced prostate cancer: Miniature 3D bone-like tissue models show effects of anti-androgens

Anti-androgen therapy can fuel spread of bone tumors in advanced prostate cancer: Miniature 3D bone-like tissue models show effects of anti-androgens -- ScienceDaily

sciencedaily.com

Dr Bock, under the mentorship of Distinguished Professor Dietmar Hutmacher, from QUT Centre for Biomedical Technologies, has focused her research on bone metastases from breast and prostate cancers.

She developed 3D miniature bone-like tissue models in which 3D printed biomimetic scaffolds are seeded with patient-derived bone cells and tumour cells to be used as clinical and preclinical drug testing tools.

The research team investigated their hypothesis that traditional anti-androgen therapy had limited effect in the microenvironment of prostate cancer bone tumours. The team's findings are published in *Science Advances*.

"We wanted to see if the therapy could be a contributor of cancer cells' adaptive responses that fuelled bone metastasis," Professor Hutmacher said.

"We developed an all-human, microtissue-engineered model of metastatic tissue using human bone-forming cells, prostate cancer cells and 3D printing."

Cancer biologist Distinguished Professor Judith Clements said the team bioengineered the microenvironment of a bone tumour to assess the effects of two clinically routinely used anti-androgen therapies -- enzalutamide and bicalutamide -- on the tumour cells.

"We found that the interactions between the cancer cells, the bone and the anti-androgens significantly impacted the progress of cancer in the mineralised microenvironment of bone tumours," Professor Clements said.

"This means that the efficacy of these therapies is compromised in the presence of the bone microenvironment."

Professor Hutmacher said an important outcome of the study was the need to upscale the bone tumour microenvironment model platform and make it available to other research groups.

"This would enable the prostate cancer research community to develop therapies for a more effective treatment of advanced prostate cancer."

In future, Dr Bock will use her model with patient-derived cells from patients undergoing prostatectomy, so that it could be used as a personalised preclinical diagnostic and drug testing tool.

"By screening existing and novel drugs using the bone tumour model in the laboratory, doctors will be able to treat individual patients with an anti-cancer therapy that can best suit their clinical need," Dr Bock said.

"This has the potential to considerably improve the quality of life of patients, because patients will not have to trial a succession of drugs, each of which carry the potential of severe side-effects, and which may not work for them."

This research was supported by the National Health & Medical Research Council of Australia, Australian Research Council and the Prostate Cancer Foundation of Australia.

Prostate Cancer Foundation of Australia CEO Professor Jeff Dunn AO said the findings were significant.

"This is an important discovery that will help us to better target treatments for men with different types of prostate cancer," he said.

"The findings also demonstrate the importance of ongoing research to improve our understanding of how different treatments impact disease progression and spread.

"Notably, Australia has one of the highest incidence rates of prostate cancer internationally, with 1 in every 6 Australian men likely to be diagnosed during their lifetime and around 17,000 men diagnosed each year.

"While survival rates for prostate cancer are high, with over 95% of men likely to survive at least five years, we must keep up the pace of work to find curative treatments, especially for advanced disease in the bone.

"There can be no doubt that this research will build on previous discoveries to help us save lives by stopping cancer from spreading and claiming the lives of more than 3,000 men a year, as is currently the case.

"We commend the research team and congratulate PCFA grant recipient Dr Nathalie Bock for her research achievements.

"This is Australian research excellence at its finest," he said.

Could Docetaxel Have Role in Unfavorable-Risk Prostate Cancer?

Could Docetaxel Have Role in Unfavorable-Risk Prostate Cancer? | MedPage Today

medpagetoday.com

by Mike Bassett, Staff Writer, MedPage Today July 7,

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2021

— Use of chemo reduced radiation-induced cancers, and may prolong OS in low-PSA subgroup

Adding docetaxel to androgen deprivation therapy (ADT) plus radiation therapy (RT) failed to improve survival in unfavorable-risk prostate cancer, though the combination may hold benefit for certain patients, long-term results of a randomized trial found.

While the regimen did not prolong overall survival (OS) among all men with unfavorable-risk nonmetastatic cancer after a median of 10 years follow-up, it did decrease the incidence of RT-induced cancer, reported Anthony D'Amico, MD, PhD, of Dana-Farber Cancer Institute in Boston, and colleagues.

Exploratory analyses showed that men with prostate-specific antigen (PSA) levels <4 ng/mL appeared to have improved OS, previously unseen in randomized trials, driven by a reduction in prostate cancer-specific mortality, according to the findings in the *Journal of Clinical Oncology*.

"There is a reduction in radiation-induced cancers, which is quite remarkable, because those cancers are usually lethal," D'Amico told *MedPage Today*. "And if men with PSA <4 really benefit from docetaxel by decreasing prostate cancer deaths, and also benefit from having less radiation-induced cancers, that's a double win for those men."

The FDA approved docetaxel for use in men with metastatic castration-resistant prostate cancer (mCRPC) after an OS benefit was observed in randomized clinical trials. Other trials demonstrated prolonged OS when men with newly diagnosed mCRPC were treated with ADT plus docetaxel.

However, D'Amico and colleagues noted that subsequent reports from six clinical trials, including NRG Oncology RTOG 0521 and STAMPEDE, of men with unfavorable-risk nonmetastatic cancer who had docetaxel added to radical prostatectomy or ADT and RT, had negative or inconclusive results. Thus docetaxel is not recommended when managing men with unfavorable-risk prostate cancer.

The authors also pointed out that an OS benefit with a nonsignificant reduction in prostate cancer-specific mortality was seen in two of the trials where >80% of the patients had high-grade prostate cancer. There is a "plausible" hypothesis that accounts for that OS benefit and the nonsignificant reduction in prostate cancer-specific mortality, according to D'Amico's group.

"There is a subgroup of men who have a low PSA <4, but a high-grade cancer," D'Amico explained. "These are men who don't make much PSA because they are already insensitive to testosterone. They have androgen sensitive disease, and that is exactly the disease that docetaxel increases survival in, in men with metastatic disease."

D'Amico and colleagues performed a multicenter, international, randomized phase III trial from September 2005 to January 2015 in which 350 men with T1c-4N0M0 unfavorable-risk prostate cancer were assigned 1:1 to ADT and RT with or without docetaxel.

They wanted to evaluate the effect add-on docetaxel had on OS and the incidence of RT-induced cancers, as well as how that effect on OS differed within PSA subgroups.

After a median follow-up of 10.2 years, 89 of the participants died (44 in the docetaxel arm; 45 in the ADT-plus-RT-alone arm). Of these deaths, 42 were from prostate cancer (22 and 20, respectively).

OS did not significantly increase in the docetaxel arm (a restricted mean survival time over 10 years of 9.11 with docetaxel vs 8.82 years without). However, the authors also found that fewer RT-induced cancers were observed in the docetaxel arm, with 10-year estimates of 0.61% versus 4.90% without the chemotherapy (age-adjusted HR 0.13, 95% CI 0.02-0.97). There was no significant difference in the cumulative incidence of all other second cancers (HR 0.89, 95% CI 0.50-1.60).

The treatment effect of the addition of docetaxel to ADT plus RT on OS also differed in men with PSA levels <4 ng/mL versus men with PSAs of 4-20 ng/mL (adjusted HR 0.27 and 1.51, respectively), driven by less prostate-specific mortality in the docetaxel arm (0% vs 28.57%, respectively), the authors explained.

"We looked into that PSA <4 subgroup and found there was a huge benefit there, but because the study wasn't designed to look specifically in that subgroup, it's hypothesis generating," D'Amico said. He added that his group is partnering with other trials (RTOG 0521 and STAMPEDE) for a meta-analysis to further explore that possible survival benefit in that small subset of patients.

"This small group is not inconsequential," D'Amico pointed out. "This is the group of men who have the highest rate of deaths from prostate cancer. The vast majority -- more than 50% -- go on to die from prostate

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cancer when you just give them standard treatment. So this is a group with an unmet need, and if docetaxel really has an impact in this group, it will be practice changing."

As for the finding of a reduction in RT-inducted cancers, D'Amico noted that docetaxel is a radiosensitizer, "and since radiation mutates cells, and it's those cells that go on to create new cancers, maybe docetaxel is potent enough to kill those cells that are mutated."

"And this finding is not hypothesizing -- it is robust," he stressed.

D'Amico and colleagues noted that the potential future availability of oral docetaxel, with its more favorable toxicity profile than IV docetaxel, "provides the opportunity to study oral docetaxel use to reduce the risk of RT-induced cancer with minimal patient impact and across a wide variety of cancers where RT and docetaxel use is part of the management approach."

Cardiovascular toxicities associated with abiraterone compared to enzalutamide–A pharmacovigilance study

Eugene B. Cone, Stephen Reese, Maya Marchese, Junaid Nabi, Rana R. McKay, Kerry L. Kilbridge, et al., Show all authors

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Abstract

Background

Androgen deprivation therapy (ADT) is standard-of-care for advanced prostate cancer. Studies have generally found increased cardiovascular risks associated with ADT, but the comparative risk of newer agents is undercharacterized. We defined the cardiac risks of abiraterone and enzalutamide, using gonadotropic releasing hormone (GnRH) agonists to establish baseline ADT risk.

Methods

We used VigiBase, the World Health Organization pharmacovigilance database, to identify cardiac adverse drug reactions (ADRs) in a cohort taking GnRH agonists, abiraterone, or enzalutamide therapy for prostate cancer, comparing them to all other patients. To examine the relationship, we used an empirical Bayes estimator to screen for significance, then calculated the reporting odds ratio (ROR), a surrogate measure of association. A lower bound of a 95% confidence interval (CI) of ROR > 1 reflects a disproportionality signal that more ADRs are observed than expected due to chance.

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Findings

We identified 2,433 cardiac ADRs, with higher odds for abiraterone compared to all other VigiBase drugs for overall cardiac events (ROR 1•59, 95% CI 1•48—1•71), myocardial infarction (1•35, 1•16—1•58), arrythmia (2•04, 1•82—2•30), and heart failure (3•02, 2•60—3•51), but found no signal for enzalutamide. Patients on GnRH agonists also had increased risk of cardiac events (ROR 1•21, 95% CI 1•12—1•30), myocardial infarction (1•80, 1•61—2•03) and heart failure (2•06, 1•76—2•41).

Interpretation

We found higher reported odds of cardiac events for abiraterone but not enzalutamide. Our data may suggest that patients with significant cardiac comorbidities may be better-suited for therapy with enzalutamide over abiraterone.

Outcomes of metastasis-directed therapy of bone oligometastatic prostate cancer | Radiation Oncology | Full Text

July 01, 2021

Outcomes of metastasis-directed therapy of bone oligometastatic prostate cancer | Radiation Oncology | Full Text

Radiation Oncology **volume 16**, Article number: 125 (2021) Cite this article

Abstract

Background

The aim of this work was to investigate the outcome of metastasis-directed radiotherapy (MDT) in prostate cancer patients with bone metastases following current ESTRO/EORTC subclassifications for oligometastatic disease.

Methods

Clinical data of 80 consecutive oligometastatic patients with 115 bone lesions receiving MDT between 2011 and 2019 were retrospectively evaluated. Hormone-sensitive (77.5%) and castrate-resistant (22.5%) patients were included. MDT was delivered with conventional fractionated or stereotactic body radiotherapy (SBRT) techniques. Kaplan–Meier method, log rank test, as well as Cox regression were used to calculate local control (LC) and biochemical and clinical progression-free survival (bPFS/cPFS).

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Results

At the time of MDT 31% of patients had de-novo synchronous oligometastatic disease, 46% had de-novo metachronous oligorecurrence after primary treatment and 23% had either de-novo oligoprogressive disease, repeat oligometastatic disease or induced oligometastatic disease. The median BED_3 was 93.3 Gy (range 75.8–95.3 Gy). Concomitant ADT was administered in 69% of patients. After a median follow-up of 23 months the median bPFS and cPFS were 16.5 and 21.5 months, respectively. The 2-year LC rate was 98.3%. In multivariate analysis, age ≤ 70 (HR = 2.60, 95% CI 1.20–5.62, p = 0.015) and concomitant ADT (HR = 0.26, 95% CI 0.12–0.58, p = 0.001) significantly correlated with cPFS. Category of oligometastatic disease and hormone-sensitivity were predictive for cPFS in univariate analysis. Of 45 patients with biochemical relapse, nineteen patients (42.2%) had repeat oligometastatic disease. Fourteen patients (31%) underwent a second course of MDT. No patients experienced grade ≥ 3 toxicities.

Conclusions

MDT is safe and offers high local control rates in bone oligometastases of prostate cancer. At 2 years after treatment, more than 2 out of 5 patients are progression-free.

On the Lighter Side

"That's it! I did it! I finally figured out how to hit the perfect golf shot every single time!!"

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