Prostate Heidelberg Cancer Support Group

Prostate Heidelberg

August 2022 Issue 221

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

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 face-to-face PHCSG Meeting
Tuesday 16 August 10am – 12:30pm

To join via Zoom: Copy link and paste into your browser
https://us02web.zoom.us/j/84431700940?pwd=WVJ0VmJTbGlhV2N6bmFHZVpPNlZ1QT09

Contents

MEMBERSHIP

HALF CALENDAR YEAR PHCSG MEMBERSHIP (July – Dec) $10

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 Guest Speaker – Tues 16 August

Professor Avni Sali AMMBBS, PhD, FRACS, FACS, FACNEM

Professor Avni Sali AM is often referred to as the father of Integrative Medicine in Australia. In 1996 he was the Founding Head of the Graduate School of Integrative Medicine at the Swinburne University in Melbourne. In 2009 he established the not-for-profit, charitable **National Institute of Integrative Medicine (NIIM)**, and became its founding Director. In the past he was also Head of the University of Melbourne Department of Surgery at Heidelberg Hospital.

Member News

Vale Dame Olivia Newton-John

Dame Olivia Newton-John touched the lives of many people across Australia and the world, but none more so than the cancer services staff and patients at the Olivia Newton-John Centre, who she encouraged, inspired and supported every day.

Olivia was a driving force to combat cancer, for treating the whole person and looking after their mind, spirit and body.

Since the ONJ Centre opened, thousands of cancer patients have gone through the doors and accessed the world-leading cancer services. Olivia's dream was supporting people with cancer through supportive wellness therapies. She found them so helpful for her journey that she wanted everyone to have access to them.

A memorial service is being planned so that staff, patients and their families can pay their respects to Olivia. More details will be provided soon.

Tim Baker -- *Patting the Shark*

Some of you may have seen Tim Baker's article, '*Farewell, Old Friend'*, in the July 30-31 issue of *The Weekend Australian Magazine* (paywalled). In it, he describes in very blunt terms his experience with hormone treatment following diagnosis in July 2015 at the age of fifty with stage 4, metastatic prostate cancer. It is a powerful, graphic piece, foreshadowing his book, '*Patting the Shark'*, that documents his journey learning to live well with prostate cancer. Tim also blogs for the PCFA (e.g. https://www.pcfa.org.au/news-media/news/weekly-blog-not-all-super-heroes-wear-capes/

Tim Baker is an award-winning surf writer and author. Patting the Shark – A Surfer's Journey, Learning to Live Well with Cancer (Ebury Australia, $34.99), Paperback. Also available as Ebook & Audiobook.

WELCOME TO

theLONGrun

Prostate Cancer Foundation of Australia

The Long Run aims to raise awareness and funds to help men survive prostate cancer.

All it takes is what you've got - run, walk or wheel 72km in September and collect donations and rewards along the way.

Every kilometre you cover will help end the pain of prostate cancer.

Together we can help make prostate cancer history.

https://www.thelongrun.org.au/register/the-long-run-2022

Prostate Heidelberg Cancer Guest Speakers

Tues 18 October 2022 TBA

Tues 13 December 2022

Ashley Bigaran – Exercise Physiologist Austin

Ashley presently holds a position with the Baker Heart and Diabetes Institute Sports Cardiology team as their AEP and research assistant. Ashley is currently pursuing her PhD and will be exploring the factors contributing to exercise intolerance in cancer patients.

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

Prostate Cancer Cases Risk Being Detected Too Late Due to Misleading Focus on Urinary Problems

SOURCE:
3 August 2022
University of Cambridge
https://www.sciencedaily.com/releases/2022/08/220803203926.htm?utm_medium=email&utm_source=rasa_io&utm_campaign=newsletter

Men with early, curable stages of prostate cancer are missing opportunities to have their cancer detected because national guidelines and media health campaigns focus on urinary symptoms despite a lack of scientific evidence, say experts at the University of Cambridge.

Prostate cancer is the most common type of cancer in men. According to Cancer Research UK, over 52,000 men are diagnosed with prostate cancer each year and there are more than 12,000 deaths.

Over three-quarters (78%) of men diagnosed with the disease survive for over ten years, but this proportion has barely changed over the past decade in the UK, largely because the disease is detected at a relatively late stage. In England, for example, nearly half of all prostate cancers are picked up at stage three of four (stage four being the latest stage).

Despite no evidence of a link between urinary symptoms and prostate cancer, national guidelines, health advice and public health campaigns continue to promote this link. In a review published today in *BMC Medicine*, Cambridge researchers argue that not only is this unhelpful, but it may even deter men from coming forward for early testing and detection of a potentially treatable cancer.

"When most people think of the symptoms of prostate cancer, they think of problems with peeing or needing to pee more frequently, particularly during the night," said Vincent Gnanapragasam, Professor of Urology at the University of Cambridge and an Honorary Consultant Urologist at Addenbrooke's Hospital, Cambridge. "This misperception has lasted for decades, despite very little evidence, and it's potentially preventing us picking up cases at an early stage."

Prostate enlargement can cause the urinary problems often included in public health messaging, but evidence suggests that this is rarely due to malignant prostate tumours. Rather, research suggests that the prostate is *smaller* in cases of prostate cancer. A recent study -- the UK PROTECT trial -- even went as far as to say that a lack of urinary symptoms may in fact be an indicator of a higher likelihood of cancer.

Screening programmes are one way that cancers are often detected at an early stage, but in the case of prostate cancer, some argue that such programmes risk overwhelming health services and leading to men being treated for relatively benign disease.

Testing for prostate cancer involves a blood test that looks for a protein known as a prostate-specific antigen (PSA) that is made only by the prostate gland; however, it is not always accurate. PSA density is significantly more accurate than PSA alone in predicting a positive biopsy and is used in everyday clinical practice.

The researchers point to evidence that there is a misconception that prostate cancer is always symptomatic: a previous study found that 86% of the public associated prostate cancer with symptoms, but only 1% were aware that it could be asymptomatic.

"We urgently need to recognise that the information currently given to the public risks giving men a false sense of security if they don't have any urinary symptoms," said Professor Gnanapragasam.

"We need to emphasise that prostate cancer can be a silent or asymptomatic disease, particularly in its curable stages. Waiting out for urinary symptoms may mean missing opportunities to catch the disease when it's treatable.

"Men shouldn't be afraid to speak to their GP about getting tested, and about the value of a PSA test, especially if they have a history of prostate cancer in their family or have other risk factors such as being of Black or mixed Black ethnicity."

The researchers say they are not advocating for an immediate screening programme, and acknowledge that changes in messaging could mean more men approaching their GPs for a PSA test, potentially resulting in unnecessary investigations and treatment. However, they argue that there are ways to reduce the risk of this happening. These include the use of algorithms to assess an individual's risk and whether they need to be referred to a specialist, and for those who are referred, MRI scans could help rule out 'indolent' (mild) disease or negative findings, reducing the risks of an unnecessary biopsy.

"We're calling on organisations such as the NHS, as well as patient charities and the media, to review the current public messaging," said Professor Gnanapragasam.

"If men were aware that just because they have no symptoms doesn't necessarily mean they are cancer free, then more might take up offers for tests. This could mean more tumours identified at an earlier stage and reduce the numbers of men experiencing late presentation with incurable disease."

Does Testosterone Cause Prostate Cancer?

SOURCE:
13 July 2022
https://www.pcf.org/c/does-testosterone-cause-prostate-cancer/?utm_source=NewsPulse&utm_medium=email&utm_campaign=JUL22NP

As men age, their testosterone levels can fall: by one estimate, 39% of men aged 45-85 have blood testosterone levels considered low (less than 300 ng/mL). Many have no symptoms, but some men may experience symptoms such as low mood, low energy, weight gain, and low sex drive, leading them to seek evaluation and treatment. In consultation with their doctor, they may consider testosterone supplements. Testosterone supplementation is becoming more common: between 2000 and 2011, the number of prescriptions of testosterone filled by U.S. pharmacies increased tenfold.

What does this have to do with prostate cancer? Prostate cancer is related to male hormones, and medications that block testosterone are used to treat certain types of prostate cancer. Men taking testosterone supplements might worry whether they are putting themselves at risk for prostate cancer in the future. Patients who have been diagnosed with prostate cancer and who previously took supplements may wonder: did the testosterone cause my cancer?

Fuel for *existing* prostate cancer

In his 2018 book *The Virility Paradox* (BenBella Books), PCF's President and CEO, Dr. Chuck Ryan, wrote extensively on the complicated role of testosterone in the human body. He notes that testosterone does not cause prostate cancer, but it can *fuel* prostate cancer that already exists. Biologically, there is a difference between *initiating* cancer vs. *promoting* cancer once it has already started. Testosterone does the latter for prostate cancer.

If a man taking testosterone is diagnosed with prostate cancer, it's not a cause-and-effect relationship. However, men taking testosterone should be monitored by a physician, including checking their PSA. This may lead to a greater likelihood of being diagnosed with prostate cancer – simply because a doctor is looking for it.

Testosterone after prostate cancer

Men can live for decades following therapy for localized prostate cancer, and may develop symptoms of low testosterone as they age. Men who have taken hormone therapy (androgen deprivation therapy) may have trouble recovering to normal testosterone levels. Are supplements a treatment option? Several studies suggest that testosterone therapy may be safe in select patients with a history of prostate cancer, but there is not enough evidence to definitively quantify the risks vs. the benefits. Long-term, randomized clinical trials are needed.

For treatment of advanced prostate cancer, researchers are investigating the role of high-dose testosterone supplementation. Known as bipolar androgen therapy, testosterone is given at scheduled intervals while patients are also taking hormone-blocking therapy. This causes alternating ("bipolar") very high and very low testosterone levels. Unable to adapt to the rapidly-changing environment, the cancer cells die.

Talk to your doctor

If you are considering testosterone supplements to treat symptoms of low testosterone, talk to your doctor to gain a thorough understanding of the benefits and risks. If you've had prostate cancer, be sure to tell your doctor, and note any history of prostate or other cancer in your family. Ask about getting a baseline PSA level before you start the medication, and follow your doctor's recommendations about monitoring your testosterone and PSA levels while you're taking the supplements, and beyond.

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

Treatment Intensification Patterns and Utilization in Patients With mCSPC

SOURCE:
1 August 2022
Advanced Prostate Cancer
https://www.practiceupdate.com/c/138277/67/11/?elsca1=emc_enews_weekinreview&elsca2=email&elsca3=practiceupdate_advancedprostatecancer&elsca4=advancedprostatecancer&elsca5=newsletter&rid=NTMyMjc0MDc4NjM0S0&lid=20849595

Patients with mCSPC experience a longer overall survival with treatment intensification by addition of novel hormonal therapy (NHT) [enzalutamide, abiraterone, apalutamide] or docetaxel to androgen deprivation vs androgen deprivation alone.

This study used the IQVIA™ [clinical research company) claims-based dataset to assess the real-world first-line treatment patterns in patients with metastatic castration-sensitive prostate cancer (mCSPC). Reports regarding the first-line treatment patterns used from 2015 to 2021 were obtained (N = 66,844). Urologists prescribed first-line novel hormonal therapy for 12% of the patients, whereas medical oncologists prescribed first-line novel hormonal therapy for 32% of the patients. Medical oncologists were also found to prescribe chemotherapy for 20% of the patients, which increased the total proportion of patients receiving treatment intensification as the first-line therapy to 52%.

Despite convincing evidence regarding the efficacy of treatment intensification, a significant [number] of the patients are not receiving the doublet combination strategy, which is considered the standard of care for treatment of men with mCSPC. – *Kamal Sahu MD*

Both medical oncology and urology providers need to improve their treatment intensification efforts for men with mCSPC to increase their patients' overall survival.

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

Home-based Exercise Programs for Cancer Survivors Show Promise

SOURCE:
7 July 2022
Becky Campbell
https://www.pcf.org/c/home-based-exercise-programs-for-cancer-survivors-show-promise/?utm_source=NewsPulse&utm_medium=email&utm_campaign=JUL22NP

Sedentary behavior increased during the pandemic, but "stay at home" restrictions have also provided an opportunity to examine home-based exercise programs, according to a new paper by PCF-funded researcher Christina Dieli-Conwright, PhD, MPH of the Dana Farber Cancer Institute, and colleagues. The team reviewed 12 studies of exercise interventions in people with cancer that were all home-based and adapted for pandemic restrictions. The approaches broadly included:

- Self-directed, unsupervised: recommendation to adhere to exercise guidelines or to complete a daily exercise program with accompanying resources (e.g., video)
- Self-directed, with regular guidance: online videos, smart watches, and printed materials supplemented with regular phone calls or messages to patients
- Virtually supervised interventions: one-on-one or group exercise sessions over videoconferencing

Although this review did not aim to determine which approach was most effective, it did yield some preliminary information about home-based exercise programs in cancer survivors and identified challenges and areas for further research. For example, in the virtually supervised programs, adherence was quite high, ranging from 84%-94%. In two trials in breast and prostate cancer, attendance and retention were actually higher in the virtual sessions held during the pandemic, compared with in-person supervision prior to COVID-19.

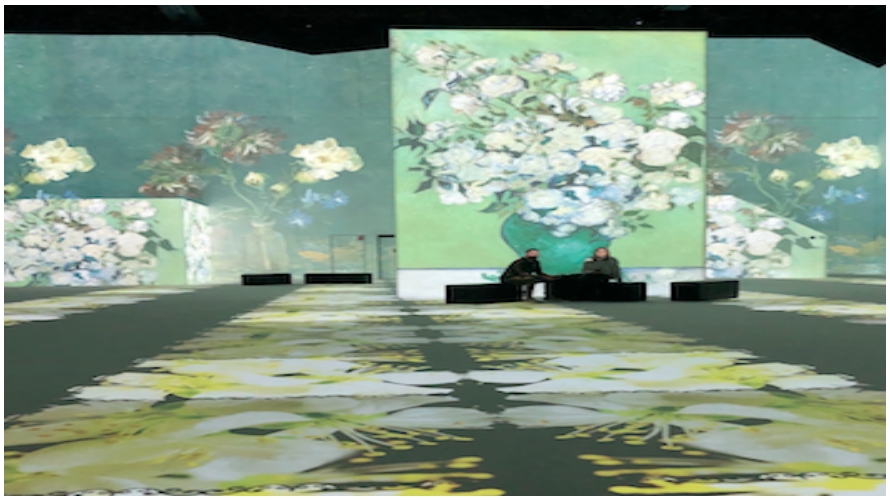
The researchers concluded that virtually-supervised interventions may be feasible, safe, and have the potential to improve outcomes in cancer survivors such as fatigue and anxiety. More research is needed to understand their impact on important health outcomes such as physical function and survivorship.

In carrying out future studies, patient safety is paramount. Participants need training on proper use of equipment to maximize effectiveness and minimize the risk of injury. People undergoing cancer treatment may have different symptoms day-to-day, as well as other health conditions that may affect their ability to exercise. While home-based exercise avoids barriers (e.g., travel time, potential exposure to germs), it presents other challenges (e.g., lack of suitable space at home, technology access). Researchers will need to address these and other open questions as they develop high-quality exercise programs to support healthy cancer survivorship.

If you've found an exercise routine that works for you—Keep it up! Aiming to get started with exercise? See Dr. Dieli-Conwright's suggestions https://www.pcf.org/c/diy-home-fitness-work-with-what-you-have-start-small-and-do-great-things/ and ask your care team for more ideas. If you like the idea of exercise in a group setting but are hesitant to go to a crowded gym, look for outdoor options over the summer.

Exercise participation among cancer survivors has been shown to improve quality of life and physical functioning, yet only 10%-30% of survivors meet physical activity guidelines. In prostate cancer, aerobic exercise after prostate cancer diagnosis may reduce the risk of prostate cancer recurrence or death by up to 60 percent.

Prostate Cancer Foundation
Curing Together.



Novel Urine-based Liquid Biopsy Launched in US prostate Cancer Market

The miR Sentinel urine-based liquid biopsy for assessing the risk of aggressive prostate cancer has been made commercially available in the United States, according to miR Scientific, the developer of the assay.[1]

Specifically, the miR Sentinel molecular test uses a biostatistical algorithm to examine small noncoding RNAs isolated from urinary exosomes and determine an individual's risk of aggressive prostate cancer. According to the company, the test is intended to facilitate clinicians in the management of men aged 45 and above who are at risk for prostate cancer.

At the 2022 AUA Annual Meeting, researchers share a study showing evidence of the test's efficacy. The research included about 1100 men at clinical sites in the United States and Puerto Rico. In at-risk men, the miR Sentinel test detected molecular evidence of prostate cancer with 98.5% sensitivity. Further, the test had an 83% prognostic sensitivity when distinguishing between clinically significant and non-significant prostate tumors.

The researchers also looked at a subset of men for whom MRI-guided and TRUS biopsies did not agree on whether the individual had prostate cancer. For this group, the miR Sentinel correctly identified 71 (99%) of 72 cases in which men had been found to have prostate cancer by either biopsy type. miR Scientific further noted in a news release that, "87% of men with PSA levels <3 found to have pathologic grade group 2 through 5 upon biopsy were identified by the miR Sentinel test as having molecular evidence of intermediate or high risk of aggressive disease."

In the news release, Laurence Klotz, MD, FRCSC, CM, chief medical officer at miR Scientific, and professor of Surgery and Chair of Prostate Cancer Research at University of Toronto Sunnybrook, stated, "Accurate assessment of a man's individual risk related to prostate cancer is one of the cornerstones of appropriate patient management. The miR Sentinel test has the potential to provide a significant improvement over the current tools that are available to physicians. The implementation of such an innovation into practice could have a dramatic impact on outcomes through appropriately guiding the need for further diagnostic workup in men with elevated risk of significant cancer and guiding treatment in those subsequently diagnosed."

SOURCE:
20 July 2022
https://www.urologytimes.com/view/novel-urine-based-liquid-biopsy-launched-in-us-prostate-cancer-

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

Review of Outdated Prostate Cancer Screening Guidelines in Australia

In response to PCFA advocacy, the RACGP (The Royal Australasian College of General Practitioners) has finally agreed to overhaul the Red Book code of practice on PSA testing that has been instrumental in late diagnosis.

Press coverage of the change can be found at:
https://mail.google.com/mail/u/0/#inbox/WhctKKXgkHHZGKLKKFddQgLWNnMdhQSvKJHpnvFSSzgbVlRRgDRFkzPrDfTtZRFfmRqdsDG

Healthy Lifestyle Cuts Prostate Cancer Mortality Among High-Risk Men

SOURCE:
27 May 2022
https://www.europeanurology.com/article/S0302-2838(22)02342-9/fulltext

Objective

To examine whether men at an increased genetic risk of prostate cancer can offset their risk of disease or disease progression by adhering to a healthy lifestyle.

Design, setting, and participants

We prospectively followed 12 411 genotyped men in the Health Professionals Follow-up Study (1993–2019) and the Physicians' Health Study (1983–2010). Genetic risk of prostate cancer was quantified using a polygenic risk score (PRS). A healthy lifestyle was defined by healthy weight, vigorous physical activity, not smoking, and a healthy diet.

Outcome measurements and statistical analysis

Overall and lethal prostate cancer events (metastatic disease/prostate cancer–specific death) were analysed using time-to-event analyses estimating hazard ratios (HRs) and lifetime risks.

Results and limitations

During 27 yr of follow-up, 3005 overall prostate cancer and 435 lethal prostate cancer events were observed. The PRS enabled risk stratification not only for overall prostate cancer, but also for lethal disease with a four-fold difference between men in the highest and lowest quartiles (HR, 4.32; 95% confidence interval [CI], 3.16–5.89). Among men in the highest PRS quartile, adhering to a healthy lifestyle was associated with a decreased rate of lethal prostate cancer (HR, 0.55; 95% CI, 0.36–0.86) compared with having an unhealthy lifestyle, translating to a lifetime risk of 1.6% (95% CI, 0.8–3.1%) among the healthy and 5.3% (95% CI, 3.6–7.8%) among the unhealthy. Adhering to a healthy lifestyle was not associated with a decreased risk of overall prostate cancer.

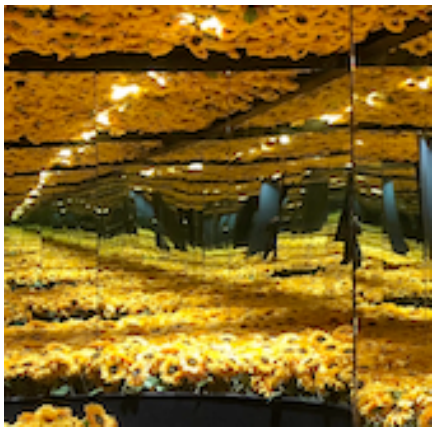
Conclusions

Our findings suggest that a genetic predisposition for prostate cancer is not deterministic for a poor cancer outcome. Maintaining a healthy lifestyle may provide a way to offset the genetic risk of lethal prostate cancer.

Patient summary

This study examined whether the genetic risk of prostate cancer can be attenuated by a healthy lifestyle including a healthy weight, regular exercise, not smoking, and a healthy diet. We observed that adherence to a healthy lifestyle reduced the risk of metastatic disease and prostate cancer death among men at the highest genetic risk. We conclude that men at a high genetic risk of prostate cancer may benefit from adhering to a healthy lifestyle.

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



Active Surveillance Plus Enzalutamide Monotherapy vs Active Surveillance Alone in Patients With Low- or Intermediate-Risk Localized Prostate Cancer

TAKE-HOME MESSAGE

This phase II, open-label, randomized clinical trial enrolled 227 patients with low- or intermediate-risk localized prostate cancer under active surveillance, randomized them 1:1 to either receive enzalutamide monotherapy for 1 year or undergo continued active surveillance, and evaluated the time to pathological (defined by an increase in the primary or secondary Gleason pattern or increase in cancer-positive cores) or therapeutic progression (defined by the earliest occurrence of primary therapy for prostate cancer). Enzalutamide treatment significantly reduced the risk of prostate cancer progression by 46.0%. The most commonly reported adverse event was fatigue, observed in 55.4% of patients, followed by gynecomastia in 36.6% of patients.

In patients with low- to intermediate-risk prostate cancer who would otherwise be treated with active surveillance, enzalutamide monotherapy significantly delayed the time to progression, increased the odds of obtaining a negative biopsy result, and was well-tolerated. – Yael Kusne MD PhD

Abstract

IMPORTANCE

There are few published studies prospectively assessing pharmacological interventions that may delay prostate cancer progression in patients undergoing active surveillance (AS).

OBJECTIVE

To compare the efficacy and safety of enzalutamide monotherapy plus AS vs AS alone in patients with low-risk or intermediate-risk prostate cancer.

DESIGN, SETTING, AND PARTICIPANTS

The ENACT study was a phase 2, open-label, randomized clinical trial conducted from June 2016 to August 2020 at 66 US and Canadian sites. Eligible patients were 18 years or older, had received a diagnosis of histologically proven low-risk or intermediate-risk localized prostate cancer within 6 months of screening, and were undergoing AS. Patients were monitored during 1 year of treatment and up to 2 years of follow-up. Data analysis was conducted in February 2021.

INTERVENTIONS

Randomized 1:1 to enzalutamide, 160 mg, monotherapy for 1 year or continued AS, as stratified by cancer risk and follow-up biopsy type.

MAIN OUTCOMES AND MEASURES

The primary end point was time to pathological or therapeutic prostate cancer progression (pathological, ≥1 increase in primary or secondary Gleason pattern or ≥15% increased cancer-positive cores; therapeutic, earliest occurrence of primary therapy for prostate cancer). Secondary end points included incidence of a negative biopsy result, percentage of cancer-positive cores, and incidence of a secondary rise in serum prostate-specific antigen (PSA) levels at 1 and 2 years, as well as time to PSA progression. Adverse events were monitored to assess safety.

SOURCE:
16 June 2022
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9204619/

RESULTS

A total of 114 patients were randomized to treatment with enzalutamide plus AS and 113 to AS alone; baseline characteristics were similar between treatment arms (mean [SD] age, 66.1 [7.8] years; 1 Asian individual [0.4%], 21 Black or African American individuals [9.3%], 1 Hispanic individual [0.4%], and 204 White individuals [89.9%]). Enzalutamide significantly reduced the risk of prostate cancer progression by 46% vs AS (hazard ratio, 0.54; 95% CI, 0.33-0.89; P = .02). Compared with AS, odds of a negative biopsy result were 3.5 times higher; there was a significant reduction in the percentage of cancer-positive cores and the odds of a secondary rise in serum PSA levels at 1 year with treatment with enzalutamide; no significant difference was observed at 2 years. Treatment with enzalutamide also significantly delayed PSA progression by 6 months vs AS (hazard ratio, 0.71; 95% CI, 0.53-0.97; P = .03). The most commonly reported adverse events during enzalutamide treatment were fatigue (62 [55.4%]) and gynecomastia (41 [36.6%]). Three patients in the enzalutamide arm died; none were receiving the study drug at the time of death. No deaths were considered treatment-related.

CONCLUSIONS AND RELEVANCE

The results of this randomized clinical trial suggest that enzalutamide monotherapy was well-tolerated and demonstrated a significant treatment response in patients with low-risk or intermediate-risk localized prostate cancer. Enzalutamide may provide an alternative treatment option for patients undergoing AS.

Treatment of Metastatic Hormone Sensitive PCa

SOURCE:
15 June 2022
https://www.researchreview.com.au/au/home.aspx

Prostate cancer is the most commonly diagnosed cancer and second leading cause of cancer deaths in Australian men. In 2021, it was estimated that there would be new cases of prostate cancer in Australia and that men would have a 1 in 8 (13%) risk of being diagnosed by the age of 85 years. In addition, there were expected to be 3,323 prostate cancer deaths with a 1 in 55 (1.8%) risk of dying. Between 2013 and 2017, the 5-year survival rate for Australian men with prostate cancer was 96%. In 2021, it was estimated that 12% of all cancer deaths in men were due to prostate cancer.

In common with most malignancies, treatment for prostate cancer is undertaken predominantly to prolong survival and maintain quality of life. Current guidelines from the American Urological Association/American Society for Radiation Oncology/Society of Urologic Oncology (AUA/ASTRO/SUO) and European Society of Medical Oncology (ESMO) recommend that clinicians discuss treatment options with men who have prostate cancer based on life expectancy, comorbidities, patient preferences and tumour characteristics.

For men with clinically local or locoregional prostate cancer, standard treatments include watchful waiting, active surveillance, radical prostatectomy, external beam radiotherapy and low-dose-rate brachytherapy. If a patient has symptomatic progression but is not suitable for, or unwilling to have, treatment with curative intent, watchful waiting with delayed ADT may also be appropriate. ADT typically consists of either surgical castration (orchiectomy) or medical castration. Agents used for medical castration include luteinizing hormone-releasing hormone agonists or antagonists, antiandrogens and other androgen suppressants.

Metastatic prostate cancer is rarely curable, and management typically focuses on relieving symptoms and slowing disease progression. For men with mHSPC, guidelines recommend treatment with first-line ADT in combination with either apalutamide, abiraterone/prednisone, docetaxel or enzalutamide.

Eventually, almost all metastatic prostate cancers become resistant to androgen ablation. Although there is scant evidence regarding maintenance of hormone suppression when androgen-independent progression occurs, the general consensus among specialists is that treatment should continue. In men with non-metastatic castration-resistant prostate cancer (CRPC), guidelines recommend apalutamide, darolutamide or enzalutamide for those with M0 disease and a high risk of progression. For men with metastatic CRPC, recommendations include:

- Abiraterone or enzalutamide for asymptomatic/mildly symptomatic men with docetaxel-naïve disease
- Docetaxel
- Abiraterone, enzalutamide and cabazitaxel for men in the post-docetaxel setting
- A bisphosphonate or denosumab for men with bone metastases at risk of skeletal-related events
- Ra for men with bone-predominant, symptomatic disease without visceral metastases

Treatment of metastatic hormone-sensitive prostate cancer

Until recently, ADT was the only treatment available for men with mHSPC. Now, several combination regimens have become available and guidelines recommend first-line ADT in combination with either apalutamide, abiraterone/prednisone, docetaxel or enzalutamide for the treatment of mHSPC. ADT alone is now only recommended in men who are unfit for apalutamide, abiraterone, enzalutamide and docetaxel. For men with low volume mHSPC, guidelines recommend combining radiotherapy of the primary tumour with systemic treatment.

The benefit of adding apalutamide to ADT was demonstrated in the phase 3 TITAN study (see below for more detail). In TITAN, 1052 participants were randomised to ADT in combination with apalutamide or placebo. The addition of apalutamide to ADT was shown to significantly reduce the risk of death compared with placebo (median OS not reached vs 52 months, p<0.0001).

The phase 3 LATITUDE and STAMPEDE studies demonstrated the benefit of adding abiraterone to ADT. In LATITUDE, 1199 participants were randomised to ADT in combination with abiraterone plus prednisone or placebo. Median OS was shown to be significantly longer in the abiraterone plus prednisone group compared with the placebo group (53 months vs 37 months; p<0.0001). In STAMPEDE, 1917 participants were randomised to ADT in combination with abiraterone plus prednisolone or ADT alone. There were 184 deaths in the abiraterone plus prednisone group compared with 262 deaths in the ADT-alone group (hazard ratio [HR] 0.63, 95% confidence interval [CI] 0.52–0.76, p<0.001).

The phase 3 CHAARTED and GETUG-AFU 15 studies investigated the benefit of adding docetaxel to ADT. In CHAARTED, 790 participants were randomised to ADT plus docetaxel or ADT alone. Median OS was 58 months with ADT plus docetaxel vs 44 months with ADT alone (p<0.001). In GETUG-AFU 15, 385 participants were randomised to ADT plus docetaxel or ADT alone. Median OS was 59 months with ADT plus docetaxel vs 54 months with ADT alone.

The benefit of adding enzalutamide to ADT was demonstrated in the phase 3 ARCHES and ENZAMET studies. In ARCHES, 1150 participants were randomised to ADT plus enzalutamide or placebo. The risk of radiographic progression or death was significantly reduced with ADT plus enzalutamide compared with ADT plus placebo

(continued page 11)

(median not reached vs 19 months, p<0.001). In ENZAMET, 1125 participants were randomised to ADT plus enzalutamide or ADT plus standard nonsteroidal antiandrogen therapy (standard-care group). The proportion of participants with OS at 3 years was 80% in the enzalutamide group compared with 72% in the standard-care group.

Despite the benefits shown in phase 3 clinical studies, and recommendations in guidelines, new combination regimens with ADT are not being used as often as ADT alone for the treatment of mHSPC. This is possibly due to concerns about the toxicity of chemotherapy, extended exposure to steroids, the need for patient monitoring, and a lack of long-term follow up from clinical studies. Therefore, there is a need for long-term safety data. The 44-month follow up of ADT plus apalutamide in the TITAN study are presented in further detail below.

Expert comment
A recent paradigm shift in the management of mHSPC was based of the observation that the upfront combination of systemic therapies results in significantly improved oncological outcomes and substantially greater survival compared with traditional treatment sequencing. This was first shown for docetaxel, but has subsequently been demonstrated for a range of androgen receptor signalling inhibitors (ARSIs). Patients with high volume metastatic disease appear to preferentially benefit from chemo-hormonal therapy, whereas the same clinical bias is not observed for ARSIs, suggesting these agents may be the better choice for older men or those with co-morbidities that may affect their ability to tolerate docetaxel, or those with lower volume metastatic disease. However, although approved by the Therapeutic Goods Administration for use in mHSPC, re-imbursement on the Pharmaceutical Benefits Scheme is currently only available for patients with castration resistant disease. So, although the evidence is there to support a change in practice, funding arrangements are a significant barrier to more widespread implementation in Australia.

Apalutamide
Apalutamide is an orally administered, androgen receptor (AR) inhibitor that binds directly to the ligand-binding domain of the AR. In preclinical studies, apalutamide was shown to prevent AR nuclear translocation, inhibit DNA binding, impede AR-mediated transcription, and lack AR agonist activity. In mouse models of prostate cancer, apalutamide administration was shown to decrease tumour cell proliferation and increase apoptosis, which led to inhibition of tumour growth and tumour regression.

In Australia, apalutamide is indicated for the treatment of:
- mHSPC
- Non-metastatic CRPC

The recommended dose of apalutamide is 240 mg (four 60 mg tablets) administered orally once daily. Patients should concurrently receive a gonadotropin-releasing hormone analogue, unless they have had a bilateral orchiectomy.

Apalutamide has special warnings and precautions for use for ischaemic cardiovascular events and ischaemic cerebrovascular disorders, fractures, falls, seizure, hypothyroidism and QT interval prolongation. The most common adverse reactions (≥10%) that occurred more frequently with apalutamide (2% over placebo) in the TITAN and SPARTAN studies (SPARTAN was conducted in participants with non-metastatic CRPC) were fatigue, arthralgia, rash, decreased appetite, fall, weight decreased, hypertension, hot flush, diarrhoea and fracture.

Please refer to the Erlyand (apalutamide) Australian Product Information for full prescribing details.

Apalutamide in patients with metastatic hormone-sensitive prostate cancer: final survival analysis of the randomised, double-blind, phase 3 TITAN Study

Summary
Apalutamide plus ADT significantly reduced the risk of death by 35% compared with placebo plus ADT (median OS not reached vs 52 months, p<0.0001). Health-related quality of life (HRQoL) was maintained in both treatment groups throughout the study, and safety was consistent with previous reports.

Methods
TITAN was a phase 3, randomised, double-blind, placebo-controlled multinational study in participants with mHSPC. Participants were randomised 1:1 to apalutamide 240 mg or placebo orally once daily in addition to continuous ADT. Participants received treatment until disease progression or unacceptable toxicity. Prior treatment for mHSPC was limited to previous docetaxel, ADT for ≤6 months and one course of radiation or surgical intervention.

The dual primary end points were OS and radiographic progression-free survival (rPFS). Secondary end points were time to initiation of cytotoxic chemotherapy, time to pain progression, time to chronic opioid use and time to skeletal-related event.

Two interim analyses and the updated final analysis for OS were planned. At the first interim analysis of TITAN, OS and rPFS met statistical significance. Based on these data, the independent data and safety monitoring committee unanimously recommended unblinding the study to allow placebo-treated participants without progression to cross over to receive open-label apalutamide. After unblinding, all participants were followed for survival, with crossover participants analysed as a part of the intention-to-treat population in the placebo group.

The final analysis provided mature OS results without formal statistical inference. In the final report, updated analyses were performed for the secondary end points of time to initiation of cytotoxic chemotherapy, time to pain progression, time to chronic opioid use and time to skeletal-related event. These analyses were conducted without formal statistical retesting.

Expert comment
Apalutamide is a competitive inhibitor of the androgen receptor that has similar in vitro efficacy as enzalutamide, but better in vivo activity in xenograft models of CRPC. It is orally bio-available and relatively well tolerated and, unlike abiraterone, does not require co-administration with corticosteroids. The TITAN study included predominantly men with de novo metastatic disease, with almost two thirds of participants having high volume disease by CHAARTED criteria. Despite this, the majority of men were asymptomatic or had only mild symptoms. Consistent with the original report, treatment with apalutamide plus ADT resulted in a 35% decrease in mortality risk compared with ADT alone at 4 years, despite crossover of almost 40% of participants from the placebo to the active group after study unblinding. This is impressive considering these participants likely had less aggressive disease than those who progressed in the placebo group. When potential confounding of the HR was corrected for statistically, the potential survival advantage was closer to 50%. Secondary endpoints, including the time to initiation of cytotoxic chemotherapy, also favoured the apalatumide group and, importantly

(continued page 12)

for a drug which may be required for long periods of time, participant quality of life was maintained.

Conclusions

Apalutamide plus ADT is a well tolerated and effective treatment option for men with mHSPC. The TITAN study shows that apalutamide improves OS and delays the onset of progression of mHSPC. This efficacy is supported by data for several other endpoints, including that showing delayed castration resistance and prolonged second relapse-free survival. In the TITAN study, apalutamide maintained HRQoL and had an acceptable safety profile with long-term follow up and exposure. These findings support the early addition of apalutamide to ADT for optimal therapeutic outcomes in men with mHSPC.

Expert's concluding remarks

It is clear that the combination of ARSIs (such as apalutamide) and ADT result in improved OS in men with mHSPC compared with ADT alone. Unlike docetaxel, the effect appears to be independent of disease volume, and these treatments may be better tolerated in older men and those with co-morbidities. The downside is that they must be given indefinitely in contrast to docetaxel which is usually just 6 cycles. In addition, long-term use may lead to cumulative toxicity, for instance from the need for concomitant steroid use with abiraterone. In this respect, apalutamide appears to give considerable survival benefit without much toxicity, and importantly maintains patients' quality of life in the longer term. Despite compelling clinical evidence, the main barrier to implementation at present is rules around reimbursement, which will likely require a detailed health economics analysis to change.

Associate Professor Niall Corcoran is a urological surgeon at the Royal Melbourne and Frankston Hospitals, and a principal research fellow in the Department of Surgery, University of Melbourne. He is also the Research and Education Lead for GU oncology for the Victorian Comprehensive Cancer Centre.

Research Study

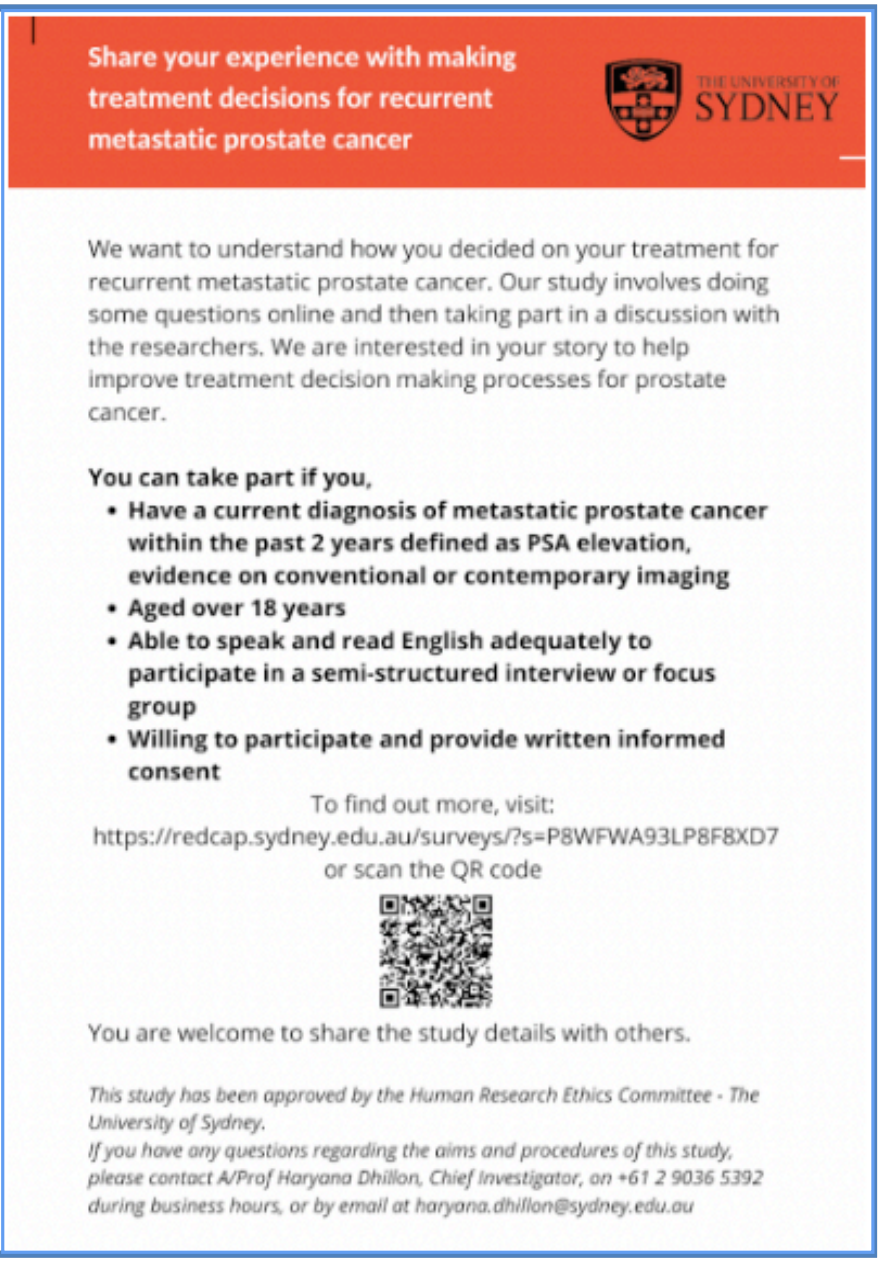
This study is the initiative of one of our members, Colin O'Brien. Colin is also a member of ANZUP's Consumer Advisory Panel (CAP). ANZUP encourages members to consider new ideas that can be developed to ultimately support patients or improve current practice.

Please complete the study if you are eligible. Your knowledge may help the 30% - 40% of men, who find they have a biochemical recurrence after their initial treatment to eliminate the disease, by improving the decision making process.

The Australian and New Zealand Urogenital and Prostate Cancer Trials Group

ANZUP is the leading cancer cooperative trials group that brings together all of the professional disciplines and groups involved in researching and treating below the belt (penile, bladder, kidney, prostate and testicular) cancers and conduct high quality clinical research.

ANZUP identifies gaps in evidence and areas of clinical need, collaborates with the leading clinicians and researchers in below the belt cancers, and communicate frequently and effectively with the broader community along the way.



Prostate Cancer Survivorship – Strategies to Help Get Your Life Back

SOURCE:
20 May 2022
Janet Farrrar Worthington
https://www.pcf.org/c/prostate-cancer-survivorship-part-3/

Matters of Survivorship: Fighting Back on ADT

ADT will try to affect your overall health, but here's the good news: you can fight back, says PCF-funded medical oncologist Alicia Morgans, M.D., M.P.H., Medical Director of Cancer Survivorship at Dana Farber Cancer Institute. **Be aware of what it might do, and you will be better able to protect yourself against its tactics.**

So here, in no particular order, are some of the things ADT might affect, and countermeasures you can take:

Bone health: Prostate cancer can affect your bones, and so can ADT, in different ways. Treating prostate cancer in the bones not only protects them, it can improve survival! ADT raises your risk of osteoporosis – but not only is this treatable, it's not a "done deal" that every man on ADT will develop it! For specific advice on keeping your bones strong, from Harvard medical oncologist Matthew Smith, M.D., Ph.D., "Avoiding fractures is so important," says Morgans. "Men who have fragility fractures (due to osteoporosis) can lose their mobility and independence, and can have some major changes in their lives until those fractures are repaired. If we simply follow the guidelines we already have on how to care for bone and prevent osteoporosis, we can improve those outcomes pretty dramatically.

"**A lot of the complications associated with ADT are absolutely things that we can address head on, try to prevent and to reverse**; for instance, we have effective therapies to counteract bone thinning and lower the risk of fracture and complications from weak bones. **Many of the known side effects of ADT are not necessarily inevitable."**

Your risk of cardiovascular disease: Here's some good news: A newer form of hormonetherapy, Orgovyx (relugolix), was approved in 2020 by the FDA for men with advanced prostate cancer, based on results of the Phase 3 HERO study. It lowers testosterone, but it works in a different way. It's also administered differently – a once-daily pill instead of a shot – and it has a **significantly lower risk of major adverse cardiovascular events** compared to Lupron (leuprolide). If you have cardiovascular risk factors, such as high blood pressure, high cholesterol, a family history of cardiovascular disease, diabetes or pre-diabetes, if you're overweight or if you smoke: **heart disease needs to be on your radar, because ADT can make it worse.**"Multiple studies have shown that men who have cardiovascular risk factors, particularly if they are not addressed, have higher rates of complications and even death on ADT," says Morgans. But treating these risk factors with diet, exercise, and medication if needed, can "improve overall survival and also quality of life. When your body is healthier, you feel better."

Note: For just about every category on this list, exercise is one of the answers. Men on ADT who exercise lower their risk of having cardiovascular and cognitive effects, developing insulin resistance, diabetes or pre-diabetes, obesity, and high blood pressure. "All of these are modifiable risk factors," says Morgans, who tells patients on ADT to remember **"A,B,C,D, and E," which stand for:**

Awareness: recognize the risks of complications, and fight back with diet, exercise and lifestyle changes.

Blood pressure: keeping your blood pressure healthy lowers the risk of heart attack and stroke.

Cigarette smoking: if you stop, your risk of dying of prostate cancer instantly begins to get lower.

Diet and **D**iabetes. You can lower your risk of insulin resistance with diet; particularly, trying to limit your carbohydrates. PCF has a wealth of good information on diet; download our guide, *The Science of Living Well, Beyond Cancer*.

Exercise. It can help keep your bones strong, your weight down, improve your blood pressure, and also improve your mood. Speaking of mood:

Depression: "Depression is highly treatable," says Morgans. "This is important, because evidence suggests that men treated with ADT do have higher rates of depression than men who have prostate cancer but are not receiving ADT." But depression is underdiagnosed and undertreated in men on ADT, she adds, "perhaps because of reticence to ask for help, or a perceived stigma with mental illness," or perhaps because it has crept up, and the patient hasn't recognized that there's a problem. This is where friends, family and caregivers can help. Depression can affect sleep, appetite, and memory, as well.

Cognitive changes: ADT can cause cognitive decline and dementia. However, this is more complicated than it sounds, Morgans notes. For one thing, symptoms of depression can be mistaken for cognitive decline, and can improve with antidepressants and exercise. For another, there are multiple forms of dementia, including vascular dementia. "If that risk is increased because of ADT, then a medicine that reduces the risk of major adverse vascular events could feasibly lower the risk of dementia, as well," although this remains to be proven in large-scale studies. In general, "what's good for the heart is good for the brain," and taking steps to improve your cardiovascular health will help protect your cognitive function, too. "We also have strategies and

(continued page 14)

mental tricks to help improve memory, and even medicines that may slow the progress of Alzheimer's." The key is to tell your doctor, and get further evaluation and help if needed. "The choice of therapies may help, as well," Morgans notes. "In multiple ongoing studies, some really interesting MRI data suggests that there may be differences in some distribution of blood flow in the brain" between androgen-targeted medicines, "including one study with darolutamide that has just launched."

Hot flashes: "At [it's] basic level, ADT is lowering testosterone, which keeps men's bodies functioning in a way they're used to," says Morgans. "Just as we see when women go through menopause, there are widespread changes. The constellation of symptoms is much broader than just the effects of ADT on the prostate cancer cells themselves."

Among the most annoying and persistent – and undertreated – are hot flashes, which "can affect mood, sleep, and cognition," says Morgans. A novel approach on the horizon is a "wearable," she adds. It's like an Apple watch, and can be linked to your phone. The basic idea is to stimulate the autonomic nerves on the wrist, with a cool sensation. "PCF is actively engaged in supporting work that can potentially improve quality of life and reduce hot flashes in men on ADT. This is an area with much room for improvement, where attention is needed, and pharmacologic therapies aren't as effective as we wish."

Prostate Cancer Foundation
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Earlier recurrence of prostate cancer after radical prostatectomy is associated with a greater likelihood of positive PSMA PET/CT results. *Source: Getty Images*

Study May Help Define Role of PSMA PET/CT in Recurrent Prostate Cancer

Recent findings provide clues to the optimal timing and indications for the use of 68Ga-PSMA PET/CT in men with biochemically recurrent (BCR) prostate cancer after radical prostatectomy (RP), according to a presentation at the 37th congress of the European Association of Urology held in Amsterdam, The Netherlands.

In a study of 207 patients with a median age of 62 years who underwent 68Ga-PSMA PET/CT, investigators found that PSA levels and time to BCR at the time of PSMA PET/CT affect the probability of positive findings at PSMA PET.

Among men with early recurrence or PSA persistence after RP, the study showed that PSMA PET should be recommended even at low PSA levels given its high diagnostic value, according to investigators. The opposite may be true for patients with late BCR, who may not benefit from the addition of a PET PSMA scan. These patients should be counseled carefully based on PSA levels.

Optimizing timing and indications for 68Ga-PSMA PET/CT in patients with biochemical recurrent prostate cancer after radical prostatectomy. Presented at: EAU 2022, July 1-4, 2022, Amsterdam, The Netherlands. Abstract: A0190

Source
2 August 2022
John Schjiezer
https://www.renalandurologynews.com/home/news/urology/prostate-cancer/study-may-help-define-role-of-psma-pet-ct-in-recurrent-prostate-cancer/?utm_medium=email&utm_source=rasa_io&utm_campaign=newsletter

Cancer Loves Sugar, and Sugar *Really* Loves Cancer

Isn't that sweet? Actually, no, it's more like a match made in hell – because sugar (glucose) makes many types of cancer grow faster.

SOURCE:
22 June 2020
Janet Farrar Worthington
https://www.pcf.org/c/prostate-cancers-sweet-tooth/

Scientists have long known that cancers soak up glucose like a sponge; in fact, German physiologist Otto Warburg, who found that tumors extract glucose at a rate 20 to 50 times higher than do normal cells, won the 1931 Nobel Prize for his research on metabolism.

Prostate cancer can take up sugar at a higher rate, too, says renowned scientist and PCF-funded investigator Lew Cantley, Ph.D., Director of the Sandra and Edward Meyer Cancer Center at Weill Cornell Medicine.

But Cantley's studies suggest **that it's not so much the amount of glucose in your bloodstream that helps promote cancer, as it is the level of** insulin, the hormone made by the pancreas that controls glucose. Insulin helps turn glucose into immediate energy, and also helps your body pack it away for longer-term storage. Briefly, when you eat, your blood sugar goes up; this causes your pancreas to say, "Hey! We need to make more insulin!" Insulin, like Paul Revere, then travels rapidly throughout the land, telling the cells to let the glucose in, either to be used right away or saved in muscles, fat cells, and the liver.

"Why does the tumor take up more glucose?" Cantley continues. "The main reason is that insulin can turn on the glucose transporters (proteins on cell membranes that carry glucose into cells), similar to those in the liver, muscle and fat. The presence of those glucose transporters on tumor cells is in part regulated by insulin. That's why I keep focusing on the insulin."

Cantley began studying the insulin receptor in the 1980s, when he was on the faculty at Harvard University. A few years later, after moving to Tufts University, he discovered an enzyme called **phosphoinositide-3-kinase (PI3K);** PI3K signals cells that insulin is present; the cells, in turn, open the valve that lets in sugar. Normally, PI3K does good and vital work, helping cells survive, grow and proliferate. But sometimes it goes awry; in Type II diabetes, this PI3K pathway becomes sluggish, cells don't respond appropriately to insulin and become insulin-resistant. But in cancer, even in someone who's insulin-resistant, PI3K does its job too well; glucose floods in, tumor cells feast on sugar and grow faster. "What we now know is that mutations in the PI3K pathway make tumor cells hyperactive in response to insulin."

In many cancers – sugar-loving cancers (not all cancers are addicted to sugar, but many are) – **PI3K is like a power switch that drives growth. "PI3K is the most frequently mutated cancer-promoting** gene **in humans,"** says Cantley. It may be involved in as many as 80 percent of cancers, including breast cancer, bladder cancer, and certain brain tumors.

What about prostate cancer? Well, one of the most common genetic events in prostate cancer is the loss of a gene called PTEN; cancer just knocks this gene out. "PTEN makes an enzyme that reverses what PI3K does. PI3K makes a lipid, and PTEN destroys that lipid; you have to have a balance between those two enzymes to keep growth under control. But in prostate cancer, and in breast cancer , the loss of PTEN activates production of this lipid that drives cell growth.

"This tells us we probably should try to keep insulin levels as low as possible if we have cancer, to try to keep the tumor from growing. If we can keep the diet under control, or exercise to keep glucose levels and insulin levels low, we have a much better chance of slower growth of the tumor. Our research would also argue that pharmacological intervention would be more effective if we keep insulin levels low."

Even better: Keep insulin levels as low as possible anyway, whether you have cancer or not. "This is a powerful potential cancer-prevention mechanism," says Howard Soule, Ph.D., Executive Vice President and Chief Science Officer at PCF. "Reducing processed sugar may turn out to be even more important for cancer prevention than treatment."

Can we learn to use cancer's sweet tooth as a weapon against it? Cantley's research has already led to the development of several PI3K-

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

inhibiting drugs: idelalisib, approved by the FDA in 2014 for treatment of lymphoma and leukemia, and alpelisib, approved in 2019 for treating breast cancers with mutations in PI3K. But Cantley also believes that **changing the diet – to one low in sugar, but also low in other carbohydrates, which can cause blood sugar to spike – can make cancer-fighting treatments work even better**. In a landmark 2018 paper published in *Nature*, Cantley and colleagues showed in mice that by severely restricting carbohydrates "and keeping the insulin level low, tumors would respond much more dramatically to drugs that are already approved to treat them. *Tumors we had never been able to shrink in mice, we could shrink with a low-glucose diet.*

"That's my obsession now, to get that message out there. Endocrinologists tell patients to exercise more and eat less sugar to keep diabetes under control, but for me, it's **even more critical to keep insulin levels low in order to get better outcomes for cancer patients."** Cantley's research suggests that "if you have a mutation in the PI3K pathway that causes cancer, and you're eating a lot of simple carbohydrates, every time your insulin goes up, it's making the tumor grow."

How can this knowledge help slow the growth of prostate cancer? Here's one example: "For prostate cancer patients with low Gleason scores who are on active surveillance, it makes perfect sense to pay a lot of attention to what you eat. Try to keep your consumption of sugary drinks as low as possible. Keeping sugar down is the best thing you can possibly do." It used to be, Cantley notes, Japanese men hardly ever got prostate cancer. "But second-generation Japanese Americans have prostate cancer in similar rates to Caucasians. It's clearly lifestyle," the Western diet. "The truth probably is that some Japanese men in their 90s had some level of prostate cancer, but didn't consume enough sugar for the cancer to advance."

Here's another: If you are on ADT for metastatic prostate cancer, you are more likely to gain weight, and also to develop insulin resistance. One way to fight this is by limiting your sugar and simple-to-digest carbs. Bonus: keeping insulin down may also help slow down the cancer. Watch out for protein drinks, too; many are loaded with sugar.

What about the ketogenic diet? It's low in carbs and high in fats. "I'm not preaching the ketogenic diet; I don't eat it myself," says Cantley, who says he weighs the same now as he did in high school. "I eat what my grandparents ate: a healthy diet, lots of raw vegetables, some animal fat, healthy vegetable fats, an intermediate amount of protein. I don't avoid fats, but I prefer olive oil on salads, and healthy fats from fish and avocado," instead of loading up on butter and cheese. "I eat more protein than the ketogenic diet would recommend, and I do occasionally eat rice and pasta."

But here's the kicker: "The one thing I'm fanatic about is **not drinking anything with sugar**: no orange juice, no apple juice, no soda. I'll *eat* an orange, but I won't grind it up and *drink* it." Sugar in liquid form is rapidly digested, which results in "glucose peaks, followed by insulin peaks."

What about alcohol? "A dry martini is probably safer than wine; there's not much sugar in there." However, Cantley adds, "I do drink wine, but as low in sugar as possible."

Exercise is a great way to divert sugar into someplace safe: the muscles. "Muscle is where you store a lot of sugar in your body. If you drink a sugary drink after exercising, your insulin goes up, and you drive all that glucose into your muscle. Whether you're exercising at the time you drink a sugary drink, or you just put on muscle from exercise in general, there's still a benefit: insulin won't spike." However, exercise doesn't make it safer to drink a lot of sugary drinks, because…

Sugary drinks are bad. It's not just sodas; sweet teas and coffee drinks have more sugar than you may realize. Even sports drinks are loaded with sugar. In 2019, Cantley and colleagues published another landmark paper in *Science*, involving mice with polyposis syndrome (mice genetically predisposed to developing polyps in the colon). They demonstrated **that sugary drinks can dramatically drive the growth of intestinal polyps.** "We gave mice high-fructose corn syrup, and their polyps grew two to three times faster." Fructose is a different sugar from glucose, and although "fructose is not consumed by tumors, it goes straight to the liver and turns into fat. Fructose makes you fat. But the other issue is that *intestinal epithelial cells can directly consume fructose*. We think this explains why there has been a doubling to tripling rate of colorectal cancer in young adults."

Consuming sugar in liquid form is worse than having *that same amount of sugar in solid form*. Cantley explains: "If you eat an apple, it takes a long time to get to the colon. By the time it gets there, all that sugar has leached out. But if you have that same amount of sugar in a drink, that watery sugar gets to the colon pretty quickly. That's independent of the insulin elevation (discussed above), and it's another scary reason why young people should avoid drinking sugary drinks, no matter how much you exercise. You may be a champion marathon runner, but if you're drinking sugary drinks all the time to keep up your energy, this is a real warning that you should pay attention to."

Now, back to prostate cancer: Would taking a PI3K-inhibitor help slow cancer's growth? As is often the case with prostate cancer, it's not that simple. It turns out that there are two different kinds of PI3K, an alpha and a beta form that can contribute to prostate cancer. "When prostate cancer loses PTEN, it uses PI3K alpha *and* beta form redundantly to drive the tumor." This means that a drug that targets only the alpha form probably won't be as effective in prostate cancer as in other forms of cancer, where only the alpha form of PI3K is involved.

However, "our preclinical findings are overwhelmingly supportive, and the retrospective data in patients strongly suggests" that **one day, in addition to surgery, radiation,** hormonal therapy **or other treatments for prostate cancer, patients will be prescribed a precision diet to make the treatment more successful**. "The more we learn about cancer metabolism, we are understanding that cancers are addicted to particular things. For many cancers, that thing is sugar."

Dr. Cantley discloses that he is a founder of a company called Faeth that is providing meals designed to improve responses to cancer therapy. He is also a founder of Petra Pharmaceuticals that focuses on drugs that target PI Kinases. In addition, he periodically consults for other companies that are developing PI 3-Kinase inhibitors.

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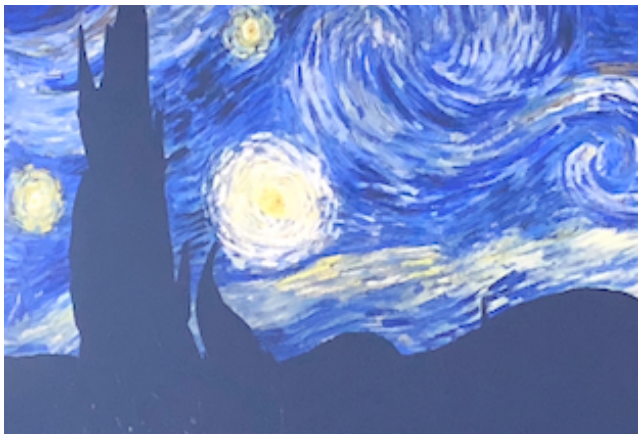

Matters of Survivorship: Sexual Health

SOURCE:
20 May 2022
Janet Farrar Worthington
https://www.pcf.org/c/prostate-cancer-survivorship-part-3/

If you're dealing with prostate cancer – the disease itself, or the aftermath of treatment – then you are dealing with issues of survivorship, says PCF-funded medical oncologist Alicia Morgans, M.D., M.P.H., Medical Director of Cancer Survivorship at Dana Farber Cancer Institute.

Sexual health is "one of the most under recognized issues" for prostate cancer patients and their partners. One big reason why is that men just don't want to talk about it, either because they keep hoping it will get better, or they just decide to be stoic and carry on. "Even though we have a roadmap for how to address these issues after surgery or radiation, we often lack the support system," says Morgans. "There are way too few sexual health counselors specifically dedicated to helping men recovering from prostate cancer." And yet: "This is an area of high interest to many patients. Sexual health affects their personal experience, their mood, energy, everything they do." It also affects the health of their partners.

Although this is the issue many men wish would just go away, what they need to do is just the opposite of hoping for the best: be proactive. If you had surgery and you haven't already had this discussion with your urologist, find out what you can do for penile rehabilitation. This may include pills such as Viagra, Cialis, or other PDE5 inhibitors; vacuum devices for stretching the penis to protect against scar tissue formation; in-office or at-home treatment with a small TENS unit to stimulate nerve regeneration and help with return of urinary control; penile injection; or a penile implant.

Don't suffer in silence! Don't listen to anyone, yourself included, who thinks, "Your cancer has been cured. Just be happy with that." There are many steps you can take to recover your sexual health – but they won't happen if you don't ask for help.

Intimacy: This is not the same as sexual health, but men on ADT and their partners still need intimacy. If your oncologist or medical center does not provide counseling in this area, ask for a referral to a sexual health counselor, and keep this in mind: **you are not alone,** whether you're the patient or his partner. There are thousands of couples dealing with this issue, as well. Your doctor also may be able to recommend support groups, online and affiliated with local medical centers.

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Continence Products

- **Depend** starter Packs by Kimberly- Clark are available from: www.dependcare.com.au
- **Tena** samples are available from: https://tena.com.au

All products are available from supermarkets and pharmacies.

For help with the cost of products visit:

CONTINENCE AIDS PAYMENT SCHEME

https://www.servicesaustralia.gov.au/individuals/services/medicare/continence

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

Continence Foundation of Australia for assistance with incontinence aids
HELPLINE 1800 33 0066

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

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.

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PHCSG Committee

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)

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

January 2022
- Links between Gut Microbiome & Aggressive PCa
- Radpid 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
- Viagara Linked to Lower Risk of Alzheimer's
- Ductal Adencarcinoma
- 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 Manadating Bone Protecting Agents

February 2022
- Why Aren't More Men Electing to Have an Orchiectomy?
- Could More Testosterone be the Key to Fighting PCa? Part one
- Inflammation from ADT may Cause Fatigue
- Optimal Duration of ADT Depends on the Type of Radiation
- How does ADT Affect the Brain?
- Pomegranate may Help Reduce Certain Cancers – Study
- The Perils & Pitfalls of PSA in Advanced PCa
- One Man's Mission to Make PCa Fix Open for All
- Physical exercise can Improve Quality of Life
- Gather My Crew
- Does One Recover Testosterone Faster when Stopping LHRH Antagonist or Agonist?
- Clinical Trials & Studies

March 2022
- Will PSA Testing be Replaced? Novel Screening Approches
- How Bipolar Androgen Therapy Works
- Bipolar Androgen Therapy and the Immune System
- The Role of SBRT
- On Metabolic Syndome, Statin Drugs & PCa Progression
- Yoga Improves QoL in Men Newly Diagnoses with PCa
- The Trials & Tribulations of Managing Men with mHSPCa
- How Enzalutamide Impacts QoL in Metastatic Cancer
- Low-meat and Meat-free Diets associated with lower overall cancer risk
- Transdermal Oestradiol for Androgen Suppression
- PCa Test Cuts False Positives
- Trial to Evaluate Men Starting ADT
- Who goes on ADT with RT to Treat Intermediate Risk PCa
- Darolutamide & Surival in mHSPC
- Effect of High Dose Vitamin D on Bone Density & Strength
- How Important is Bone Mineral Density for Men on ADT
- Bipolar Androgen Therapy – A Patient's Guide
- The D-Health Trial – Effect of Vitamin D on Mortality
- Does Estradiol Improve Cognitive Function for men on ADT?
- SBRT or Convemntional RT for Macroscopic Prostate Bed Recurrence
- To continue ADT – or Not?
- Biochemical Definition of Cure with Brachytherapy of PCa
- New Radiotracer increases Accuracy
- Less Meat, Less PCa?
- PCa's Sweet Tooth
- RP vs RT in Ductal Carcinoma of Prostate
- Survival after RP vs RT in Nodai Positive PCa

April 2022
- Apalutamide no on the PBS
- The Benefit of Exercise
- Ex Med and Hospital exercise programs for patients wit PCa
- Gut Environment changes due to ADT
- Effect of Statins on Advanced PCa or abiraterone/enzalutamide
- Researchers identify five types of bacteria in men with aggressive PCa
- Curative treatments didn't work – what should I do?
- Molecular Mechanisms of Coffee on PCa
- ADT use & duration with RT for Localised PCa
- Association of Muscle Mass after RP
- Is ADT Necessary when you take Abiraterone?
- Obesity Linked to Improved Survival in Advanced PCa
- A Novel Oral Cytoskeleton Disruptor – experimental drug Sabizabulin
- Survival Benefit to Debulking with radiation
- QoL in mHSPC men taking Enzlautamide
- Cleveland Clinic Study Links Microbiome to Aggressive PCa
- Portable Method for PSA Screening
- Clinical Trials

May 2022
- Apalutamide now on the PBS
- The Benefit of Exercise
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- QoL in mHSPC men taking Enzlautamide
- Cleveland Clinic Study Links Microbiome to Aggressive PCa
- Portable Method for PSA Screening

June 2022
- My Cancer Care Record
- Common Blood Test Results Explained
- Don't Allow Statistics to Dictate Your Treatment
- Getting Second Doctor's Opinion
- Primary Care Use of FRAX / Quality of Life in in the Stampede Trial
- Penile Traction Therapy
- SPPORT Trial
- Persistent Testosterone Suppression after Cessation of ADT for localised PCa
- MSK SScientists Identify New Subtype of PCa
- Clinical Efficacy of Bipolar Androgen Therapy with MCRPCa
- Three steps Further
- Treatment Intensification in mHSPCa
- On The Radar /
- Mediterranean Style Dietary with High Interval Training
- Clinical Trials

July 2022
- My Cancer Care Record
- Prostate Cancer Australia's most common cancer
- My Cancer Care Record/ 4 Doxetacel vs Nonsteroidal Antiandrogen with ADT for High Volume mHSPCa
- Treatment Intensification in mHSPCa
- Clinically localised PCa: AUA/ASTRO
- ASCO 2022: Enzamet Update: Benefit Adding Enzalutamide
- Role of Radiotherapy in Oligometastatic HSPCa/
- 8 Review of a plant based diet
- Recent Advances in Management of mPCa
- Multivitamin Use not linked to PCa Risk
- Lu-PSMA-617 Outperforms Cabazitaxel in mPCa
- Commomwealth Seniors Health Card – changing
- Olaparib in BCRA mutated mCRPCa
- Partners of PCa sufferers made ill
- ADT Risk Factors for Depression & Anxiety
- MRI scans detect more accurately than new imaging techniques
- Information Session 'Call the Plumber"

August 2022
- Prostate Cancer Cases Risk Being Diagnosed Too Late
- Does Testosterone Cause Prostate Cancer?
- Treatment Intensification Patterns and Utilization
- Home Based Exercise Programs Show Promise
- Novel Liquid-based Biopsy Launched in US
- Healthy Lifestyle Cuts PCa Mortality Among High Risk Men
- Active Surveillance Plus Enzalutaimde Monotherapy Vs Active Surveillance
- Treatment of Metastatic Hormone Sensitive Prostate Cancer
- Strategies to Help Get Your Life Back
- Study May Help Define Role of PSMA PET Scan in Recurrent PCa
- Cancer Loves Sugar & Sugar *REALLY* Loves Cancer
- Matters of Survivorship – Sexual Health

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

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
- Novatis 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 thel level of your Testosterone matter when on ADT?
- Stay Bone-Healthy
- ADT and the risk of Cariovascular 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 Resportion 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 & ENZAp

October 2021
- Continuous vs Intermittant 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 lomger
- 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 Coul d Improve Outcomes for Advanced Patients
- PCa Trials – Recruiting
- Promising Treatments & New Methods