Prostate Heidelberg Cancer Support Group

Prostate Heidelberg

April 2022 Issue 217

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 19 April 10am – 12:30pm

To join via Zoom: Copy link and paste into your browser

https://us02web.zoom.us/j/81304479071?pwd=WWNjbGJiK2pCMi8xdmFJdlRwQWsxUT09#

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

Contents

Member News

The Prostic Consumer Summit at the Sofitel had some useful information and it was great to see some of our members attending in person. The consumer session is available at: https://www.youtube.com/watch?v=beXdcZrq-EM

To date most Lu therapy is given to mCRPCa patients. However clinical trials (Bullseye – USA) & (UpFront - Australia) are being held to test the hypothesis if ^{177}Lu-PSMA is an effective treatment in oligometastatic hormone-sensitive prostate cancer (oHSPC) to prolong the progression-free survival (PFS) and postpone the need for androgen deprivation therapy (ADT). The results should be available in 2024.

We are lining up new speakers for the year, and encourage you attend. Unfortunately our speaker for April has had to pull out at the last minute so our meeting will be a general discussion and round robin. We will start at our usual time of 10am.

Finally please don't forget to renew your membership. Bank details on the front cover.

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

PCFA has partnered with the University of Southern Queensland (USQ) to develop, trial and evaluate a nurse led survivorship intervention for men on Androgen Deprivation Therapy (ADT), also known as Hormone Therapy.

If you've started hormone therapy in the last 3 months (or are about to start), we would love to hear from you. We are seeking people to take part in an interview which should take no longer than 30-40 minutes of your time to help us better understand the impact of survivorship care interventions.

Interviews will be conducted by telephone or Zoom at a time most convenient to you. You will be required to sign a consent form if you choose to take part. By signing the consent form, you indicate that you understand the information and give your consent to participate in the research study.

If you would like to take part in the study, or find out more, please contact the PCFA's Director of Nursing, Sally Sara via email: Sally.Sara2@usq.du.au.

Note:
This study has been approved by the University of Southern Queensland Human Research Ethics Committee. If you have any concerns about the ethical conduct of this study, you may contact the University of Sothern Queensland, Manager of Research Integrity and Ethics on (07) 4631 1839 or email researchintegrity@usq.edu.au and quote this number [USQ HREC Approval number]. The Manager of Research Integrity and Ethics is not connected with this research project and can address your concerns in an unbiased manner.

Who in the Real World Goes on ADT Along with Radiotherapy to Treat Intermediate Risk Prostate Cancer?

Source:
23 February 2022
https://www.lifeonadt.com/life-on-adt-blog/2022/2/23/who-in-the-real-world-goes-on-adt-along-with-radiotherapy-to-treat-intermediate-risk-prostate-cancer

Clinical trials have shown a benefit to adding ADT to radiotherapy for men treated for unfavourable intermediate risk prostate cancer (PCa). However, for men with *favorable* intermediate risk PCa, adding ADT to radiotherapy doesn't appear to be much more beneficial than radiotherapy alone.

ADT has many side effects and it is a patient's choice whether he goes on ADT or not. So, who in the real world elects to take ADT and who avoids it when treated for intermediate risk PCa?

Researchers in the United States conducted a retrospective cohort study to explore trends or variations in ADT use across the country. To do so, they examined data from the National Cancer Database on over 100,000 men diagnosed with PCa, who were undergoing radiotherapy between 2004 -2016. Approximately 60% had favorable (i.e., only one risk factor) and 40% had unfavorable (i.e., more than one risk factor) for intermediate risk disease. Here risk factors were defined according to National Comprehensive Cancer Network criteria. They included: Gleason score 7, PSA 10 – 20 ng/ml, or clinical stage T2b – T2c.

Men < 60 years of age were less likely to receive ADT. The authors postulate that younger men may be less inclined to accept treatment with ADT because of treatment-related side effects; e.g., hot flashes, weight gain, decreased libido. Black men were more likely to receive ADT compared to white men. Additionally, men who lived > 120 miles from the treatment centre were less likely to receive ADT versus those who lived < 60 miles away.

The authors concluded that treatment recommendations are not followed consistently, resulting in some men being "overtreated," and others being "undertreated." To make the best decision on treatment for PCa, patients need to understand their disease characteristics—i.e., what constitutes unfavourable versus favourable intermediate risk PCa—and the contexts in which treatment with ADT has survival benefits when added to radiotherapy.

To read the full study, see: https://www.advancesradonc.org/article/S2452-1094(22)00011-2/fulltext

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

Darolutamide and Survival in Metastatic, Hormone - Sensitive Prostate Cancer

Source:

https://www.nejm.org/doi/full/10.1056/NEJMoa2119115?query=TOC&cid=NEJM%20eToc,%20February%2024,%202022%20DM758850_NEJM_Non_Subscriber&bid=842714399

Abstract

BACKGROUND

Darolutamide is a potent androgen-receptor inhibitor that has been associated with increased overall survival among patients with nonmetastatic, castration-resistant prostate cancer. Whether a combination of darolutamide, androgen-deprivation therapy, and docetaxel would increase survival among patients with metastatic, hormone-sensitive prostate cancer is unknown.

METHODS

In this international, phase 3 trial, we randomly assigned patients with metastatic, hormone-sensitive prostate cancer in a 1:1 ratio to receive darolutamide (at a dose of 600 mg [two 300-mg tablets] twice daily) or matching placebo, both in combination with androgen-deprivation therapy and docetaxel. The primary end point was overall survival.

RESULTS

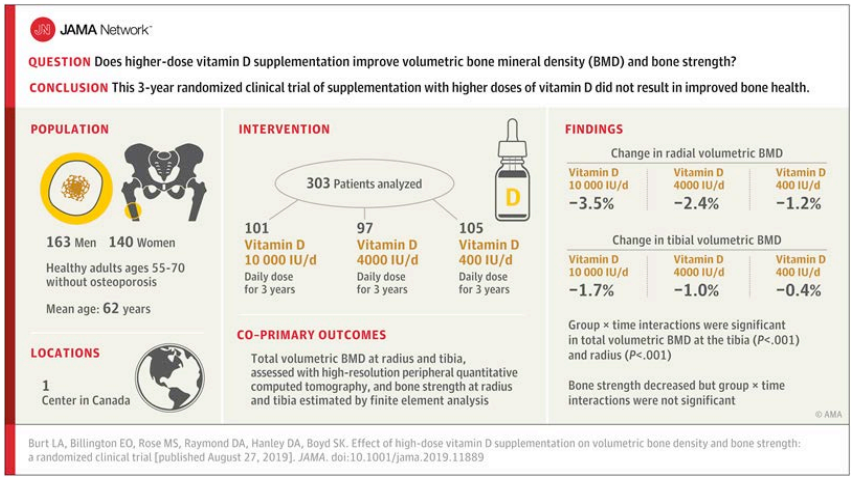
The primary analysis involved 1306 patients (651 in the darolutamide group and 655 in the placebo group); 86.1% of the patients had disease that was metastatic at the time of the initial diagnosis. At the data cutoff date for the primary analysis (October 25, 2021), the risk of death was significantly lower, by 32.5%, in the darolutamide group than in the placebo group (hazard ratio 0.68; 95% confidence interval, 0.57 to 0.80; P<0.001). Darolutamide was also associated with consistent benefits with respect to the secondary end points and prespecified subgroups. Adverse events were similar in the two groups, and the incidences of the most common adverse events (occurring in ≥10% of the patients) were highest during the overlapping docetaxel treatment period in both groups. The frequency of grade 3 or 4 adverse events was 66.1% in the darolutamide group and 63.5% in the placebo group; neutropenia was the most common grade 3 or 4 adverse event (in 33.7% and 34.2%, respectively).

CONCLUSIONS

In this trial involving patients with metastatic, hormone-sensitive prostate cancer, overall survival was significantly longer with the combination of darolutamide, androgen-deprivation therapy, and docetaxel than with placebo plus androgen-deprivation therapy and docetaxel, and the addition of darolutamide led to improvement in key secondary end points. The frequency of adverse events was similar in the two groups.

(Funded by Bayer and Orion Pharma; ARASENS ClinicalTrials.gov number,

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



Effect of High-Dose Vitamin D Supplementation on Volumetric Bone Density & Bone Strength

Source:
August 27, 2019
https://jamanetwork.com/journals/jama/article-abstract/2748796

Key Points

Question Does higher-dose vitamin D supplementation improve bone mineral density (BMD, measured using high-resolution peripheral quantitative computed tomography) and bone strength (measured as failure load)?

Findings In this randomized clinical trial that included 311 healthy adults, treatment with vitamin D for 3 years at a dose of 4000 IU per day or 10 000 IU per day, compared with 400 IU per day, resulted in statistically significant lower radial BMD (calcium hydroxyapatite; −3.9 mg HA/cm^3 and −7.5 mg HA/cm^3, respectively); tibial BMD was significantly lower only with the daily dose of 10 000 IU. There were no significant differences in bone strength at either the radius or tibia.

Meaning Among healthy adults, supplementation with higher doses of vitamin D did not result in improved bone health; further research would be needed to determine whether it is harmful.

Abstract

Importance Few studies have assessed the effects of daily vitamin D doses at or above the tolerable upper intake level for 12 months or greater, yet 3% of US adults report vitamin D intakes of at least 4000 IU per day.

Objective To assess the dose-dependent effect of vitamin D supplementation on volumetric bone mineral density (BMD) and strength.

Design, Setting, and Participants Three-year, double-blind, randomized clinical trial conducted in a single center in Calgary, Canada, from August 2013 to December 2017, including 311 community-dwelling healthy adults without osteoporosis, aged 55 to 70 years, with baseline levels of 25-hydroxyvitamin D (25[OH]D) of 30 to 125 nmol/L.

Interventions Daily doses of vitamin D_3 for 3 years at 400 IU (n = 109), 4000 IU (n = 100), or 10 000 IU (n = 102). Calcium supplementation was provided to participants with dietary intake of less than 1200 mg per day.

Main Outcomes and Measures Co-primary outcomes were total volumetric BMD at radius and tibia, assessed with high resolution peripheral quantitative computed tomography, and bone strength (failure load) at radius and tibia estimated by finite element analysis.

Results Of 311 participants who were randomized (53% men; mean [SD] age, 62.2 [4.2] years), 287 (92%) completed the study. Baseline, 3-month, and 3-year levels of 25(OH)D were 76.3, 76.7, and 77.4 nmol/L for the 400-IU group; 81.3, 115.3, and 132.2 for the 4000-IU group; and 78.4, 188.0, and 144.4 for the 10 000-IU group. There were significant group × time interactions for volumetric BMD. At trial end, radial volumetric BMD was lower for the 4000 IU group (−3.9 mg HA/cm^3 [95% CI, −6.5 to −1.3]) and 10 000 IU group (−7.5 mg HA/cm^3 [95% CI, −10.1 to −5.0]) compared with the 400 IU group with mean percent change in volumetric BMD of −1.2% (400 IU group), −2.4% (4000 IU group), and −3.5% (10 000 IU group). Tibial volumetric BMD differences from the 400 IU group were −1.8 mg HA/cm^3 (95% CI, −3.7 to 0.1) in the 4000 IU group and −4.1 mg HA/cm^3 in the 10 000 IU group (95% CI, −6.0 to −2.2), with mean percent change values of −0.4% (400 IU), −1.0% (4000 IU), and −1.7% (10 000 IU). There were no significant differences for changes in failure load (radius, $P = .06$; tibia, $P = .12$).

Conclusions and Relevance Among healthy adults, treatment with vitamin D for 3 years at a dose of 4000 IU per day or 10 000 IU per day, compared with 400 IU per day, resulted in statistically significant lower radial BMD; tibial BMD was significantly lower only with the 10 000 IU per day dose. There were no significant differences in bone strength at either the radius or tibia. These findings do not support a benefit of high-dose vitamin D supplementation for bone health; further research would be needed to determine whether it is harmful.

How Important is Bone Mineral Density for Men

Source:
27 August 2019
https://www.lifeonadt.com/life-on-adt-blog/2022/4/6/how-important-is-bone-mineral-density-testing-for-

Because ADT can cause a loss of bone mineral density, men on ADT have an increased risk of bone fractures. However, if one is aware of the risks and takes appropriate action, this risk can be managed. Here the old adage, 'knowledge is power,' is surprisingly relevant.

Dual-energy x-ray absorptiometry (DXA, also abbreviated DEXA) screening is used to assess bone mineral density and is the standard tool for monitoring bone health. Yet, despite ADT's risk to bone density, research suggests that DXA screening is under-utilized.

A recent study out of the United States looked at the rates of DXA screening among men with localized/regional prostate cancer who were starting ADT. The researchers used data from a national health database to examine rates of DXA screening among nearly 55,000 men (66-99 years of age), who were initiating ADT.

Only 7.9% of men underwent DXA screening shortly before or after starting ADT.

Subsequently while on ADT, 17.5% of men developed a bone fracture, and 7.7% of the men developed a major osteoporotic fracture. Of note, this study excluded men with metastatic disease, in order to rule out fractures related to bone metastases.

Importantly, DXA screening was associated with a 9.1% lower risk of major fracture among those who underwent DXA screening versus those who didn't. It's likely there are multiple factors contributing to this result, but the authors note: "Men who received DXA screening were more likely to receive bone-modifying agents (18.8%) than those who did not (1.8%)."

It may also be true that getting a DXA scan educates/informs (i.e., "sensitizes") patients to the osteoporotic risk of ADT. Patients may thus be more inclined to do exercises (e.g., impact loading exercises) and take medication, if prescribed, to protect their bones. In that sense, the DXA diagnostic procedure ends up being not just diagnostic, but having therapeutic value in and of itself.

To read the full article, see:
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790600

Bipolar androgen therapy (BAT): A patient's guide

Source:
31 March 2022
https://onlinelibrary.wiley.com/doi/10.1002/pros.24328

Abstract

Bipolar androgen therapy (BAT) is a new treatment concept for men whose prostate cancer has become resistant to standard hormone-blocking therapy. Over the past decade, we have performed a series of clinical studies testing BAT in asymptomatic men with castration-resistant prostate cancer. The key findings from these clinical studies are that BAT (a) can be safely administered to asymptomatic patients with metastatic castrate-resistant prostate cancer; (b) does not produce symptomatic disease progression; (c) produces sustained prostate-specific antigen and objective responses in 30%–40% of patients; and (d) can resensitize and prolong response to subsequent antiandrogen therapy. The concept of BAT has generated significant interest from men with prostate cancer, their families, and their physicians. Here we provide a "Patient's Guide" that answers questions about BAT in a form that is accessible to patients, their families, and physicians. Our goal is to provide information to help patients make the most informed decisions they can regarding their prostate cancer treatment.

The D-Health Trial: a Randomised Controlled Trial of the Effect of Vitamin D on Mortality

Source:
10 January 2022
https://www.thelancet.com/journals/landia/article/PIIS2213-8587(21)00345-4/fulltext

Background

The effect of supplementing unscreened adults with vitamin D_3 on mortality is unclear. We aimed to determine whether monthly doses of vitamin D_3 influenced mortality in older Australians.

Methods

We did a randomised, double-blind, placebo-controlled trial of oral vitamin D_3 supplementation (60 000 IU per month) in Australians 60 years or older who were recruited across the country via the Commonwealth electoral roll. Participants were randomly assigned (1:1), using automated computer-generated permuted block randomisation, to receive one oral gel capsule of either 60 000 IU vitamin D_3 or placebo once a month for 5 years. Participants, staff, and investigators were blinded to study group allocation. The primary endpoint was all-cause mortality assessed in all participants who were randomly assigned. We also analysed mortality from cancer, cardiovascular disease, and other causes. Hazard ratios (HRs) and 95% CIs were generated using flexible parametric survival models. This trial is registered with the Australian New Zealand Clinical Trials Registry, ACTRN12613000743763.

Findings

Between Feb 14, 2014, and June 17, 2015, we randomly assigned 21 315 participants, including 10 662 to the vitamin D group and 10 653 to the placebo group. In 4441 blood samples collected from randomly sampled participants (N=3943) during follow-up, mean serum 25-hydroxy-vitamin D concentrations were 77 (SD 25) in the placebo group and 115 (SD 30) nmol/L in the vitamin D group. Following 5 years of intervention (median follow-up 5·7 years [IQR 5·4–6·7]), 1100 deaths were recorded (placebo 538 [5·1%]; vitamin D 562 [5·3%]). 10 661 participants in the vitamin D group and 10 649 participants in the placebo group were included in the primary analysis. Five participants (one in the vitamin D group and four in the placebo group) were not included as they requested to be withdrawn and their data to be destroyed. The HR of vitamin D_3effect on all-cause mortality was 1.04 [95% CI 0·93 to 1·18]; p=0·47)and the HR of vitamin D_3 effect on cardiovascular disease mortality was 0·96 (95% CI 0·72 to 1·28; p=0·77). The HR for cancer mortality was 1·15 (95% CI 0·96 to 1·39; p=0·13) and for mortality from other causes it was 0·83 (95% CI 0·65 to 1·07; p=0·15). The odds ratio for the per-protocol analysis was OR 1·18 (95% CI 1·00 to 1·40; p=0·06). In exploratory analyses excluding the first 2 years of follow-up, those randomly assigned to receive vitamin D had a numerically higher hazard of cancer mortality than those in the placebo group (HR 1·24 [95% CI 1·01–1·54]; p=0·05).

Interpretation

Administering vitamin D_3 monthly to unscreened older people did not reduce all-cause mortality. Point estimates and exploratory analyses excluding the early follow-up period were consistent with an increased risk of death from cancer. Pending further evidence, the precautionary principle would suggest that this dosing regimen might not be appropriate in people who are vitamin D-replete.

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

Does a Bit of Add-back Estradiol Improve Cognitive Function for Men on ADT?

Source
25 March 2022
https://www.lifeonadt.com/life-on-adt-blog/2022/3/25/does-a-bit-of-add-back-estradiol-improve-cognitive-function-for-men-on-adt

A new study out of Australia looked at whether the use of transdermal (i.e., applied to the skin) estradiol improved cognitive function for men on ADT. The study was inspired by some evidence suggesting that estradiol is cognitively protective for women before menopause. One may suppose that estradiol may cognitively benefit men on ADT, if it protects them from hot flashes that disrupt their sleep. Indeed, a good night's sleep helps keep one mentally alert during the day. So that sounds reasonable.

Men in the study were randomly assigned to receive either transdermal estradiol as a topical gel or a placebo while on ADT. All the men were administered a huge battery of cognitive tests at baseline and again at one, three and six months. As such, this was a rigorous, well-designed study.

However, the paper had a negative result. Adding estradiol showed no major effect on cognition for prostate cancer patients with castrate levels of testosterone from ADT.

A big problem was that there were only 39 men in each group. With sample sizes so small, it is not surprising that no major differences were found between the two groups.

This study is a testament to how the COVID-19 pandemic has disrupted quality-of-life research in prostate cancer. Sadly, this study was under powered because the pandemic forced the researchers to prematurely close the study.

This research is too interesting and too important to be abandoned completely. One hopes that the researchers will either be able to extend the study once the pandemic is under control or that others will follow up on the research.

With small sample sizes, it's particularly important to match participants as closely as possible on each arm of a study…and as closely as possible on as many criteria as possible. Indeed, the men in both groups had a mean age of 72 years and were very similar in most other ways. However, one might wonder whether patients who are much younger might see some benefit from the add-back estradiol not detected in this study. That is based on the fact that hot flash intensity and bother is greater for younger men.

We hope this research will not be abandoned completely. Indeed, we would like to see it revisited in future studies involving larger sample sizes and a more diverse patient population.

Stereotactic or Conventional Radiotherapy for Macroscopic Prostate Bed Recurrence: a Propensity Score Analysis

Source:
7 March 2022
https://www.urotoday.com/recent-abstracts/urologic-oncology/prostate-cancer/135901-stereotactic-or-conventional-radiotherapy-for-macroscopic-prostate-bed-recurrence-a-propensity-score-analysis.html

To assess outcomes between salvage radiation therapy (SRT) with curative intent and stereotactic radiotherapy for macroscopic prostate recurrence (SSRT) after radical prostatectomy (RP). In order to compare these two different options, we compared their outcomes with a propensity score-based matched analysis.

Data from 185 patients in seven Italian centres treated for macroscopic prostate bed recurrence after RP were retrospectively collected. To make a comparison between the two treatment groups, propensity matching was applied to create comparable cohorts.

After matching, 90 patients in the SRT and SSRT groups were selected (45 in each arm). Kaplan-Meier analysis did not show any significant differences in terms of BRFS (Biochemical Recurrent Free Survival) and PFS (Progression Free Survival) between matched populations ($p = 0.08$ and $p = 0.8$, respectively). Multivariate models show that treatment was not associated with BRFS, neither in the whole or matched cohort, with HR of 2.15 (95%CI 0.63-7.25, $p = 0.21$) and 2.65 (95%CI 0.59-11.97, $p = 0.21$), respectively. In the matched cohort, lower rate of toxicity was confirmed for patients undergoing SSRT, with acute GI and GU adverse events reported in 4.4 versus 44.4% ($p < 0.001$) and 28.9 versus 46.7% ($p = 0.08$) of patients, and late GI and GU adverse events reported in 0 versus 13.3% ($p = 0.04$) and 6.7 versus 22.2% ($p = 0.03$) of patients, respectively.

Considering the favourable therapeutic ratio of this approach and the lower number of fractions needed, SSRT should be considered as an attractive alternative to conventional SRT in this setting.

To Continue Androgen Deprivation Therapy or Not?

Source
2 March 2022
Chris McNamara
https://onlinecommunity.pcfa.org.au/t5/Research-Blog/BLOG-To-continue-androgen-deprivation-therapy-or-not/ba-p/6861

The concept of intermittent androgen deprivation therapy (IADT) is well established. After a patient has been initiated on ADT for an induction period of between 6-12 months, they may then be offered a treatment holiday. The benefit of this treatment approach is to minimise treatment related side effects (such as compromised sexual function, hot flushes, depression, fatigue and cardiovascular risk) and improve quality of life. It may also resensitise the tumour and prolong survival to castration resistance. There is also a cost benefit.

Who qualifies for IADT?

Patients who achieve a PSA less than 4 ng/mL during the initial induction period, have poor tolerability to continuous ADT, have non-metastatic disease, or metastasis that is limited to lymph nodes (glands) and are not candidates for chemotherapy such as docetaxel, have locally advanced disease, ideally older but highly motivated, have Gleason scores >7, and have longer PSA doubling time. IADT may lead to slower time to cancer progression and improved overall survival.

What is a typical IADT protocol?

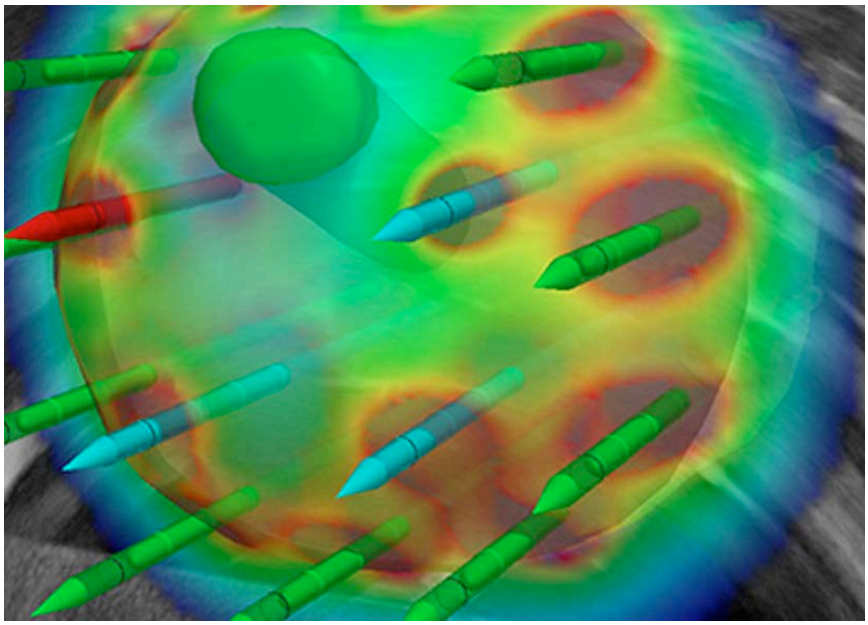
There is no formal recommendation for the optimal protocol, but this is a guide: After the initial induction period where the PSA has reached less than 4 ng/mL for metastatic disease or less than 0.5ng/ml for those who have recurrent disease after primary treatment (surgery or radiation), the off-treatment phase can begin. During this time disease progression is monitored by testing PSA and testosterone levels every 3-6 months and a clinical review. If the PSA reaches 4-10 ng/ml for non-metastatic cancer and 10-20ng/ml for metastatic cancer or if the patient exhibits evidence of radiological or symptomatic progression, then treatment has to be re-initiated. Further imaging studies such as CT, bone scan or PET-based imaging may be requested. If there is no progression then a new induction phase is implemented for another 6 months before an ADT holiday can be trialled again.

The American Urological Association and National Comprehensive Cancer Network guidelines suggest IADT may be offered for patients with biochemical failure without metastases, and the European Association of Urology considers IADT for asymptomatic metastatic patients. This variation in recommendations has influenced the implementation of IADT by practitioners. There is limited research into the patterns of IADT usage. Cheung et al from the University of Toronto investigated a cohort of 8544 eligible patients and discovered that only 16,4% received IADT[1]. This statistic varied per region from 11.4%-24.8%. Those who had recurrence after radiation, or a prostatectomy were more likely to be placed on IADT with a prevalence of 26.6%. Those who had higher incomes were also more likely candidates, whereas those in rural areas experienced variation in their access to services and poorer survival. Radiation oncologists were more likely to prescribe IADT over urologists and number of years in practice was a positive influencer. Some of the cited reasons for initiating IADT by doctors was patient age, lower PSA, desire to maintain sexual function, associated illnesses, and patient request, which may reflect attempts to minimize side effects in lower-risk patients.

Where indicated, IADT has a potential impact on patients' quality of life and cancer outcomes. Further research is required, particularly in the Australian context, to ascertain local prescribing patterns and impact on overall survival. This may shape treatment guidelines and redress any inequalities in care. Current trials are investigating combination treatments including targeted interventions (radiation and intratumoural therapy) and medications (abiraterone or immunotherapy such as nivolumab) to increase the time before re-initiation of ADT by controlling the primary disease[2].

Prostate Cancer Foundation of Australia

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.



A Biochemical Definition of Cure Following Brachytherapy of Prostate Cancer

As part of a special course on brachytherapy for prostate cancer from the American Brachytherapy Society (ABS) and *Grand Rounds in Urology*, Juanita M. Crook, MD, FRCPC, Professor of Radiation Oncology at the University of British Columbia in Kelowna, discusses the development of a biochemical definition of cure following low-dose-rate (LDR) prostate brachytherapy. She begins with some background, explaining that the interpretation of post-radiation PSA values has been challenging. She relates that the 1996 ASTRO consensus conference defined biochemical failure as 3 consecutive rises after the nadir with failure backdated to midway between the nadir and the first rise, while the 2005 Phoenix consensus conference defined biochemical failure as 2 ng/ml > nadir, a definition still widely used today. Dr. Crook emphasizes that neither definition was meant to be a trigger for intervention, and neither attempted to define cure. She then discusses research on the importance of PSA nadir in LDR brachytherapy which showed that if PSA at 4 years was less than 0.2 to 0.4 ng/ml, patients tended to do well, but if it was greater than 1.0, the majority were going to fail. Dr. Crook considers another study on long-term PSA stability after LDR brachytherapy which found that 86% of patients had stable PSA at a median followup of 89 months. She also briefly notes that a study of intermediate-risk patients undergoing external beam radiation therapy (EBRT) + high-dose-rate brachytherapy boost found similar results to the studies of LDR brachytherapy regarding the importance of PSA nadir. Dr. Crook then goes into detail about a study she and her colleagues conducted to define a biochemical definition of cure following LDR brachytherapy by identifying a PSA threshold value at an intermediate follow-up time that is associated with long-term (10-15 year) freedom from prostate cancer. She explains that by using prospectively-collected data sets combined from 7 institutions, she and her colleagues were able to determine that patients with a PSA ≤ 0.2 ng/ml by 4-5 years have a 99% probability of being free of clinical failure at 10-15 years. Dr. Crook concludes that PSA ≤ 0.2 ng/ml should be adopted as biochemical definition of cure for comparison with surgical series, but highlights that those patients not achieving this threshold PSA should not be considered as having "failed" but should continue to be monitored with the understanding that they are at higher risk of subsequent clinical failure.

Source
April 2022
Juanita M Crook MD FRCPC
https://grandroundsinurology.com/a-biochemical-definition-of-cure-following-brachytherapy-of-prostate-cancer/?utm_campaign=ABS%20Course&utm_medium=email&_hsmi=208919219&_hsenc=p2ANqtz-99av6hBHYpnOIfx7Vymt0YnuVXko0m8ng4RXsAzMjlCGj5kQuK477HWvuyzbc20Ol05xlP0WWrVeS9c6flWmfNT3rShg&utm_content=208919219&utm_source=hs_email

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

New Radiotracer Yields Huge Increase in Accuracy of Localizing PCa Relapses

Source
28 March 2022
Saarland University
https://sciencesources.eurekalert.org/news-releases/947867

Prostate cancer is the most common malignant tumour in men in Germany, with about 62,000 new cases diagnosed each year[1]. Worldwide, there are more than 1.3 million new cases a year. As with many other types of malignant tumours, prostate cancer responds well to treatment if caught in its early stages. The survival rate for patients who undergo radiation therapy or have their prostate gland surgically removed is around 90%. However, even if the prostate gland has been removed, there is still a risk of metastasis. 'Metastasis can occur if the surgeon was not able to extract all of the tumour during the operation and tiny fragments of cancerous tissue are still present. This may mean that the cancer returns many months later even though the original tumour is no longer present,' explains Samer Ezziddin, Professor of Nuclear Medicine and Director of the Department of Nuclear Medicine at the Saarland University Medical Center.

For several years, medical scientists have been using a reliable method of detecting both metastases, where the cancer has spread to other parts of the body, and local recurrences, where the cancer has reappeared in the same place that it was first detected. The technique, known as PSMA-PET/CT imaging, is performed using a positron emission tomography scanner. The method is used when prostate-specific antigen (PSA) is detected in the blood of patients whose prostate has already been removed. Prostate-specific antigen is produced by both the prostate gland and by prostate tumour tissue. The presence of measurable quantities of PSA in the blood of a man whose prostate has been surgically removed therefore indicates that the primary tumour, which may have been removed a considerable period of time ago, has metastasized or recurred. However, it is often unclear where precisely these PSA-producing metastases are located. A prostate carcinoma that has spread to other parts of the body can mean that PSA is found in the patient's bones, lymph nodes or liver. In the PSMA-PET/CT imaging technique, the focus is on detecting a protein molecule known as PSMA (prostate-specific membrane antigen) that is attached to the surface of the prostate tumours cells and can thus be used to identify the locations of the metastases. 'The problem is that other non-prostate related pathologies can also result in the presence of PSMA,' explains Samer Ezziddin. For example, PSMA can be produced following a bone fracture due to the increased formation of blood vessels in the tissue surrounding the fracture site. Similarly, small and completely harmless vascular tumours, known as haemangiomas, can also express PSMA.

This is where modern imaging technology comes into play. 'Since about 2014 or 2015 we've been using PSMA-PET/CT to see where metastases or local recurrences have formed,' says Professor Ezziddin. 'The technique involves injecting a radiopharmaceutical into the patient's vein. The radiopharmaceutical is a tracer compound containing a weakly radioactive substance that is able to attach itself to the PSMA molecule. After a while, the PET-CT image shows us the distribution of PSMA molecules, which allows us to identify where a tumour is located or to map the distribution of metastatic sites.

So far, short-lived radiotracers such as gallium-68-labelled PSMA ligands have been the markers of choice. The 68Ga isotope has a half-life of 68 minutes, so for about an hour after injection, the radiologists can see precisely where the tracer has ended up and thus identify the likely site of a tumour. But on a PET-CT image it is not always easy to distinguish between a malignant tumour and harmless structures such as haemangiomas. 'In around half the cases we look at, we don't see any abnormalities in a conventional PSMA-PET/CT image,' says Ezziddin.

Ezziddin and his team have therefore been testing a new radiopharmaceutical that contains the isotope zirconium 89 (89Zr), which has a significantly longer half-life and has not fully decayed even after several days. 'The results were stunning,' says Samer Ezziddin. 'We examined twenty patients whose conventional PSMA-PET/CT scans were all negative. That is to say, we were unable to find any evidence of metastases or other tumour tissue in the original images. But when we used the zirconium-89-labelled radiotracer, we found early-stage tumours and metastases in all of the patients in our small sample group.

As a result, these patients could be treated using radiation therapy much earlier than would otherwise have been the case. Because the medical team now knew the precise location of the cancer cells, they were able to subject these regions to a very precise and much higher dose of radiation. Normally, the medical staff are much less certain of where the cancer cells are located, and therefore have to take a less targeted approach, which has the associated risk of exposing surrounding healthy tissue to radiation, something they would ideally wish to avoid. Without the

(continued page 12)

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

new radioisotope tracer, a negative result from a conventional PSMA-PET/CT scan would have meant that these metastases and local recurrences would have gone undetected for far longer. 'And that, of course, means that a patient's chances of survival are considerably diminished,' explains Samer Ezziddin.

'But the longer half-life also allows us to examine other patients, too. If we have patients who previously had a mildly positive or indeterminate PSMA-PET/CT scan, we can now use the new technique to identify those regions in which higher levels of PSMA were only due to the presence of benign pathologies and thus distinguish them from true prostate cancer aetiologies,' says Professor Ezziddin. 'In contrast to a region with a malignant prostate tumour, these other regions will no longer be visible on the PET/CT image.' The reason for this behaviour lies in the slightly different structure of a PSMA molecule bound to the membrane of a prostate cancer cell than one bound to, say, the surface of blood vessel cells. After a few days, the radiotracer is no longer attached to these harmless regions but is still bound to the cancer tissue. The accuracy of the imaging results is thus enhanced enormously when the tracer molecule contains zirconium 89 as the radionuclide.

Although the results that Professor Ezziddin and his team have produced are from a case study and not a peer-reviewed study, the huge relevance of their findings for many patients, has prompted Ezziddin to publicize the surprisingly clear-cut results from this small pilot study. It may thus be possible to help patients whose metastases would previously have been detected much later using conventional PSMA-PET/CT imaging.

'At a conservative estimate, I would say that each year between 100,000 and 200,000 men worldwide could benefit from this new technique,' says Ezziddin.

Less Meat, Less Prostate Cancer?

Source
8 March 2022
https://www.pcf.org/blog/less-meat-less-prostate-cancer/

People often have questions about whether specific foods—such as meat—might increase their risk of prostate cancer or other diseases.

A new study of more than 200,000 men in the U.K. found that men who were vegetarian, and men who ate fish (but no meat), were less likely to be diagnosed with prostate cancer compared to men who often ate meat.

People who signed up for the study answered questions about their diet and were classified as regular meat-eaters (eating meat, including poultry, more than 5 times per week), low meat-eaters (5 or fewer times per week), eating fish but no meat, and eating no meat (vegetarian/vegan). They also provided blood samples and other physical data. They were followed for several years, and any cancer diagnosis was recorded.

About 60% of men were regular meat-eaters. Vegetarians/vegans were 31% less likely to be diagnosed with prostate cancer during the follow up-period vs regular meat-eaters. Men who ate fish, but no meat, were 20% less likely to get prostate cancer. Being a low meat-eater did not affect risk of prostate cancer.

It's important to note that the study found a *connection* (or association) between diet and prostate cancer risk, and does not *prove* cause and effect. Men who often ate meat may differ from men who were vegetarian and men who ate fish in other ways that affect health, such as smoking, exercise, and body mass index (BMI). The researchers considered this, and accounted for it as much as possible in their analysis, but there may be other factors that could not be measured.

What You Can Do

It can feel discouraging to limit your diet by making a list of foods to avoid. Instead, focus on the positive: *filling* your plate with foods that boost your overall health, such as brightly-colored vegetables, legumes, and whole grains. In fact, a study by PCF-funded researchers Dr. Stacy Loeb and Dr. Lorelei Mucci investigated the benefits of "healthful plant-based diet." While not vegetarian per se, it is rich in whole, plant-based foods, while minimizing animal products, refined grains, and sweets. This type of diet is linked to a lower risk of advanced and fatal prostate cancer, especially in men younger than 65. (See Dr. Mucci's presentation on the study here.)

If you do eat meat, consider using it as a flavor-enhancing condiment rather than the "main event." Or, if you enjoy a steak on a special occasion, pair it with generous serving of roasted broccoli instead of scalloped potatoes.

Prostate Cancer's Sweet Tooth

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

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.

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-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

(continued page 14)

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* a n 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."

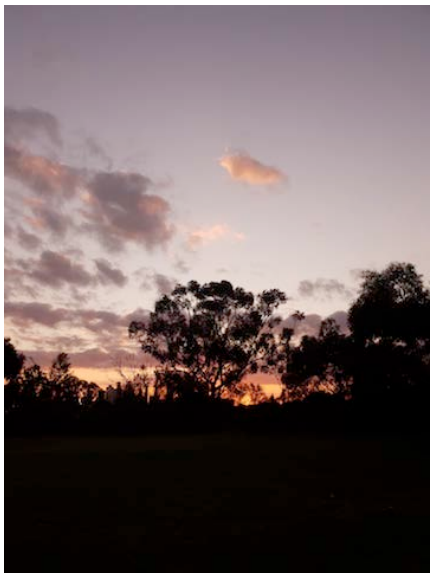
Survival after Radical Prostatectomy vs. Radiation Therapy in Ductal Carcinoma of the Prostate

Authors: Chierigo F et al.

https://www.researchreview.com.au/getmedia/146b225a-4286-47b3-b340-52d9f98d2303/Prostate_Cancer_Research_Review_Issue_51.pdf.aspx?ext=.pdf

Summary: This retrospective analysis of data from the US Surveillance, Epidemiology, and End Results (SEER) database (2004-2016), compared cancer- specific mortality between radical prostatectomy (n = 303) and external beam radiotherapy (n= 66) in patients with ductal carcinoma of the prostate. Radical prostatectomy patients were older, with higher PSA values, higher clinical T-stage and higher Gleason grade groups. Five-year cancer-specific mortality rates were 4.2% for radical prostatectomy versus 10% for radiotherapy (HR 0.40; 95% CI 0.16-0.99; p = 0.048). Multivariate analysis revealed that the central tendency of the HR for radical prostatectomy versus radiotherapy approached one. Propensity score matching of 124 radical prostatectomy versus 53 radiotherapy patients showed no protective effect of radical prostatectomy (HR 1.16; 95% CI 0.23-5.73) nor did inverse probability of treatment weighting (HR 0.97; 95% CI 0.35-2.66).

Comment: Ductal variant prostate cancer has a significantly poorer clinical outcome compared to the much more prevalent acinar histological type, and the optimal treatment strategy is unclear. This study reports on treatment outcomes following radiation treatment or radical prostatectomy over a 12- year period using data from the SEER database. Overall, >80% of patients were treated with surgery, which on crude analysis appeared to be associated with improved cancer-specific mortality, which disappeared once a propensity score matched analysis was undertaken in a smaller subset corrected for PSA, stage and grade. What is clear is that ductal variant histology is lethal (5-year cancer-specific mortality of 5-10%), so more work is needed to improve patient treatments and outcomes.



Survival After Radical Prostatectomy vs Radiation Therapy in Clinical Node-Positive Prostate Cancer

Abstract

To compare overall mortality (OM), cancer-specific mortality (CSM), and other cause mortality (OCM) rates between radical prostatectomy (RP) versus radiotherapy (RT) in clinical node-positive (cN1) prostate cancer (PCa).

MATERIALS AND METHODS

Within Surveillance, Epidemiology, End Results (SEER) (2004-2016), we identified 4685 cN1 PCa patients, of whom 3589 (76.6%) versus 1096 (24.4%) were treated with RP versus RT. After 1:1 propensity score matching (PSM), Kaplan-Meier plots and Cox regression models tested the effect of RP versus RT on OM, while cumulative incidence plots and competing-risks regression (CRR) models addressed CSM and OCM between RP and RT patients. All analyses were repeated after the inverse probability of treatment weighting (IPTW). For CSM and OCM analyses, the propensity score was used as a covariate in the regression model.

RESULTS

Overall, RT patients were older, harbored higher prostate-specific antigen values, higher clinical T and higher Gleason grade groups. PSM resulted in two equally sized groups of 894 RP versus 894 RT patients. After PSM, 5-year OM, CSM, and OCM rates were, respectively, 15.4% versus 25%, 9.3% versus 17%, and 6.1% versus 8% for RP versus RT (all $p < 0.001$) and yielded respective multivariate hazard ratios (HRs) of 0.63 (0.52-0.78, $p < 0.001$), 0.66 (0.52-0.86, $p < 0.001$), 0.71 (0.5-1.0, $p = 0.05$), all favoring RP. After IPTW, Cox regression models yielded HR of 0.55 (95% confidence interval [CI] = 0.46-0.66) for OM, and CRR yielded HRs of 0.49 (0.34-0.70) and 0.54 (0.36-0.79) for, respectively, CSM and OCM, all favoring RP (all $p < 0.001$).

CONCLUSIONS

RP may hold a CSM advantage over RT in cN1 PCa patients.

TAKE-HOME MESSAGE

- This retrospective, observational study assessed the differences in clinical outcomes among patients with clinical node-positive (cN1) prostate cancer undergoing radiotherapy (RT) versus radical prostatectomy (RP). After propensity score matching, the 5-year overall mortality (OM), cancer-specific mortality (CSM), and other-cause mortality (OCM) rates for RT versus RP were 15.4% versus 25%, 9.3% versus 17%, and 6.1% versus 8%, respectively. After inverse probability of treatment weighting, the multivariable Cox regression model for OM produced a hazard ratio of 0.55 (P < .001), while multiple competing risks regression models produced hazard ratios of 0.49 and 0.54 for CSM and OCM, respectively (P < .001).
- These findings highlight that, in comparison with RT, RP was associated with lower CSM and OCM, and should be considered for patients with cN1 prostate cancer.

– Vinay Mathew Thomas, MD

SOURCE
15 March 2022
https://www.practiceupdate.com/journalscan/92120/67/11?elsca1=emc_enews_weekinreview&elsca2=email&elsca3=practiceupdate_advancedprostatecancer&elsca4=advancedprostatecancer&elsca5=newsletter&rid=NTMyMjc0MDc4NjM0S0&lid=20849595

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

PCa Clinical Trials & Studies

For Further information on current and recruiting trials visit:

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

Update to a randomized controlled trial of lutetium-177-PSMA in Oligo-metastatic hormone-sensitive prostate cancer: the BULLSEYE trial

8 November 2021

The BULLSEYE trial is a multicenter, open-label, randomized controlled trial to test the hypothesis if 177Lu-PSMA is an effective treatment in oligometastatic hormone-sensitive prostate cancer (oHSPC) to prolong the progression-free survival (PFS) and postpone the need for androgen deprivation therapy (ADT). The original study protocol was published in 2020. Here, we report amendments that have been made to the study protocol since the commencement of the trial.

Two important changes were made to the original protocol: (1) the study will now use 177Lu-PSMA-617 instead of 177Lu-PSMA-I&T and (2) responding patients with residual disease on 18F-PSMA PET after the first two cycles are eligible to receive additional two cycles of 7.4 GBq 177Lu-PSMA in weeks 12 and 18, summing up to a maximum of 4 cycles if indicated. Therefore, patients receiving 177Lu-PSMA-617 will also receive an interim 18F-PSMA PET scan in week 4 after cycle 2. The title of this study was modified to; "Lutetium-177-PSMA in Oligo-metastatic Hormone Sensitive Prostate Cancer" and is now partly supported by Advanced Accelerator Applications, a Novartis Company.

We present an update of the original study protocol prior to the completion of the study. Treatment arm patients that were included and received 177Lu-PSMA-I&T under the previous protocol will be replaced.

ClinicalTrials.gov NCT04443062 . First posted: June 23, 2020.

Phase II evaluation of stereotactic ablative radiotherapy (SABR) and choline-PET/CT–identied oligometastatic castration-resistant prostate cancer

Authors: Zhang H et al.

https://www.researchreview.com.au/getmedia/146b225a-4286-47b3-b340-52d9f98d2303/Prostate_Cancer_Research_Review_Issue_51.pdf.aspx?ext=.pdf

Summary: This phase II trial examined the use of stereotactic ablative radiotherapy (SABR) in 89 patients (128 lesions) with oligometastatic CRPC. The median OS was 29.3 months while the 1-year OS was 96% and the 2-year OS was 80%. Biological PFS (PSA) was 40% at 1 year and 21% at 2 years, while local PFS was 84.4% at 1 year and 75.3% at 2 years. There were no grade ≥3 adverse events. High baseline tumour- reactive T cell levels predicted superior local-, biological-, and distant-PFS. High baseline effector memory T cell levels were associated with improved biological PFS.

Comment: One of the interesting phenomena associated with radiation treatment is the abscopal effect, whereby treatment of one metastatic lesion can produce regression in other, non-treated deposits. It has long been suspected that this has an immunological basis, which has led to hope that high-dose radiation to metastatic lesions can prime otherwise non-responsive tumours to immunotherapy such as ICIs. Against this background this biomarker study investigated the role of various immune biomarkers as predictors of response to SABR in oligometastatic mCRPC. Patients with higher levels of anti-tumour immune reactivity at baseline demonstrated better tumour response, whereas patients who experienced an increase in anti-tumour reactivity after SABR (about 30%) had signicantly improved OS. Maybe combination with an ICI in this population is the way forward.

Prostate Heidelberg Cancer Support Group Meetings

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

21 June: Assoc Prof Joseph Ischia Urological Surgeon

16 August: Boston Scientific

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.

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

April 2022
- 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

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