

## MEMBERSHIP

FULL CALENDAR  
YEAR PHCSG  
MEMBERSHIP \$20

Join our Monthly  
meetings on the third  
Tuesday (Feb – Dec)  
10am – 12:30pm

EFT Payments to:  
Prostate Heidelberg CSG  
BSB 083 256  
Acct 583244292

# Prostate Heidelberg Cancer Support Group

PHCSG provides  
information, education  
and support for those  
affected by Prostate  
Cancer. At our meetings  
we are committed to:

- showing respect to members, speakers and guests
- allowing members to speak without interruption
- respecting confidentiality

# Prostate Heidelberg

January 2022

Issue 214

## For Education, Information and Support

Meeting Hall: Ivanhoe Uniting Church 19 Seddon Street, Ivanhoe  
POB 241 Ivanhoe Victoria 3079  
Email: prostateheidelberg@gmail.com  
Website: www.prostateheidelberg.info

**Next PHCSG Meeting** – **Tuesday 15 February**  
10am – 12:30pm

**To join via Zoom:** Copy link and paste into your browser  
<https://us02web.zoom.us/j/84450281030?pwd=cnVJZzl5a3cweEljUG5GWjBJSUNBZz09>

## Wishing members a Safe & Healthy 2022

PHCSG provides support, education and awareness of prostate cancer (PCa) in the community. PCa is one of the most common cancers among men in Australia. Although mortality rates have declined in recent years, there has been an increase in incidence and diagnoses. Two years of the Covid-19 pandemic hasn't encouraged men to seek help and testing - crucial to ensure early detection.

We look forward to welcoming and supporting existing and new members to our first meeting of the New Year on Tuesday 15 February. Please be advised, that as a precautionary measure, it will once again be via Zoom!

In this month's newsletter we highlight:

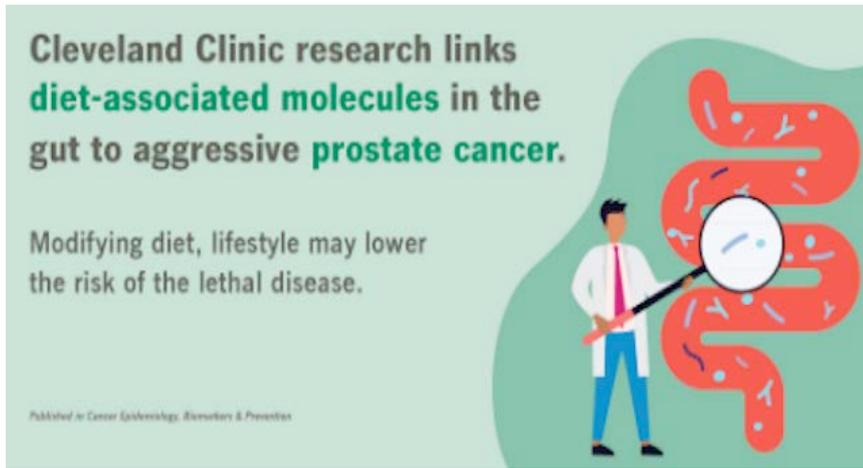
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- 

If there is anything you want to talk through in relation to your treatment or wellbeing please don't hesitate to ring:

Max Shub 0413 777 342

Mike Waller 0438 616 240

Michael Meszaros 0407 837 538



# Cleveland Clinic Study Links Gut Microbiome and Aggressive PCa

## Researchers uncover how diet, lifestyle modifications may lower risk of lethal disease.

Source:  
12 Jan 2022  
<https://newsroom.clevelandclinic.org/2021/10/28/cleveland-clinic-study-links-gut-microbiome-and-aggressive-prostate-cancer/>

Cleveland Clinic researchers have shown for the first time that diet-associated molecules in the gut are associated with aggressive prostate cancer, suggesting dietary interventions may help reduce risk. Findings from the study were published in *Cancer Epidemiology, Biomarkers & Prevention*.

### Prevention

While more research will be necessary, the study's lead author Nima Sharifi, M.D., says findings from the team's analysis of nearly 700 patients may have clinical implications for diagnosing and preventing lethal prostate cancer.

"We found that men with higher levels of certain diet-related molecules are more likely to develop aggressive prostate cancer," said Dr. Sharifi, director of Cleveland Clinic's Genitourinary Malignancies Research Center. "As we continue our research in this area, our hope is that one day these molecules can be used as early biomarkers of prostate cancer and help identify patients who can modify their disease risk by making dietary and lifestyle changes."

In this study, Dr. Sharifi and his collaborators – including Stanley Hazen, M.D., Ph.D., and Eric Klein, M.D. – analyzed data from patients previously enrolled in the National Cancer Institute's Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial.

They studied baseline levels of certain dietary nutrients and metabolites (byproducts produced when a substance is broken down in the gut) found in patients' blood serum prior to prostate cancer diagnosis. They compared serum levels between healthy patients and those who later received a prostate cancer diagnosis and died from the disease.

The researchers found that men with elevated levels of a metabolite called phenylacetylglutamine (PAGIn) were approximately two or three times more likely to be diagnosed with lethal prostate cancer. This metabolite is produced when microbes in the gut break down phenylalanine, an amino acid found in many plant- and animal-based protein sources like meat, beans and soy.

In addition to PAGIn, researchers also discovered that elevated levels of two nutrients abundant in animal products, including red meat, egg yolks and high-fat dairy products, called choline and betaine, also were linked with increased risk for aggressive prostate cancer.

While these nutrients and gut metabolites have been studied previously in heart disease and stroke, this is the first time that gut microbiome metabolites have been studied clinically in relation to prostate cancer outcomes.

Dr. Hazen was the first to identify PAGIn's association with increased cardiovascular disease risk. The findings were published in 2020 in *Cell*. "Interestingly, we found that PAGIn binds to the same receptors as beta blockers, which are drugs commonly prescribed to help lower blood pressure and subsequent risk of cardiac events," said Dr. Hazen, director of Cleveland Clinic's Center for Microbiome & Human Health and chair of Lerner Research Institute's Department of Cardiovascular & Metabolic Sciences. "This suggests that part of beta blockers' potent efficacy may be due to blocking the metabolite's activity."

"New insights are emerging from large-scale clinical datasets that show use of beta blockers is also associated with lower mortality due to prostate cancer," said Dr. Sharifi, who is a staff physician in Lerner Research Institute's Department of Cancer Biology. "We will continue to work together to investigate the possible mechanisms linking PAGIn activity and prostate cancer disease processes in hopes of identifying new therapeutic targets for our patients."

The research team also will continue to explore the reliability of using choline, betaine and PAGIn as biomarkers of aggressive prostate cancer and how dietary interventions can be used to modulate their levels and reduce patients' subsequent disease risk.



# Rapid Prostate Cancer Screening Kits

Source:  
5 January 2022  
Cornell University  
[https://www.sciencedaily.com/releases/2022/01/220105202807.htm?utm\\_medium=email&utm\\_source=rasa\\_io](https://www.sciencedaily.com/releases/2022/01/220105202807.htm?utm_medium=email&utm_source=rasa_io)

The proof-of-concept test, described online Nov. 12 in the journal *Current Research in Biotechnology*, is inexpensive and uses a test strip and a small cube-shaped 1.6-inch reader to quantify a marker of prostate cancer -- called prostate-specific antigen (PSA) -- from a drop of blood in minutes.

"We'll be able to take a drop of blood in a community setting such as a barbershop and be able to deliver results in 10 to 15 minutes right there, which can indicate when somebody needs to come in for further tests," said Dr. Saurabh Mehta, the Janet and Gordon Lankton Professor in the Division of Nutritional Sciences and the paper's senior author. Balaji Srinivasan, a research associate in Mehta's research group, is the paper's first author.

"It's creating that first point of contact that hopefully builds rapport and brings health care services to the people at the point of need," Mehta said.

The kit comes with a test strip, similar to those found in at-home COVID-19 antigen or pregnancy tests. Users would draw a drop of blood and apply it to the test strip, and in about 15 minutes, two lines appear on the strip.

The color of the two lines is due to 150-nanometer gold nanoshells, which greatly enhance the test's sensitivity to detect PSAs and make the lines appear more intense in their presence, Srinivasan said. While a

pregnancy test gives a positive or negative result, the cube reader senses the intensity of the test strip lines and then calculates and displays a measurement of PSA concentration in the blood.

"Another advantage of test strips is that the technology to make them really cheap or mass produce them has been around for many years," Srinivasan said. He estimates that PSA test kits may be mass produced and sold for a few dollars each.

While a different PSA test kit developed by a private company has been approved by the FDA, it works by putting a blood sample into a microfluidic channel and has a larger bench-top analyzer, making it less portable and more expensive to own and operate.

Study co-author David Erickson, the S.C. Thomas Sze Director and Sibley College Professor in the Sibley School of Mechanical and Aerospace Engineering, has worked with Mehta to also develop a mobile phone-based system to detect infectious diseases, inflammation and nutritional deficiencies in saliva. Meanwhile, co-author Dr. David Nanus, professor of medicine in the Division of Hematology and Medical Oncology and a member of the Meyer Cancer Center at Weill Cornell Medicine, reached out to Mehta wanting to collaborate on a portable PSA screening device to reach underserved populations.

A highly portable and rapid prostate cancer screening kit could provide early warning to populations with higher incidence of prostate cancer and particularly those with limited access to health care.

PLEASE NOTE:  
Treatments may vary in Australia. Please ensure you discuss your diagnosis and treatment options with your consulting specialist



# How Much Should You Eat?

Source:  
<https://www.pcf.org/blog/how-much-should-you-eat/>

As the New Year begins, many people look at their lifestyle habits and think about ways to feel healthier in the coming months.

Two key pieces of eating well are 1) the best foods and 2) the optimal amount of food. #1 has some variation among individuals, but research has consistently shown that a variety of brightly-colored vegetables supplies the body with the cancer-fighting, immune-boosting nutrients everyone needs. Whole grains, high-quality, plant-based proteins, and healthy fats such as olive oil round out a healthy eating plan.

But how much of each type of food?

Government and doctor recommendations for portion sizes have not increased over time, but anyone who has eaten out at a restaurant knows that the amount of food you are served is often more than you can eat. Opportunities to pay a fraction more money to “supersize” your soda or get a bowl of pasta the size of your head are everywhere.

When you eat excess food, it triggers your body to convert calories to fat. Portion sizes are where the rubber meets the road: it is important to eat appropriate amounts of various healthy foods at each sitting.

There’s more variation among people in how much food they need each day. It depends on several factors such as body size and composition, age, any medical conditions, and activity level. If you’re training for a 5K run or you lift weights 3x/week, you may need more food. If you’re trying to lower your BMI, or you just turned 60, you may need less food than you did in the past. If you’re starting—or just finishing—cancer treatment, talk to your doctor about any special dietary considerations.

And then there’s the pandemic. For many people, activity levels took a nosedive. In one large international survey, 66% of people reported that they were unable to maintain their usual level of activity. Older people reported greater declines in activity. Not only did we stop going to the gym, but as we stayed more at home, we got less “incidental” daily physical activity, like walking over to the printer at the office or to the neighborhood coffee shop to meet a friend. As your circumstances change, so will the amount of food you need.



**How much should you eat?**  
 That’s where a little precision comes in. Each individual is different. These are just a few guidelines to help you make the best choices for you.

Category	Size	Frequency
Brightly-Colored Vegetables	6-8 cups	Daily
Healthy Added Fats (e.g., extra virgin olive oil*)	1-3 tbsp	Daily
Fruit	3 cups/pieces	Daily
Whole Grains (eg. Rice, Quinoa)	½ cup cooked	Per meal
Nuts & Seeds	1 oz	Daily
Breads, Pastas, Desserts	1 serving	3x per week
Protein	1 serving <sup>†</sup>	Per meal

\*Extra virgin olive oil has antioxidant and anti-inflammatory properties which exceed many other oils.  
<sup>†</sup>Serving size is between a palm and a fist, depending on your level of exercise.

Why are Pasta and Bread with Dessert?

Most pastas and breads are made of refined grains. Highly refined grains (such as white flour) behave similarly to sugar in your body. Read your labels, choose carefully, and balance your daily choices (e.g., if you have a sandwich at lunch, skip the whole grains at that meal). If this feels like a big change to you all at once, take it a little bit at a time every week

Learn to be your own researcher to make the best treatment decisions, by being proactive and an advocate for your own health

# Abiraterone/ADT Combo Associated With High Metastasis-Free Survival Rate in Non-Metastatic Prostate Cancer

Source:  
January 11, 2022  
Matthew Fowler  
<https://www.cancer-network.com/view/abiraterone-adt-combo-associated-with-high-metastasis-free-survival-rate-in-non-metastatic-prostate-cancer>

A meta-analysis of 2 phase 3 randomized trials found that combination therapy including androgen deprivation therapy led to higher rates of metastasis-free survival for patients with high-risk non-metastatic prostate cancer.

A combination regimen consisting of abiraterone acetate and prednisolone with or without enzalutamide plus androgen deprivation therapy (ADT) was associated with higher rates of metastasis-free survival (MFS) compared with androgen deprivation therapy alone for patients with high-risk non-metastatic prostate cancer, according to results from a meta-analysis of phase 3 trials published in *The Lancet*.

A total of 180 MFS events were observed in the combination therapy groups compared with 306 events in the control groups after a median follow-up of 72 months. Of the events that took place in the combination therapy groups, 52% were deaths compared with 38% in the control groups. Six-year MFS was 82% and 69% in the combination therapy and control groups, respectively.

"[Patients] with high-risk non-metastatic prostate cancer who receive ADT with combination therapy have significantly better metastases-free survival and overall survival than those who receive ADT alone," the investigators wrote. "Two years of abiraterone and prednisolone added to ADT and, if indicated, radiotherapy should be considered a new standard treatment for non-metastatic prostate cancer with high-risk features."

The meta-analysis focused on 2 two randomized phase 3 trials conducted utilizing the Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy (STAMPEDE, MRC-PR08) platform. The first compared ADT with ADT plus abiraterone and prednisolone and the second analyzed ADT compared

with ADT plus abiraterone, prednisolone, and enzalutamide.

Eligibility criteria required patients to have confirmed prostate adenocarcinoma, a WHO performance status of 0 to 2, and no evidence of distant metastases via conventional imaging. Additionally, patients were required to have high-risk disease or be relapsing with high-risk features.

Protocol recommended that patients receive standard of care ADT for 3 years. Radiotherapy was required after randomization for node-negative patients and encouraged for node-positive patients. The combination therapy regimen consisted of abiraterone acetate at 1000 mg and prednisolone at 5 mg, with or without enzalutamide at 160 mg.

The primary end point for the meta-analysis was MFS. Some key secondary end points included overall survival (OS), cancer-specific survival, failure-free survival, progression-free survival (PFS), and toxicity.

A total of 1974 non-metastatic patients were randomly assigned within both trials, including 455 to the control group and 459 to the combination therapy group in the abiraterone trial from November 15, 2011, to January 17, 2014. In the abiraterone and enzalutamide trial, 533 patients were randomized to the control group and 527 received the combination therapy from July 29, 2014, to March 31, 2016.

The median age of patients was 68 years (IQR, 63-73) and the median prostate-specific antigen level was 34 ng/ml (IQR, 14.7-47). Additionally, 39% of patients were node positive. The median time from randomization to combination therapy initiation was 1.4 weeks (IQR, 1.0-2.7), and median time from ADT initiation to combination therapy was 8.4 weeks (IQR, 5.1-11.3).

MFS was significantly longer in the combination therapy groups (not reached [NR]; IQR, not estimable [NE]-NE) vs the control groups (NR; IQR, 97-NE; HR, 0.53; 95% CI, 0.44-0.64;  $P < .0001$ ).

A subgroup analysis of 294 MFS events in the abiraterone trial and 192 events in the abiraterone and enzalutamide trial highlighted a notable effect in both trials, respectively (abiraterone trial: HR, 0.54; 95% CI, 0.43-0.68;  $P < .0001$ ; abiraterone/enzalutamide trial: HR, 0.53, 95% CI, 0.39-0.71;  $P < .0001$ ) with no evidence of between-trial heterogeneity.

In terms of OS, a total of 147 deaths and 236 deaths in the combination therapy and control groups were observed, respectively. OS was longer in the combination therapy groups (median, NR; IQR, NE-NE) compared with the control groups (median, NR; IQR, 103-NE; HR, 0.60; 95% CI, 0.48-0.73;  $P < .0001$ ). The 6-year survival rate was 86% in the combination therapy groups compared with 77% in the control groups.

Grade 3 or higher adverse effects (AEs) during the first 24 months were observed in 29% of patients in the abiraterone trial control group and 32% of patients in the abiraterone and enzalutamide trial control group. The combination therapy groups had rates of grade 3 or higher AEs of 37% and 57% in the abiraterone trial and abiraterone enzalutamide trials, respectively.

"These results might suggest that, by preventing relapse and death from prostate cancer, patients treated with combination therapy are more likely to live longer and die from another cause," the investigators wrote.



# Terbium-161 clinical study collaboration

Theranostics is an emerging field using radioactive molecules for both the diagnosis and treatment of cancer. It is a game-changer for some patients, enabling truly personalized medicine and providing the ability to treat what you see and see what you treat.

In this first-in-class clinical trial, <sup>161</sup>Tb, a radioactive compound, will be linked to a small molecule targeting prostate specific membrane antigen (PSMA) to treat men with advanced prostate cancer. Like currently used Lutetium-177 (<sup>177</sup>Lu), <sup>161</sup>Tb emits a beta radiation that travels only a few millimeters enabling targeted killing of cancer cells. In addition, <sup>161</sup>Tb emits another type of radiation called Auger electronic which have higher linear energy transfer and travel less than the width of a single cell. Laboratory experiments have shown that <sup>161</sup>Tb is superior to <sup>177</sup>Lu by eradicating tiny, microscopic tumor deposits.

As part of this agreement, Isotopia will supply <sup>161</sup>Tb to support a first-in-human pilot study conducted by the Prostate Cancer Theranostics and Imaging Centre of Excellence (ProSTIC) at Peter Mac. Professor Michael Hofman, ProSTIC Director, said: "Peter Mac has led groundbreaking studies that show radioactive substances targeting PSMA prolong life and improve quality-of-life in men with advanced prostate cancer. This new world first clinical trial using <sup>161</sup>Tb, a next generation targeting, has the potential [to] further improve outcomes for men with prostate cancer."

Dr. Eli Shalom, CEO of Isotopia said: "We are excited to start this collaboration with the experts at Peter Mac and lay the foundation for <sup>161</sup>Tb to be used for the development of innovative radiopharmaceuticals. We are honored to work with Professor Hofman to determine the clinical advantages in comparison to <sup>177</sup>Lu-PSMA that will accelerate the development of a new generation of therapeutic isotopes to be used in targeted therapy.

Isotopia will start building its own <sup>161</sup>Tb based pipeline starting with PSMA I&T all the way from clinical trials to commercialization."

## About Peter Mac

Peter MacCallum Cancer Centre is a world-leading cancer research, education and treatment centre and Australia's only public health service solely dedicated to caring for people affected by cancer.

The Prostate Cancer Theranostics and Imaging Centre of Excellence (ProSTIC) at Peter Mac performs state-of-the-art research to deliver new paradigms for treatment of prostate cancer driven by seamless integration of clinical trials, pre-clinical and discovery research. The multi-disciplinary team includes nuclear medicine, medical oncology, radiation oncology, urology and laboratory-based doctors and research with a strong patient-centred philosophy. The Centre of Excellence is funded by a grant from the Prostate Cancer Foundation (PCF) with support from the Peter MacCallum Cancer Foundation.

## About Isotopia

Isotopia Molecular Imaging Ltd. is a collaboration between The Metrontario Group and some of Israel's leading scientists in the field of radiopharmaceuticals and sterile manufacturing. The Isotopia development team is a multidisciplinary team consisting of professional Quality Assurance, Chemists, Microbiologists, Engineers Operations and Logistics. The experienced Isotopia team, together with its GMP certified plant – by the IL MOH and US FDA – and centralized radio-nuclear pharmacy, cyclotron facility, carrier free <sup>177</sup>Lu production site, are a well-established platform for development. Isotopia creates collaborations between the scientific and medical community to further develop and experiment with new markers for imaging applications, molecular therapy and providing CMO services.

Source:

9 November 2021

<https://www.pnewsire.com/news-releases/isotopia-and-the-peter-maccallum-cancer-centre-announce-terbium-161-clinical-study>

Peter MacCallum Cancer Centre, world leading cancer research, education and treatment center and Isotopia Molecular Imaging Limited (Isotopia), a global supplier of radioisotopes for targeted therapies, have signed a clinical research and supply agreement for the medical radioisotope no-carrier-added Terbium-161 (n.c.a. Tb-161), an innovative therapeutic isotope used for targeted cancer treatment.



Source:  
[https://www.practiceupdate.com/C/121215/56?elsca1-emc\\_enews\\_to\\_pic-alert](https://www.practiceupdate.com/C/121215/56?elsca1-emc_enews_to_pic-alert)

# Electrical Pudendal Nerve Stimulation vs Pelvic Floor Muscle Training Plus Transanal Electrical Stimulation for Post-Prostatectomy Urinary Continence

## OBJECTIVE

To assess the short-term efficacy of electrical pudendal nerve stimulation (EPNS) versus pelvic floor muscle training (PFMT) plus transanal electrical stimulation (TES) for the early treatment of post-radical prostatectomy urinary incontinence (PRPUI) and explore its mechanism of action.

## SUBJECTS AND METHODS

A parallel designed randomized controlled trial was conducted at a research institute and a university hospital. Ninety-six PRPUI patients were allocated to EPNS group (64 cases) and PFMT+TES group (32 cases) and treated by EPNS and biofeedback-

assisted PFMT plus TES, 3 times a week for 8 weeks, respectively. Outcome measurements were improvement rate, scores of the International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form (ICIQ-UI SF) and the number of used diapers.

## RESULTS

After 24 treatments, the efficacy rate of 68.7% in EPNS group was significantly higher than that of 34.4% in PFMT+TES group (P=0.005). The ICIQ-UI SF score, and urine leakage amount score, diaper score, symptom and quality of life improved significantly in both groups and showed Therapy x

Treatment interaction, and the above scores in EPNS group were significantly lower than these in PFMT+TES group. Perineal ultrasonographic recordings showed that PFM movement amplitude during EPNS ( $\geq 1$ - $< 3$  mm) was similar to that during PFMT, however, PFM movement EMG amplitude was significantly higher during EPNS than during PFMT (P<0.001).

## CONCLUSIONS

EPNS is more effective than PFMT+TES in short-term (8 weeks) treatments of early urinary incontinence after radical prostatectomy. Its mechanism of action is that EPNS can excite the pudendal nerve and simulate PFMT.

Source:  
8 September 2020  
<https://www.urotoday.com/recent-abstracts/urologic-oncology/prostate-cancer/123765-identifying-prostate-surface-antigen-patterns-of-change-in-patients-with-metastatic-hormone-sensitive-prostate-cancer-treated-with->

# Identifying PSA Patterns of Change in Patients with mHSPC treated with Abiraterone & Prednisone

While most patients with metastatic hormone-sensitive prostate cancer (mHSPC) will initially respond to androgen deprivation therapy (ADT) plus abiraterone acetate with prednisone (AA/P), the majority will develop castration-resistant disease. The ability to track early prostate-specific antigen (PSA) changes may alert clinicians to those more likely to progress and initiate subsequent therapies earlier before clinical or radiographic progression develops.

Historically with ADT alone or docetaxel-based chemotherapy, a non-detectable PSA at 7 months was considered a predictor of overall survival. However, there has not been a standard time frame established for patients treated with adrenal biosynthesis inhibitors. Our results showed a significant association between the degree of PSA decline at 3 months and serologic progression in mHSPC patients treated with ADT plus AA/P. Moreover, a PSA reduction  $< 98\%$  from baseline and PSA  $> 3.0$  ng/mL at 3 months were associated with a significantly shorter castration-resistant prostate cancer (CRPC)-free survival.

These findings support evaluating response to ADT plus AA/P for mHSPC as early as 3 months after initiation of therapy. Since castration-resistant disease is associated with high morbidity and mortality, it is important to identify patients with aggressive disease early to help maintain quality of life and prevent increased exposures to the healthcare system.



# Giant Study Finds Viagra Is Linked to Almost 70% Lower Risk of Alzheimer's

Source:  
PETER DOCKRILL  
6 DECEMBER 2021

<https://www.sciencealert.com/giant-study-finds-viagra-is-linked-to-almost-70-lower-risk-of-alzheimer-s>

Usage of the medication sildenafil – better known to most as the brand-name drug Viagra – is associated with dramatically reduced incidence of Alzheimer's disease, new research suggests.

According to a study led by researchers at the Cleveland Clinic, taking sildenafil is tied to a nearly 70 percent lower risk of developing Alzheimer's compared to non-users.

That's based on an analysis of health insurance claim data from over 7.2 million people, in which records showed that claimants who took the medication were much less likely to develop Alzheimer's over the next six years of follow up, compared to matched control patients who didn't use sildenafil.

It's important to note that a associations like this – even on a huge scale – are not the same as proof of a causative effect. For example, it's possible that the people in the cohort who took sildenafil might have something else to thank for their improved chances of not developing Alzheimer's.

Nonetheless, the researchers say the correlation shown here – in addition to other indicators in the study – is enough to identify sildenafil as a promising candidate drug for Alzheimer's disease, the viability of which can be explored in future randomized clinical trials designed to test whether causality does indeed exist.

"Notably, we found that sildenafil use reduced the likelihood of Alzheimer's in individuals with coronary artery disease, hypertension, and type 2 diabetes, all of which are comorbidities significantly associated with risk of the disease, as well as in those without," explains computational biologist and senior

author of the study, Feixiong Cheng from the Cleveland Clinic.

It's not the first time sildenafil use has been linked with better health outcomes, with the drug previously showing promise in a range of different scientific contexts, including cancer and malaria research among others.

Here, Cheng's team began by building over a dozen endophenotype modules, using computational techniques to map genetic factors that could hypothetically govern the manifestation of Alzheimer's disease.

With 13 of these modules in hand, the researchers then looked at what kinds of FDA-approved drugs might hypothetically help against the identified phenotypes.

Out of over 1,600 such medications already approved by the FDA, sildenafil turned out to be one of the most promising candidates.

That might sound baffling – given the drug is so far used in the main only for treating erectile dysfunction and pulmonary hypertension – in the research community, there were already signs the sildenafil compound might have other kinds of health benefits, given its interactions with the amyloid and tau proteins implicated in Alzheimer's pathology.

"Recent studies show that the interplay between amyloid and tau is a greater contributor to Alzheimer's than either by itself," Cheng says.

"We hypothesized that drugs targeting the molecular network intersection of amyloid and tau endophenotypes should have the greatest potential for success... Sildenafil, which has been shown to significantly improve cognition and

memory in preclinical models, presented as the best drug candidate."

The hypothesis appears to be borne out by the health insurance data, with the team finding sildenafil users had a 69 percent reduced risk of Alzheimer's disease compared to non-users – a reduction that was notably stronger than other kinds of medications also investigated in the study, including losartan, metformin, diltiazem, and glimepiride.

Of course, the researchers emphasize that none of this establishes causality, but on that front there may be other promising leads.

In separate experiments studying human brain cells in vitro to explore how sildenafil might confer protection against Alzheimer's cognitive decline, the researchers observed that neurons treated with the drug showed elevated growth and reduced tau accumulation.

It's early days, but those effects could well have something to do with the reduced chances of developing Alzheimer's in the insurance cohort. To that end, it's important to follow these leads further, the team says.

"We are now planning a mechanistic trial and a phase II randomized clinical trial to test causality and confirm sildenafil's clinical benefits for Alzheimer's patients," Cheng says.

"We also foresee our approach being applied to other neurodegenerative diseases, including Parkinson's disease and amyotrophic lateral sclerosis, to accelerate the drug discovery process."

The findings are reported in [Nature Aging](#).



# MP67-19 Ductal Adenocarcinoma of the Prostate: A Systematic Review and Meta-Analysis of Incidence, Presentation and Management

Source:

[https://www.urotoday.com/conference-highlights/siu-2021/133864-siu-2021-role-of-psma-pet-in-mrtpc-and-psma-rt.html?utm\\_source=newsletter\\_9837&utm\\_medium=email&utm\\_campaign=uroalerts-oncology-daily](https://www.urotoday.com/conference-highlights/siu-2021/133864-siu-2021-role-of-psma-pet-in-mrtpc-and-psma-rt.html?utm_source=newsletter_9837&utm_medium=email&utm_campaign=uroalerts-oncology-daily)

## Context

Ductal adenocarcinoma (DAC) is relatively rare, but is nonetheless the second most common subtype of prostate cancer. First described in 1967, opinion is still divided regarding its biology, prognosis, and outcome.

## Objectives

To systematically interrogate the literature to clarify the epidemiology, diagnosis, management, progression, and survival statistics of DAC.

## Materials and methods

We conducted a literature search of five medical databases from inception to May 04 2020 according to PRISMA criteria using search terms "prostate ductal adenocarcinoma" OR "endometrioid adenocarcinoma of prostate" and variations of each.

## Results

Some 114 studies were eligible for inclusion, presenting 2 907 170 prostate cancer cases, of which 5911 were DAC. [Correction added on 16 January 2021 after the first online publication: the preceding statement has been corrected in this current version.] DAC accounts for 0.17% of prostate cancer on meta-analysis (range 0.0837%-13.4%). The majority of DAC cases were admixed with predominant acinar adenocarcinoma (AAC). Median Prostate Specific Antigen at diagnosis ranged from 4.2 to 9.6 ng/mL in the case series.

DAC was more likely to present as T3 (RR1.71; 95%CI 1.53-1.91) and T4 (RR7.56; 95%CI 5.19-11.01) stages, with far higher likelihood of metastatic disease (RR4.62; 95%CI

3.84-5.56; all P-values < .0001), compared to AAC. Common first treatments included surgery (radical prostatectomy (RP) or cystoprostatectomy for select cases) or radiotherapy (RT) for localized disease, and hormonal or chemotherapy for metastatic disease. Few studies compared RP and RT modalities, and those that did present mixed findings, although cancer-specific survival rates seem worse after RP.

Biochemical recurrence rates were increased with DAC compared to AAC. Additionally, DAC metastasized to unusual sites, including penile and peritoneal metastases. Where compared, all studies reported worse survival for DAC compared to AAC.

## Conclusion

When drawing conclusions about DAC it is important to note the heterogenous nature of the data. DAC is often diagnosed incidentally post-treatment, perhaps due to lack of a single, universally applied histopathological definition. As such, DAC is likely underreported in clinical practice and the literature. Poorer prognosis and outcomes for DAC compared to AAC merit further research into genetic composition, evolution, diagnosis, and treatment of this surprisingly common prostate cancer sub-type.

## Patient summary

Ductal prostate cancer is a rare but important form of prostate cancer. This review demonstrates that it tends to be more serious at detection and more likely to spread to unusual parts of the body. Overall survival is worse

with this type of prostate cancer and urologists need to be aware of the presence of ductal prostate cancer to alter management decisions and follow-up.

## DISCUSSION

### Recommendations and limitations

We find the increased likelihood of peritoneal metastases after treatment of ductal adenocarcinoma with radical prostatectomy to be particularly noteworthy. Is this perhaps because of the opportunity for seeding during radical prostatectomy? Compared to more peripheral AAC, peri-urethral DAC cells are more likely to extravasate from ducts into the peritoneum during urethral dissection and prostate manipulation in surgery. We hypothesize that radiotherapy or perhaps radical cystoprostatectomy may be more suitable than conventional radical prostatectomy, in avoiding this potentially iatrogenic complication. There is certainly an opportunity for assessment of this intervention and outcome in the setting of a randomized trial, although such a trial would be difficult given the relatively infrequent nature of DAC and the fact that it is often not detected until inspection of the surgical specimen, rather than at diagnostic biopsy.

Additionally, in light of increased post-operative metastatic spread with DAC, and the possibility of lower PSA production, it may be beneficial to monitor such men with imaging (MP-MRI ± Prostate Specific Membrane Antigen [PSMA]-Positron Emission Tomography [PET]) in addition to PSA.

Source:

[https://www.practiceupdate.com/c/128320/3/1/?elsca1=emc\\_enews\\_top-10&elsca2=email&elsca3=practiceupdate onc&elsca4=oncology&elsca5=newsletter&rid=NTMyMjc0MDc4NjM0S0&lid=20844139](https://www.practiceupdate.com/c/128320/3/1/?elsca1=emc_enews_top-10&elsca2=email&elsca3=practiceupdate onc&elsca4=oncology&elsca5=newsletter&rid=NTMyMjc0MDc4NjM0S0&lid=20844139)

## Bipolar Androgen Therapy vs Enzalutamide in Castration-Resistant Metastatic PCa

Written by Brian E. Lewis MD, MPH, FACP

This was a prospective phase II study wherein men with metastatic castration-resistant prostate cancer (mCRPC) who were asymptomatic and had progressed on abiraterone were randomized to receive testosterone at a dose of 400 mg every 28 days (the bipolar androgen therapy [BAT] group) or enzalutamide. Upon progression, patients received the opposite therapy, and PSA response was again evaluated. There was a 50% PSA reduction in 28.2% of men on BAT therapy compared with 25.5% of men taking enzalutamide. There was similar progression-free survival of 5.7 months in the two arms, and overall survival of 32.9 and 29 months in the BAT arm and enzalutamide arm, respectively. Interestingly, 77.8% of patients who received BAT followed by enzalutamide had a PSA50 response compared with 21.3% among those who received BAT after enzalutamide. The patients who underwent BAT followed by enzalutamide also had an improved progression-free survival response of 28.2 months versus 19.6 months with enzalutamide followed by BAT.

It is interesting that patients who received BAT prior to enzalutamide seemed to continue to respond or to have renewed response to enzalutamide. This suggests that BAT may “re-sensitize” prostate cancer cells to next-generation hormonal therapies.

Source:  
December 2021

[https://www.researchgate.net/publication/357031937\\_Real-world\\_first-line\\_systemic\\_therapy\\_patterns\\_in\\_metastatic\\_castration-resistant\\_prostate\\_cancer](https://www.researchgate.net/publication/357031937_Real-world_first-line_systemic_therapy_patterns_in_metastatic_castration-resistant_prostate_cancer)

## Real-World First-Line Systemic Therapy Patterns in Metastatic Castration-Resistant PCa

Several systemic therapies have demonstrated a survival advantage in metastatic castration resistant prostate cancer (mCRPC). Access to these medications varies significantly worldwide. In Australia until recently, patients must have received docetaxel first, unless unsuitable for chemotherapy, despite no evidence suggesting superiority over androgen receptor signalling inhibitors (ARSIs). Our study investigated real-world systemic treatment patterns in Australian patients with mCRPC.

The electronic CRPC Australian Database (ePAD) was interrogated to identify mCRPC patients. Clinicopathological features, treatment and outcome data, stratified by first-line systemic therapies, were extracted. Comparisons between groups utilised Kruskal-Wallis

tests and Chi-Square analyses. Time-to-event data were calculated using Kaplan-Meier methods and groups compared using log-rank tests. Factors influencing overall survival (OS) and time to treatment failure (TTF) were analysed through Cox proportional hazards regression models. We identified 578 patients who received first-line systemic therapy for mCRPC. Enzalutamide (ENZ) was most commonly prescribed (n = 240, 41%), followed by docetaxel (DOC, n = 164, 28%) and abiraterone (AA, n = 100, 17%). Patients receiving ENZ or AA were older (79, 78.5 years respectively) compared with DOC (71 years, p = 0.001) and less likely to have ECOG performance status 0 (45%, 44%, 59% in ENZ, AA and DOC groups respectively p < 0.0001). Median TTF was significantly higher in those receiving ENZ (12.4 months) and AA (11.9

months) compared to DOC (8.3 months, p < 0.001). PSA50 response rates and OS were not statistically different.

Time to developing CRPC > 12 months was independently associated with longer TTF (HR 0.67, p < 0.001) and OS (HR 0.49, p = 0.002). In our real-world population, ENZ and AA were common first-line systemic therapy choices, particularly among older patients and those with poorer performance status. Patients receiving ENZ and AA demonstrated superior TTF compared to DOC, while OS was not statistically different. Our findings highlight the important role of ARSIs, given the variability of access worldwide.

The Walter and Eliza Hall Institute of Medical Research.



# Cancer Breakthrough: Exercise May Stop Disease in its Tracks

Forget bedrest: ECU research has shown exercise may be a key weapon in cancer patients' battle against the disease.

Source:  
05 Oct 2021  
<https://www.ecu.edu.au/newsroom/articles/research/cancer-breakthrough-exercise-may-stop-disease-in-its-tracks>

Exercise causes muscles to secrete proteins called myokines into our blood – and researchers from ECU's Exercise Medicine Research Institute have learned these myokines can suppress tumour growth and even help actively fight cancerous cells.

A clinical trial saw obese prostate cancer patients undergo regular exercise training for 12 weeks, giving blood samples before and after the exercise program.

Researchers then took the samples and applied them directly onto living prostate cancer cells.

Study supervisor Professor Robert Newton said the results help explain why cancer progresses more slowly in patients who exercise.

"The patients' levels of anti-cancer myokines increased in the three months," he said.

"When we took their pre-exercise blood and their post-exercise blood and placed it over living prostate cancer cells, we saw a significant suppression of the growth of those cells from the post-training blood.

"That's quite substantial indicating chronic exercise creates a cancer suppressive environment in the body."

## A formidable team

PhD candidate and research lead Jin-Soo Kim said while myokines could signal cancer cells to grow slower – or stop completely – they were unable to kill the cells by themselves.

However, he said myokines can team up with other cells in the blood to actively fight cancer.

"Myokines in and of themselves don't signal the cells to die," Mr Kim said.

"But they do signal our immune cells – T-cells – to attack and kill the cancer cells."

Professor Rob Newton.

Professor Newton said exercise also complements other prostate cancer treatments such as androgen deprivation therapy, which is both effective and commonly prescribed but can also lead to significant reduction in lean mass and an increase in fat mass. This can result in sarcopenic obesity (being obese with low muscle mass), poorer health and cancer outcomes.

All study participants were undergoing ADT and were obese, with the training program seeing them maintain lean mass while losing fat mass.

## A fighting future

The study focused on prostate cancer due it being the most common non-skin cancer among men and the high number of patient fatalities – however Professor Newton said the findings could have a wider impact.

"We believe this mechanism applies to all cancers," he said.

ECU is carrying out further studies, including a trial where patients with advanced-stage prostate cancer are put through a six-month exercise program.

Though results are still pending, Professor Newton said preliminary findings were encouraging.

"These men have high disease burden, extensive treatment side-effects and are very unwell, but they still can produce anti-cancer medicine from within.

"It's important as it may indicate why men even with advanced cancer, if they're physically active, don't succumb as quickly."

'Myokine expression and tumour-suppressive effect of serum following 12 weeks of exercise in prostate cancer patients on ADT' was published in *Medicine and Science in Sports and Exercise*.

# Large International Evaluation Reveals AI Accurately Diagnoses Prostate Cancer



Researchers at Karolinska Institutet in Sweden have together with international collaborators completed a comprehensive international validation of artificial intelligence (AI) for diagnosing and grading prostate cancer. The study, published in *Nature Medicine*, shows that AI systems can identify and grade prostate cancer in tissue samples from different countries equally well as pathologists. The results suggest AI systems are ready to be responsibly introduced as a complementary tool in prostate cancer care, researchers say.

The international validation was performed via a competition called PANDA. The competition lasted for three months and challenged more than 1000 AI experts to develop systems for accurately grading prostate cancer.

“Only ten days into the competition, algorithms matching average pathologists were developed. Organising PANDA shows how competitions can accelerate rapid innovation for solving specific problems in healthcare with the help of AI,” says Kimmo Kartasalo, a researcher at the Department of Medical Epidemiology and Biostatistics at Karolinska Institutet and corresponding author of the study.

A problem in today’s prostate cancer diagnostics is that different pathologists can arrive at different conclusions even for the same tissue samples, which means that treatment decisions are based on uncertain information. The researchers believe the use of AI technology holds great potential for improved reproducibility, that is, increased consistency of the assessments of tissue samples irrespective of which pathologist performs the evaluation, leading to more accurate treatment selection.

## Accurate diagnostics

The KI researchers have shown in earlier studies that AI systems can indicate if a tissue sample contains cancer or not, estimate the amount of tumour tissue in the biopsy, and grade the severity of prostate cancer, comparably to international experts. However, the main challenge associated with implementing AI in healthcare is that AI systems are often highly sensitive towards data that differ from the data used for training the system, and may consequently not produce reliable and robust results when applied in other hospitals and other countries.

“The results from PANDA show for the first time that AI systems can produce an equally accurate diagnosis and grading of prostate cancer in an international setting as human pathologists. The next step is controlled studies for evaluating how to best introduce AI systems in patient care,” says Martin Eklund, associate professor at the Department of Medical Epidemiology and Biostatistics at Karolinska Institutet and the last author of the study.

“Future studies should also include a larger variety of rare but unusually challenging biopsies as well as samples from countries with more varied ethnicity and demographics,” he continues.

## Not a replacement for human experts

AI-based assessment of prostate cancer biopsies has the potential to improve diagnostic quality and thus ensure more consistent and equal care for the patients, at a lower cost.

“The idea is not for AI to replace human experts, but rather to function as a safety net to avoid pathologists missing cancer cases and to help in standardising the assessments. AI can also be an option in those parts of the world that today completely lack pathology expertise,” says Lars Egevad, professor at the Department of Oncology-Pathology at Karolinska Institutet and one of the experts on prostate pathology who co-authored the study.

The study was performed in collaboration with colleagues from Radboud University Medical Center in the Netherlands, Google Health in the USA and the University of Turku in Finland. It was financed by the Swedish Research Council, the Swedish Cancer Society and the Swedish Prostate Cancer Federation, among others. Several authors have industry connections and patents related to prostate cancer diagnostics or machine learning for medical images, and some have received monetary compensation from companies. Full disclosure of potential conflicts of interest can be found in the scientific article.

Source:  
13 January 2022

<https://www.sciencedaily.com/releases/2022/01/220113111518.htm#:~:title=01%2F220113111518.htm:Researchers%20have%20completed>

Learn to be your own researcher to make the best treatment decisions, by being proactive and an advocate for your own health



# Study provides New Insights into Molecular Drivers of Treatment Resistance in Prostate Cancer

*"Prostate cancer, even metastatic disease, responds well to androgen deprivation treatment, but tumors almost always recur."*

Dominic Smiraglia, PhD, co-senior author and study leader, Associate Professor of Oncology, Department of Cell Stress Biology, Roswell Park

An international research team co- led by scientists at Roswell Park Comprehensive Cancer Center and The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute has identified an important accelerator of treatment-resistant prostate cancer. The study, published today in *Cell Reports*, provides insight into how loss or mutation of the NCOR2 gene accelerates the progression of prostate cancer to a more lethal form of the disease.

Standard prostate cancer treatment uses drugs that target and block the androgen receptor, a protein that binds to male hormones to drive the development of cancer cells in the prostate. Blocking this driving force is highly effective, at least initially. Unfortunately, the benefits of androgen-deprivation therapy are often short-lived. Prostate cancer is the second leading cause of cancer deaths among men, primarily because many patients with aggressive forms of the disease eventually experience progression or recurrence despite treatment. There is a need for new insights into the mechanisms of prostate cancer recurrence, which are multiple and complex, in order to develop new therapeutic targets.

To better understand the molecular

drivers of treatment resistance, a team of researchers co- led by Dr. Smiraglia and Moray Campbell, PhD, Associate Professor of Pharmaceutics and Pharmacology at The Ohio State University College of Pharmacy and member of the OSUCCC – James Molecular Carcinogenesis and Chemoprevention Research Program, set out to examine the role of NCOR2 (which stands for nuclear receptor corepressor 2/silencing mediator for retinoid and thyroid hormone receptors), a gene that is mutated in some prostate cancers, in the development and progression of treatment-resistant cancer.

"A role for NCOR2 in prostate cancer has been proposed for a long time, and the current study is the first to ask where it binds in the genome, what genes it regulates and how this impacts the effectiveness of androgen deprivation therapy," says Dr. Campbell.

Analyzing clinical samples from 707 men with primary, nonmetastatic prostate cancer, the researchers found that reduced expression of NCOR2 was significantly associated with increased levels of serum prostate specific antigen (PSA), an indicator of prostate cancer progression. A subset of 136 men received androgen-deprivation therapy, and among these men, those with higher levels of NCOR2 were significantly less likely to experience a rise in PSA levels than

men with low expression of this gene.

The scientists then reduced NCOR2 expression in a preclinical laboratory model of prostate cancer and found that disease recurrence after androgen-deprivation therapy was accelerated. Genetic and epigenetic changes traditionally associated with cancer were also observed, including increased DNA hypermethylation, suggesting that this gene rewires the epigenome to make prostate cancer cells more resistant to androgen therapy.

"In all of our analyses, we found that loss of NCOR2 not only accelerated prostate cancer recurrence but also induced a shift in cellular identity to neuroendocrine prostate cancer, which is a more lethal form of the disease," says Dr. Smiraglia.

The faster time to recurrence upon loss of NCOR2 suggests that a reduction in this protein could make some cells resistant to the effects of androgen depletion and opens a new avenue for specific treatments targeting this molecule.

Co-first authors of the study, "Reduced NCOR2 expression accelerates androgen deprivation therapy failure in prostate cancer, are Mark Long, PhD, an Assistant Professor of Oncology in Biostatistics & Bioinformatics at Roswell Park, and Justine Jacobi, a predoctoral trainee in Dr. Smiraglia's lab.

Source:  
14 December 2021

<https://www.news-medical.net/news/20211214/Study-provides-new-insights-into-molecular-drivers-of-treatment-resistance-in-prostate-cancer.aspx#:~:text=Solove%20Research%20Institute%20has%20identified,lethal%20form%20of%20the%20disease>

Source:  
ASCO 2021

<https://www.urotoday.com/conference-highlights/asco-2021/asco-2021-prostate-cancer/130101-asco-2021-decreased-fracture-rate-by-mandating-bone-protecting-agents-in-the-eortc-1333-peaceiii-trial>

# Decreased Fracture Rate by Mandating Bone Protecting Agents in the EORTC 1333/PEACEIII Trial

ASCO 2021: Decreased Fracture Rate by Mandating Bone Protecting Agents in the EORTC 1333/PEACEIII Trial Combining Ra223 with Enzalutamide Versus Enzalutamide Alone: An Updated Safety Analysis

Beginning with the introduction of docetaxel for metastatic castration resistant prostate cancer (mCRPC) in 2004, there has been a dramatic and rapid proliferation of systemic therapy options in advanced prostate cancer including a number of novel hormonal therapies (including abiraterone acetate and enzalutamide), second-line chemotherapy (cabazitaxel), bone-targeting agents (radium-223) and other targeted agents (including olaparib, rucaparib, and pembrolizumab), each of which has proven survival benefits.

In addition to these treatments, it is recognized that both androgen-deprivation therapy for prostate cancer and metastatic disease itself is associated with risk of fracture, due to the osteoporotic events and skeletal-related events, respectively. Bone protective agents, with differing doses for these differing indications, may reduce both bone loss and skeletal-related events.

For patients treated with androgen deprivation therapy and an androgen receptor pathway inhibitor, up to 11% of patients may have fragility or osteoporotic fractures and up to 40% of patients may have disease-related skeletal-related events. As a result, guidelines routinely recommend bone protective agents.

As suggested by the success of monotherapy in mCRPC, there has been interest in combination therapies. The ERA-223 trial of abiraterone acetate and radium-223 was launched. However, the trial was unblinded prematurely due to a higher-than-expected rate of fractures and deaths with the combination approach.

Additionally, in the ERA-223 trial, most fractures occurred at sites without evidence of metastatic disease, suggesting an osteoporotic mechanism. Further, use of bone protective agents at study entry was low in this cohort

(40%). However, post hoc analyses suggested that bone protective agents reduced fractures in both the experimental and control arms. In parallel to the ERA-223 trial, the randomized phase III EORTC-1333-GUCG (NCT02194842) trial compares enzalutamide vs. a combination of Radium 223 and enzalutamide in men with asymptomatic or mildly symptomatic metastatic castration resistant prostate cancer (mCRPC).

As noted above, ERA-223 (NCT02043678) was prematurely unblinded in November 2017 due to a significant increase in the rate of fractures in the combination of abiraterone and radium-223. This led to an amendment in the EORTC-1333-GUCG trial to mandate use of bone protecting agents (BPA).

As skeletal fractures, pathological or not, are a frequent and underestimated adverse event of systemic treatment of advanced prostate cancer, the authors sought to assess whether this mandated use of BPA (zoledronic acid or denosumab) would mitigate the risk of fractures in this patient population was unclear. Building on preliminary data previously reported, in the Prostate, Testicular, and Penile Oral Abstract Session at the 2021 American Society of Clinical Oncology 2021 Annual Meeting held on Tuesday, June 8th, 2021, Dr. Gillessen presented updated safety results from the EORTC 1333 / PEACE III trial of radium-223 and enzalutamide, specifically examining the effect of mandated bone protective agents on fracture risk with longer follow-up.

As of the data cut-off of January 28, 2021, the EORTC-1333-GUCG trial had enrolled 253 patients in total of whom 134 were enrolled after BPA were mandated and 119 who were enrolled prior. Patients were randomized as planned to enzalutamide + radium-223 or enzalutamide alone.

In this analysis focusing on skeletal safety, the authors estimated the fracture rate using the cumulative incidence method in the safety population of 237 (122 after making BPA mandatory) treated patients. The

authors used competing risk models utilizing death in absence of fracture as competing event with time-to-event models using censoring at last follow-up.

Utilization of BPA was significantly increased by the amendment: among those in the combination enzalutamide + radium-223 arm, overall use of 69.5% and use after the amendment was 95.2%. Similarly, overall use in the enzalutamide arm was 73.1% with 95% of patient enrolled after the amendment receiving BPA. Notably, 13.6% of those in the combined arm and 21.8% in the enzalutamide alone arm were not receiving BPA at enrollment but initiated treatment during the on-protocol treatment with 55.9% and 51.3%, respectively, receiving BPA since study entry. With a median follow-up of 36.7 months in patients prior to the amendment mandating BPA and 23.1 months among those patients receiving BPA, a total of 39 patients reported a fracture. The vast majority of these events (30 patients: 20 in the enzalutamide + radium-223 and 10 in the enzalutamide only arm) occurring in patients not receiving BPA while 9 events occurred on those receiving BPA (4 of which occurred in patients receiving enzalutamide and radium-223).

The cumulative incidence of fracture was similar among patients who received BPA (with a numerically lower incidence among those receiving the combination of enzalutamide and radium-223) while, among those who did not receive BPA, rates of fractures were higher in patients receiving the combination of enzalutamide.

This updated analysis of the EORTC-1333-GUCG trial demonstrates evidence of effect modification for the risk of fracture with the combination of enzalutamide and radium-223: without BPA, this risk increased while, with BPA, the cumulative incidence is very low for patients treated with either combination therapy or enzalutamide alone. This analysis further emphasizes the importance of administering bone protective agents to prevent skeletal complications.

## PCa Clinical Trials & Studies

For Further information on current and recruiting trials visit:

<https://www.anzup.org.au/content.aspx?page=prostatecancertrialdetails>

Psma Intensity Can be Altered by Androgen and Phospho-SrC Obstruction

Trial ID NCT04925648  
Phase 2  
Anticipated Start Date 18/10/21

Location  
Kingshorn Cancer Centre, St Vincent's Sydney  
Peter Mac Melbourne

The study's purpose is to understand the appearance of your prostate-specific membrane antigen (PSMA) PET scan after you take 14 days of treatment with a drug called dasatinib alone or in combination with anti-testosterone drug call darolutamide.

Who is it for? You may be eligible to join this study if you have metastatic prostate cancer and had a recent PSMA scan showing low PSMA uptake

Study Details:

Participants will receive dasatinib 100 mg daily or dasatinib 100 mg daily and darolutamide 600 mg twice daily for 14 days. They will undergo another PSMA PET scan after 14 days. Participants will be followed up on day 7 of treatment and 30 days after treatment.

It is hoped that this research will provide insight into the mechanism of PSMA expression in advanced prostate cancer.

Like all treatment decisions, you have to weigh how you feel about the potential benefits against the potential risks. No one

## Prostate Heidelberg Cancer Support Group Meetings

UPFRONTPSMA

A Randomised Phase 2 Study of Sequential 177Lu-PSMA617 and Docetaxel Versus Docetaxel in Metastatic Hormone-Naive Prostate Cancer

Protocol No 18/047

Patients with a diagnosis of de novo high-volume mHNPc who meet all the inclusion and exclusion criteria will be eligible for participation in this study.

Associate Professor Arun Azad (Principal Investigator) & Professor Michael Hofman (Nuclear Medicine Investigator)

140 participants

Further Information: [ClinicalTrials.gov](https://ClinicalTrials.gov):

PHCSG organizes specialists and consultants to speak to members on a regular basis.

Details to follow

## Internet Resources

Members have found the following websites useful

Prostate Cancer Foundation of Australia for guides & help  
<https://www.pcfa.org.au>  
<https://onlinecommunity.pcfa.org.au/>

Australian Cancer Trials  
Information on clinical trials  
<https://www.australiancancertrials.gov.au>

USA Prostate Cancer Foundation (Guide) PDF guide for men newly diagnosed with PC  
<https://www.pcf.org/guide/>

Us TOO International PCa Education (USA) USA PC support groups' information & newsletter  
<https://www.ustoo.org>

Cancer Council Victoria for general support services  
<https://www.cancervic.org.au>

ExMed Cancer Program  
Melbourne based 'best practice' exercise medicine program  
<https://www.exmedcancer.org.au>

ProstMate (PCFA) A companion to record PC results

Beyond Blue for help with depression and anxiety  
[HELPLINE 1300 22 4636](https://www.beyondblue.org.au)

Continence Foundation of Australia for assistance with incontinence aids  
[HELPLINE 1800 33 0066](https://www.cfau.org.au)

PCRI Prostate Digest (USA)  
Prostate Cancer Research Institute supporting research and disseminating information to educate and empower patients, families and the medical community  
<https://pcri.org/insights-newsletter>

PAACT Newsletter (USA) Patient Advocates for Advanced Cancer Treatments  
<http://paact.help/newsletter-signup/>

A Touchy Subject  
<https://www.youtube.com/channel/UCdyuxGuAuCWJbe-kZvwVSzQ>

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Mike Waller Convener  
Max Shub Co-Facilitator  
Spiros Haldas Library  
David Bellair Web Site  
Michael Meszaros Welfare Officer  
Sue Lawes Secretary/Newsletter

## PHCSG Meetings 2022 10am – 12:30pm

Tues 15 Feb  
Tues 15 March  
Tues 19 April  
Tues 16 May  
Tues 21 June  
Tues 19 July  
Tues 16 August  
Tues 20 September  
Tues 18 October  
Tues 15 November  
Tues 13 December (the second Tues to avoid the week prior to Xmas. Includes Xmas lunch – subject to COVID restrictions)

The internet is a good source for research but it should not be trusted to give you answers for your personal care. Always speak to your doctor to clarify any medical advice.

Disclaimer: Information in this newsletter is not intended to take the place of medical advice. Please ask your doctor to clarify any details that may be related to your treatment. PHCSG have no liability whatsoever to you in connection with this newsletter.

## 2022 PHCSG

### Articles

If you have any feedback or wish to include articles on specific aspects of Prostate Cancer please contact Sue at:

[prostateheidelberg@gmail.com](mailto:prostateheidelberg@gmail.com)

#### January 2022

- Links between Gut Microbiome & Aggressive PCa
- Rapid PCa Screening Kits
- How Much Should You Eat?
- Abiraterone/DT Combo Associated with High Metastasis-Free Survival Rate
- Terbiom-161 Clinical Study Collaboration
- Electrical Pudendal Nerve Stimulation vs Pelvic Floor Muscle Training
- Identifying PSA Patterns in mHSPC Treated with Abiraterone & Prednisone
- Viagra Linked to Lower Risk of Alzheimer's
- Ductal Adenocarcinoma
- BAT vs Enzalutamide in MCRPC
- Systemic Therapy Patterns in MCRPC
- Exercise May Stop Disease in its Tracks
- AI Accurately diagnoses PCa
- New Insights into Molecular Drivers of Treatment Resistance in PCa
- Decreased Fracture Rate by Mandating Bone Protecting Agents

Disclaimer: Information in this newsletter is not intended to take the place of medical advice. Please ask your doctor to clarify any details that may be related to your treatment. PHCSG have no liability whatsoever to you in connection with this newsletter.

# 2021 PHCSG Articles

If you have any feedback or wish to include articles on specific aspects of Prostate Cancer please contact Sue at:

[prostateheidelberg@gmail.com](mailto:prostateheidelberg@gmail.com)

## January 2021

- Exercise Infographic
- Sexual Dysfunction & Shared Decision Making
- FDA Approves first Oral Hormone Therapy
- Prolonged ADT Reduces Cardio Fitness
- Reducing the Burden of Out-of-Pocket Expenses
- BAT Sensitizes CRPCa to Subsequent Therapy
- Targeting Bone Mets with Radiation in Oligorecurrent Men
- Prostate Cancer Trials
- PEACE V-STORM
- UpFront PSMA Phase II
- NINJA

## February 2021

- Advantages of Coffee
- Our Biological Clock
- Statins tied to Better Outcomes
- What's New in Inflammation
- New PC Management Techniques
- About the Patch Trial
- Eating a Colourful Diet
- Dose Painting
- Advancement in Focal Therapy
- Prostate Cancer Trials
- Enza-P
- DASL-HiCaP Trial
- Lu-177-PSMA-617
- Adding Apalutamide to Radiotherapy & LHRH Agonist

## March 2021

- Challenging Your Private Health Provider
- How Research is Prioritised – Norman Swan podcast
- Metastatic PCa – Don't Accept Complacency
- An mRNA Vaccine for Cancer
- Life After Treatment – Wellness Program
- Focal Therapy – If It Sounds Too Good to be True
- Immune Checkpoints on CTCs

## April 2021

- Study finds cancer cells evade chemo by going dormant
- High Risk Localised PCa: Changing the rules
- Automated Pathological Assessment of PCa Biopsy Slides
- Final Results from TITAN Study
- SBRT for High Risk Patients
- Benefit of taking 1year of ADT after

- radiation for high risk PCa
- Novel Radiopharmaceutical beats Cabazitaxel in MCRPC
- Novartis announces phase III positive results
- Estrogen – Our Sister Hormone
- Prostate Cancer Trials
- Enzalutamide With Lu PSMA-617 Versus Enzalutamide Alone
- Darolutamide Augments Standard Therapy for Localised Very High-Risk Cancer

## May 2021

- Full on Kitchen Sink for High Risk Localized PCa
- Calcium & Vitamin D Supplements
- Favourable prognosis with adjuvant ADT after RT
- Healthy Lifestyle may offset Genetic Risk
- Additional Treatment Option
- New Type of Treatment could reawaken Immune Response
- Penile Rehabilitation
- Prostate Cancer Trial Results

## June 2021

- Dry July
- Breakthrough in Disease resistance to drugs
- PyL PSMA Pet Imaging
- Does the level of your Testosterone matter when on ADT?
- Stay Bone-Healthy
- ADT and the risk of Cardiovascular Disease
- The Pros & Cons of Orchiectomy
- Risk of Serial Biopsies
- Reflections on 10 years on AS
- Improvements on Oligo-recurrent Therapies
- Time Pressure Decisions
- Research making Chemo Friendlier
- Trial Results on Exercise

## July 2021

- Ground Breaking Early Cancer Detection
- What Should You Eat
- ADT What You Really Need to Know
- Anti Androgen Therapy
- Overall Survival with Metachronous MHSPC
- New Guidelines for Salvage Radiation
- Help for ED after RP
- Germline Testing
- Prostate Cancer Trials
- Enz-P; DASL HiCaP; NINJA; Upfront PSMA
- 45 & Up Study Results

## August 2021

- Targeting PSMA
- What is the Role of Modern Imaging
- Observation Vs SBRT for Oligometastatic PC
- Combined High-dose Salvage RT & HT in Oligorecurrent Pelvic Nodes
- Long Term Urinary & Erectile Function following RP
- Bone Resorption Inhibitors
- RT After RP
- Take Responsibility
- Prostate Cancer Trials
- UpFront PSMA & MOSES Study

## September 2021

- Targeting PSMA
- PEEK Study
- Skeletal Events & Bone Modifying Agents in Castration Resistant PC

- Abiraterone +docetaxel+ADT for Newly Diagnoses Metastatic PC
- Brief, Intense Radiation & Hormone Therapy for Very High Risk PCa
- Progression-directed Therapy for Oligoprogression
- Insights into PC metabolism
- Diagnostic Accuracy of PSMA 18F-DCFPyl PET/CT
- Risk of PC in relatives of PC
- Relugolix – Expected to Alter Treatment
- Whole-pelvic radiation Therapy for High-Risk Patients
- It's time to Retire a Common Biopsy
- Cognitive Function / Marital Status & PC Incidence
- Covid Passports
- Medical Bills: Out of Pocket Costs
- Prostate Cancer Trials
- UpFront PSMA & ENZA

## October 2021

- Continuous vs Intermittent ADT
- Predict Risk Tool
- Doubling Time Tool
- High Discontinuation Rate in AS
- AI Program Helps Detect PCa
- Plant Based Diet
- Obesity Ups MCRPCa Survival
- Impact of Hypofractionated RT on Patient Outcomes
- Controversy Around Testosterone Therapy
- Medications for ADT Hot Flashes
- Best Way to recover Urinary Continence after PR
- Diabetic Risk & ADT
- Abiraterone for NMPC
- When to Use Chemo

## November 2021

- New PCa drug helping men live longer
- What predicts who goes on continuous vs intermittent ADT
- Gut Bugs can drive PCA growth & resistance
- Exception to early salvage radiation
- PCa Urine Test
- New Strategy against Treatment resistant PCa
- Blood Test may help treat PCa
- Prostate Cancer Studies
- Caregiver Health Literacy/Supportive Care Program/access to Nutrition Info
- Optimal Dietary & Exercise

## December 2021

- PCa Thwarted by Gut Microbiota
- Exercise is Medicine
- Giving Cancer a "Brown-Out"
- Wake Up! It's Time to Address Sleep Issues
- The Complex Natural Biochemistry of a Healthy Diet
- ADT: What You Really Need to Know
- Andropause and the Treatment Nobody Talks About
- Unlocking the Secrets of Sleeping Cancer Cells
- Treatment-Related Regret
- New PCa Treatment Could Improve Outcomes for Advanced Patients
- PCa Trials – Recruiting

Disclaimer: Information in this newsletter is not intended to take the place of medical advice. Please ask your doctor to clarify any details that may be related to your treatment. PHCSG have no liability whatsoever to you in connection with this newsletter.