Prostate Heidelberg

September 20 Issue 210

MEMBERSHIP

HALF YEAR PHCSG MEMBERSHIP $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

For Education, Information and Support

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

Next PHCSG Meeting via Zoom – Tues 21 September 10am – 12:30pm

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

https://us02web.zoom.us/j/89733739029?pwd=dUUreUNQdFpRRnFxWnFXZktMZ3FKZz09

Meeting ID: 897 3373 9029
Passcode: 793545

PHCSG August

In August, we welcomed Ben Shemesh who told us about the development of the BroSupPORT portal. You can read more about it on page 17. As we continue in lockdown I'm sure we all feel the need for support, even if we don't have PCa. It was mentioned at our last meeting that very few partners/support persons join our primary members at our meetings. They, of course, are always welcome and often add new perspectives on dealing with the challenges of PCa. I have included a study from France on page 15 about the importance of a social network.

In this month's newsletter we highlight:

- 2 PEEK Study
- 3 Skeletal Events & Bone Modifying Agents in Castration Resistant PC
- 4/5 Abiraterone+docetaxel+ADT for Newly Diagnoses Metastatic PC
- 6/7 Brief, Intense Radiation & Hormone Therapy for Very High Risk PCa
- 8 Progression-directed Therapy for Oligoprogression
- 8 Insights into PC metabolism
- 9 Diagnostic Accuracy of PSMA 18F-DCFPyL PET/CT
- 10 Risk of PC in relatives of PC
- 11/12 Relugolix – Expected to Alter Treatment
- 13 Whole-pelvic radiation Therapy for High-Risk Patients
- 14 It's time to Retire a Common Biopsy
- 15 Cognitive Function / Marital Status & PC Incidence
- 16 Trials / Covid Passports
- 17 Medical Bills: Out of Pocket Costs / BroSuPORT

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 Heidelberg Cancer Support Group

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

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

Please support our Intrepid Outback PHCSG Adventurer David Campbell who will be embarking on this drive to raise money and awareness for Prostate Cancer.

David's Message:

"A diagnosis of metastatic prostate cancer seemed like a death sentence! I don't think you ever really accept it, but with support I realized I could have a quality of life… a different life!

To support [the PCFA event] I am working on my 1992 Landcruiser and 2004 youngest son to join me on this rally to raise funds today to save men's lives tomorrow.

Every dollar you donate will be a game-changer for 1 in 6 men and their families threatened with prostate cancer, boosting life-saving prostate cancer research and support provided by PCFA."

If you would like to make a donation please visit
https://fundraise.pcfa.org.au/fundraisers/davidcampbell

All monies raised by you go directly to the Prostate Cancer Foundation of Australia using funraisin
All donations over $2 tax deductible and go directly to the Prostate Cancer Foundation – no expenses are deducted from these donations, 100% of all donations go to assist with prostate cancer research.

Prostate Cancer Foundation of Australia

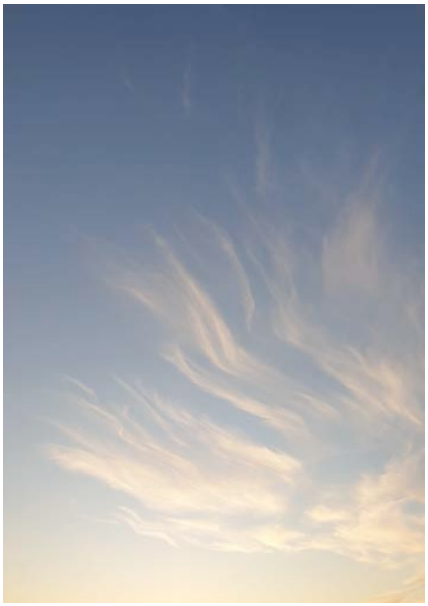
Peek Prostate Cancer Study: Personal Experience, Expectations & Knowledge

PEEK
PROSTATE CANCER AUSTRALIAN STUDY 2021

You are invited to take part in a research study to help understand people diagnosed with prostate cancer & their expectations of the health system, including opinions on access to affordable treatments and holistic care.

What is involved?: The study will include an online questionnaire that will take approximately 20 minutes to complete, as well as a structured interview by telephone that will take approximately 30 – 45 minutes, but you can take as long as you need. The structured interview is conducted with one of our nurses and is a great opportunity for people to talk about and document their experience to benefit others in the future. In our past studies, participants have found that participating in the study made them feel good because they had the chance to reflect on their experience and talk about it, and also help others in the future.
What else do I need to know? The complete patient information sheet. This has all the information you need to make a decision on whether to participate
Will I be told the results of the study? Yes! We will provide all participants with a copy of the study results.
Study sponsor: The study is being carried out by the Centre for Community-Driven Research (CCDR). CCDR are a charity that conducts research to help patients have their voice heard. CCDR are working in partnership with Prostate Cancer Foundation on this study and a grant was received from AstraZeneca (the Funder) to do this study. The Funder has no involvement in the research design, implementation or analysis. Ethics approval has been granted from University of Wollongong.

https://www.cc-dr.org/wp-content/uploads/PARTICIANT-INFORMATION-VPUBLIC.pdf



Incidence of Symptomatic Skeletal Events and Bone-Modifying Agent Use in Castration-Resistant Prostate Cancer

Source:
23 Aug 2021
Advanced Prostate Cancer
https://www.practiceupdate.com/c/121997/67/11/?elsca1=emc_enewsweekinreview&elsca2=email&elsca3=practiceupdate_advancedprostatecancer&elsca4=advancedprostatecancer&elsca5=newsletter&nd=NTMyMjc0MDc4NjM0S0&lid=20849595

Abstract

INTRODUCTION

Bone metastases occur frequently in castration-resistant prostate cancer (CRPC) and may lead to skeletal-related events (SREs), including symptomatic skeletal events (SSEs). Bone-modifying agents (BMAs) delay SREs and SSEs. However, the real-world use of BMAs is debated given the absence of demonstrated survival advantage and potential adverse events (AEs). Our retrospective study examined BMA use and SSE rates in Australian patients with CRPC.

METHODS

Patients with CRPC and bone metastases were identified from the electronic CRPC Australian Database. Patient characteristics, treatment patterns and AEs were analysed. Descriptive statistics reported baseline characteristics, SSE rates and BMA use. Comparisons between groups used t-tests and Chi-square analyses. Overall survival was calculated by the Kaplan-Meier method.

RESULTS

A total of 532 eligible patients were identified with a median age of 73 years (range: 44-97 years). BMAs were prescribed in 232 men (46%), 183 of whom received denosumab. Patients receiving first-line docetaxel for CRPC were more likely to commence BMAs than those receiving abiraterone or enzalutamide (51% vs 31% vs 38%; p = 0.004). SSEs occurred in 148 men (28%), most commonly symptomatic lesions requiring intervention (75%). At the time of initial SSEs, only 28% were receiving BMAs. Patients treated at sites with lower BMA use (<median) had higher SSE rates (32% vs 22%, p = 0.019).

CONCLUSION

In our real-world cohort, SSEs occurred in almost one-third of patients with CRPC and bone metastases, whereas less than half of patients received BMAs. The lower rate of SSEs in treatment sites with increased BMA use supports their benefit in this setting.

TAKE-HOME MESSAGE

The authors of this retrospective, real-world analysis showed that less than half of the Australian patients with castration-resistant prostate cancer (CRPC) with symptomatic bone metastases received bone-modifying agents (BMAs). BMAs were more commonly given with docetaxel compared with other first-line therapeutic agents. Less than a third of the patients were on BMAs while symptomatic skeletal events occurred, and 46% did not subsequently commence a BMA. The rate of adverse events was low (3%), and osteonecrosis of the jaw occurred in 2% of patients.

BMAs should be initiated earlier and more consistently in CRPC patients with bone metastases.

– Jing Xi, MD, MPH

Abiraterone+Docetaxel+ADT for Newly Diagnosed Metastatic Men Beats Docetaxel+ADT (or Abiraterone+ADT)

Source:
23 May 2021

https://www.prostatecancer.news/2021/05/abiraterone-docetaxel-adt-for-newly.html

The first results of the long-awaited PEACE-1 randomized clinical trial (RCT) are in. They randomized newly diagnosed metastatic men to either prostate radiation or abiraterone or standard-of-care (SOC). SOC included docetaxel for many of the men.

Radiographic progression-free survival increased by 2.5 years (from 2.0 to 4.5 yrs) with the addition of abiraterone to docetaxel. Time to castration resistance increased by 1.7 yrs (from 1.5 to 3.2 yrs).

The full results will tell us how much the prostate radiation adds, and the effect on overall survival. The analysis by metastatic burden will be important too. Meanwhile, docetaxel+abiraterone+ADT should be considered the new standard of care.

How does this combination therapy compare to previous RCTs for docetaxel or abiraterone?

Because the STAMPEDE RCTs for docetaxel and abiraterone occurred at about the same time, 566 patients were randomized to one or the other. Sydes et al. reported the outcomes after a median of 4 years of follow-up.

- Abiraterone reduced PSA more quickly, as reflected in "failure-free survival" (time to PSA increase, clinical progression, or death) and "progression-free survival" (time to first "failure" event, excluding PSA).
- Those who received docetaxel first soon caught up. There were no significant differences in "metastasis-free survival," "prostate cancer-specific survival," "overall survival," or "time to the first skeletal-related event (pain or fracture)"
- Serious toxicity (Grade 3 or greater) was also equal: 50% for docetaxel, 48% for abiraterone.

The STAMPEDE researchers (the STOPCAP group) did a meta-analysis of the STAMPEDE trials that concluded that abiraterone probably had a greater effect than docetaxel, but unlike the analysis above, it was not a direct comparison. They concluded that either should be recommended.

The other RCTs for metastatic hormone-sensitive prostate cancer (mHSPC) included STAMPEDE- abiraterone, LATITUDE- abiraterone, STAMPEDE-docetaxel, CHAARTED-docetaxel.GETUG-AFU-15(docetaxel) did not detect a difference in survival from the early use of docetaxel. 30% had prior treatment. There were differences in the populations studied in each trial that should be understood.

LATITUDE screened for more advanced patients - 80% were "high risk." High risk was defined by having 2 of 3 "high-risk" features, either: Gleason 8-10, or ≥ 3 bone metastases or visceral metastases. About half had performance status of 1 or 2 ("0" is the best performance status).

CHAARTED started by recruiting only patients with a high burden of metastases. But only 73% were *de novo*, meaning 27% had been previously treated before they entered the trial. They later opened the trial to men with fewer metastases and ended up with a small group (27%) of low burden *de novo* patients. They defined "high burden" as visceral metastases or ≥ 4 metastases with at least 1 outside the axial skeleton.

The two STAMPEDE trials recruited almost entirely (95%) *de novo* patients. 56% were "high burden" by the CHAARTED definition. 52% were "high risk" by the LATITUDE definition. 26% had performance status of 1 or 2.

PEACE1 recruited only *de novo* metastatic patients, with excellent performance status. 57% had high-risk features by the LATITUDE definition.

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

(continued page 5)

The chart shows how long it took for patients to progress on each of the early interventions. Complicating analysis, each trial used a slightly different definition of progression.

While comparison is complicated, the extension of progression-free survival by 2.5 years by adding abiraterone to docetaxel alone is impressive. Docetaxel adds 1 - 1.5 years to progression-free survival over ADT alone. Abiraterone adds 1 - 1.5 years to progression-free survival over ADT alone.

Does docetaxel *only* benefit Metastatic Hormone Sensitive PC (mHSPC) patients with a high-volume of metastases?

This has stirred much controversy. Gravis et al. argue that the overall survival improvement from docetaxel was seen in CHAARTED only among men with high-volume metastases was a real biological effect (i.e., that high-volume PC is a different disease from low-volume PC, that responds differently to chemo). Armstrong argues for a biological difference. They acknowledge, however, that the small sample size of *de novo* men with low volume metastases (n=154) and their short follow-up (only 16% had died during the 48 months of follow-up) may be underestimating the benefit in the low volume, *de novo* subgroup. Remember that in CHAARTED, the low-volume subgroup was not recruited initially, so the follow-up is shorter in the group that needs the longer follow-up.

Clarke et al. argue that STAMPEDE is the more definitive trial because its sample size of mHSPC men with low-volume metastases was over twice as great (n=362) and the follow-up was longer (62% of the docetaxel patients had died during 78 months of follow-up). They did not find evidence of heterogeneity - low-volume PC responded just as much to chemo as high-volume PC. While the effect on low volume PC was similar, the statistical confidence in its effect did not meet 95% confidence. They attribute this to insufficient sample size (power). Suzman and Antonarakis agree that chemo should be offered to *all* mHSPC men, regardless of volume of metastases.

It would seem that a meta-analysis combining the low-volume, *de novo* subgroups from both CHAARTED and STAMPEDE might be sufficiently powered to provide a more definitive answer.

Patients wishing to understand why analyses of subgroups are controversial, may be amused by this analysis of STAMPEDE subgroups. The authors found that patients born on a Monday benefited the most from abiraterone, and it was statistically significant. while patients born on a Friday had the least benefit, and it wasn't statistically significant. They further found that men diagnosed on a Monday did not benefit from abiraterone, whereas men diagnosed on other days had a statistically significant benefit. These absurd findings are sometimes known as "p-hacking" or "data dredging." This interview discusses this error and the mistake of drawing biological inferences from statistical significance. Pre-specifying subgroups is one way to avoid such errors, but drawing conclusions from inadequately powered subgroups, while tempting, should be avoided.

This controversy is reflected in the conflicting recommendations that constitute the standard of care.

The current National Comprehensice Cancer Network (NCCN) guidelines state: "Docetaxel should not be offered to men with low volume metastatic prostate cancer, since this subgroup was not shown to have improved survival in either the ECOG study or a similar European (GETUG-AFU 15) trial."

The current American Society of Clinical Oncology (ASCO) guidelines state: "Recommendation 1.2. For patients with low-volume metastatic disease (LVD) as defined per CHAARTED who are candidates for chemotherapy, docetaxel plus ADT should not be offered (Type: evidence-based, benefits outweigh harms; Evidence quality: high; Strength of recommendation: strong for patients with LVD)."

On the other hand, the current Australian Urology Associates AUA)/American Society of Radiation Oncology (ASTRO)/Society of Urologic Oncology (SUO) guidelines state: "15. In patients with mHSPC, clinicians should offer continued ADT in combination with either androgen pathway directed therapy (abiraterone acetate plus prednisone, apalutamide, enzalutamide) or chemotherapy (docetaxel). (Strong Recommendation; Evidence Level: Grade A)

Canadian Urological Association (CUA) guidelines state: "Docetaxel plus ADT may also be an option in patients with mCNPC/mCSPC with good performance status with low-volume disease (Level 2, Weak recommendation)."

National Institute for Health and Care Excellence (NICE) (UK) guidelines state: "Offer docetaxel chemotherapy to people with newly-diagnosed metastatic prostate cancer who do not have significant comorbidities."

European Urological Association (EAU) guidelines state: "Based on these data, upfront docetaxel combined with ADT should be considered as a standard in men presenting with metastases at first presentation provided they are fit enough to receive the drug [1070]"

I [the author] personally believe that the STAMPEDE researchers make a stronger case pending better data from PEACE1.

It is also possible that genomics will allow better selection of patients for early chemotherapy. Hamid et al. examined tissue collected for the CHAARTED trial. They found a subtype called "Luminal B" that was associated with improved survival from chemotherapy. This finding has not yet been validated on an independent trial. Meanwhile, DECIPHER provides the test as part of its GRID analysis.

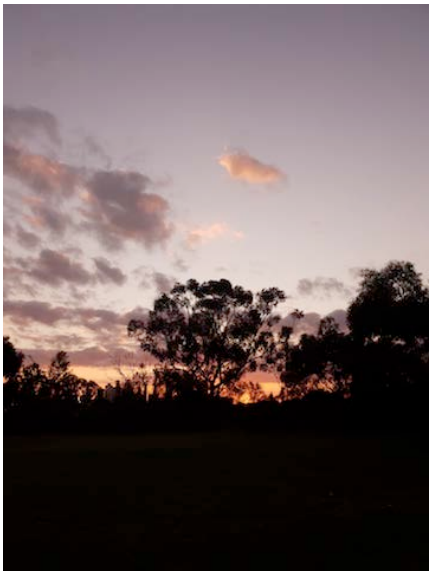
The major advantages of early chemo vs "saving it for later" are:

- Longer survival advantage
- Side effects are milder when patients are less debilitated from years of cancer
- As many as 10 infusions (usually 6) can be given if it is well tolerated
- Most patients are not resistant, so docetaxel can be repeated
- If there is resistance, cabazitaxel can be given

Time to "progression" following each early therapy

	abiraterone+docetaxel+ADT	docetaxel+ADT	abiraterone+ADT	ADT alone	Trial notes
PEACE1*	4.5 yrs	2.0 yrs			100% de novo, 100% perf. status 0, 57% high volume
STAMPEDE‡ (abiraterone)			Not reached (> 3.4 yrs)	2.0 yrs	94% de novo,26% perf.status 1 or 2, 55% high volume
LATITUDE* (abiraterone)			2.8 yrs	1.2 yrs	100% de novo, 45% perf. Status 1 or 2, 80% high volume/high risk
STAMPEDE‡ (docetaxel)		3.1 yrs		1.7 yrs	95% de novo, 56% high volume
CHAARTED§ (docetaxel)		2.8 yrs		1.7 yrs	73% de novo, 65% high volume

* time to radiographic progression or death
‡ time to first symptomatic event or death
§ time to symptoms or radiographic progression



Brief, Intense Radiation and Hormone Therapy for Very High Risk PCa

Source:
3 June 2021
https://www.prostatecancer.news/2021/06/brief-intense-radiation-and-hormone.html

Brachy boost therapy seems to have the best oncological results for men with very high-risk prostate cancer. But brachy boost therapy entails 20-25 external beam radiation treatments plus the invasive placement of radioactive seeds or needles plus at least 18 months of testosterone suppression. While the oncological results are excellent, with about 80% cure rates, there is significant risk of serious late-term urinary retention. In some men, testosterone never fully recovers.

McBride et al. reported the early results of the AASUR trial. The goal of the trial was to find a treatment with equivalent oncological outcomes, but one that is easier on the patient, with less risk of long-term toxicity. They recruited 64 patients at 4 top institutions (Memorial Sloan Kettering, Johns Hopkins, University of Michigan, and Thomas Jefferson University). All patients were "very high risk," defined as:

- any Gleason score (GS) 9 or 10, or
- 4 or more cores of GS 8, or
- 2 high-risk features (stage T3/4, GS 8, or PSA>20)
- No metastases (N0, M0)
- Patients were treated with:
  - SBRT (7.5-8.0 Gy x 5 treatments)
  - 6 months of Lupron, Erleada, and Zytiga
- After 30 months of follow-up:
  - 90% were free of biochemical failure
  - Median PSA at the last follow-up was 0.1
  - PSA remained undetectable in 40%
  - Testosterone rose to non-castrate levels at a median of 6.5 months after hormone therapy ended, and almost all rose to >150 ng/dl
  - 23% experienced transient serious toxicities, mostly hypertension
  - Quality of life scores at 1 year held for urinary and rectal domains but declined in sexual and hormone domains.

How do these results compare to other trials of radiation+ADT in high-risk patients?

Lin et al. used whole pelvic IMRT with an SBRT boost to the prostate and 2 years of ADT in 41 high- and very high-risk patients. With 4 years of follow-up, they reported 92% biochemical recurrence-free survival (bRFS).

Hoskin et al. used high dose rate brachytherapy as a monotherapy in 86 high-risk patients. Most (80%) had adjuvant ADT for a median of 6.3 months (range 1-40 months). With 4 years of follow-up, they report 87% biochemical recurrence-free survival (bRFS) among high-risk patients.

Zapatero et al. reported the results of the DART 01.03 GICOR trial of escalated dose IMRT with either short-term (4 months) or long-term (28 months) ADT. There were 185 high-risk patients with about half getting each ADT protocol. About a quarter received simultaneous radiation of their pelvic lymph nodes. With 5 years of follow-up, they report 76% bRFS among high-risk patients who got short-term ADT and 88% bRFS among high-risk patients who got long-term ADT.

Alan Pollack reported early results of the NRG Oncology 0534 or SPPORT randomized clinical trial at the ASTRO meeting in 2018. Approximately 600

(continued page 7)

Glossary of Terms:

Prostate Cancer is full of accronyms.

To help you navigate all the terms we have produced a list on our Website:

www.prostateheidelberg.info

patients with a biochemical failure after prostatectomy were treated with whole pelvic salvage radiation. They all received 4-6 months of adjuvant ADT. With 5 years of follow-up, they reported 89% bRFS. (They defined this second bRFS as nadir +2.0, as in radiation trials.)

This table summarizes these trials:

HR=high risk VHR=very high risk SV=seminal vesicles bRFS=biochemical recurrence-free survival: PSA stayed lower than nadir+2.0 ng/ml

	AASUR	**SBRT boost** (Lin)	**HDR-BT** (Hoskin)	**IMRT** DART GICOR	**IMRT** DART GICOR	**SRT** SPPORT
follow-up	2.5 yrs	4 yrs	4 yrs	5 yrs	5 yrs	5 yrs
Radiation	SBRT	IMRT+ SBRT boost	HDR-BT monotherapy	IMRT (dose escalated)	IMRT (dose escalated)	RP+SRT
Coverage area over prostate	SV	Whole pelvic	±SV (if MRI+)	• SV • 27% whole pelvic	• SV • 19% whole pelvic	Whole pelvic
Adjuvant hormone therapy	ADT+Zytiga +Erleada	93% ADT	80% ADT	ADT	ADT	ADT
Duration of hormone therapy	6 months	2 yrs	6.3 months	4 months	28 months	4-6 months
Risk	VHR	78% HR 22% VHR	HR	HR	HR	Recurrent
bRFS	**90%**	**92%**	**87%**	**76%**	**88%**	**89%**

2.5 years of follow-up is too early to draw valid conclusions. We see that most of the trials had higher bRFS even with much longer follow-up; however, only AASUR recruited very high-risk patients exclusively. ICECAP has shown that only metastasis-free survival is a valid surrogate endpoint for overall survival. A trial on high-risk patients will have to run for 8-10 years to collect a sufficient number of metastases to draw valid conclusions, so we can only look at this as an early signal.

Treatment of Pelvic Lymph Nodes

We know that the time to be able to see the first few cancerous pelvic lymph nodes is often several years, so 2.5 years of follow-up tells us little. The newly approved PSMA PET scans will be able to rule out the larger metastases (>5 mm), but will never be able to find metastases smaller than that. Waiting for visibility to make the decision to treat is a bad idea. By the time some lymph nodes are large enough or rapidly growing, the risk of spread outside the pelvic lymph node drainage area increases, and the hope of a cure may vanish.

The PSMA PET/CT is nevertheless worthwhile. While a negative scan does not change the treatment decision, a positive scan may detect occult metastases or pelvic lymph nodes that may benefit from a higher spot dose and more intense or longer hormone therapy.

We rely on validated formulas to tell us the probability that there are microscopic pelvic lymph node metastases. Two of the popular formulas are the Roach Equation and the Yale Formula.

There is a risk of overtreatment. Many high-risk patients will never require pelvic lymph node treatment, and we are awaiting evidence (RTOG 0924) that such treatment will improve survival. As we have seen bRFS is improved.

However, the only risk is that toxicity will be higher when the whole pelvis is treated. Murthy et al. showed that even at higher doses of pelvic lymph node radiation, there was no increase in acute toxicity, late gastrointestinal toxicity, and no deterioration in patient-reported quality of life scores.

Arguably, 25 extra IMRT treatments to the pelvic lymph nodes represent a patient inconvenience over the 5 SBRT prostate-only treatments. In the UCLA and Sunnybrook high-risk SBRT trials, the pelvic lymph nodes may be treated (to 25 Gy) within the same 5 treatments. So far, with limited follow-up, cancer control is high and toxicity is low.

Hormone therapy intensification

The DART 01.05 GICOR trial proved that long-term (28 months vs 4 months) ADT improves survival in high-risk patients even when treated with dose-escalated IMRT. Nabid et al. proved that 18 months is often as good as 36 months. AASUR suggests that by including both Zytiga and Erleada, the duration of hormone therapy can be shortened. But the sexual and hormone quality of life did diminish. This raises questions that can only be answered in an expanded randomized clinical trial:

- Are all 3 medications (Zytiga, Erleada, and Lupron) necessary for the benefit? The ACIS trial found that adding Erleada increased radiographic progression-free survival in mCRPC patients. There was no such synergy found in adding Xtandi to Zytiga in this non-randomized trial.
- Do they add much to Lupron alone if whole pelvic radiation is given?
- Does Lupron alone for, say, 9 months, with whole-pelvic SBRT (as in the UCLA trial) afford the same benefit with less toxicity? And would Orgovyx instead of Lupron allow for earlier testosterone recovery?
- Can genomics (Prolaris or Decipher of biopsy tissue) identify patients who might benefit from the combined hormone therapy?

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

Progression-directed Therapy for Oligoprogression in Castration-Refractory Prostate Cancer

European Urolog
https://euoncology.europeanurology.com/article/S2588-9311(19)30138-5/fulltext

In metastatic castration-refractory prostate cancer (mCRPC), state-of-the-art treatment consists of androgen biosynthesis inhibition (abiraterone), inhibition of the androgen receptor (enzalutamide), chemotherapy, or radium-223 in combination with androgen deprivation therapy (ADT). A subgroup of these patients show oligoprogression, with the progression of only a limited number of metastatic spots, while all other metastases remain controlled by ongoing systemic therapy. In a bi-institutional retrospective study, we tested the hypothesis that progression-directed therapy (PDT) targeting oligoprogressive lesions might defer the initiation of next-line systemic treatment (NEST). A total of 30 patients were diagnosed with mCRPC and experienced oligoprogression, defined as a total of three or fewer progressive lesions either at known metastatic sites and/or the appearance of new metastasis and/or local recurrence. All patients were under active ADT with or without second-line systemic treatment. All patients received PDT targeting the oligoprogressive lesions, while ongoing systemic treatment was maintained. There was median NEST-free survival of 16 mo (95% confidence interval [CI] 10–22) and progression-free survival of 10 mo (95% CI 6–15) with only minor radiotherapy- or surgery-related toxicity. These findings encourage further prospective trials.

Patient summary

In patients with metastatic castration-refractory prostate cancer, surgical treatment or high-dose radiation therapy directed to only the limited number of progressive metastatic spots, while all other metastases remained controlled by ongoing systemic therapy, led to substantial postponement of next-line systemic treatment in our study.

Study Provides Important Insights into Prostate Cancer Metabolism

Reviewed by Emily Henderon B Sc Aug 27 2021

South Australian medical researchers have identified a new way in which prostate cancer cells use glucose to grow and survive, which in turn could be the secret to destroying them.

In a new study published in the international journal eLife, researchers at Flinders University and The University of Adelaide used cutting-edge technologies to analyze this metabolic pathway in prostate cancer cells, in the process demonstrating that it represents a weakness in prostate tumors that could be exploited to develop new therapies.

Associate Professor Luke Selth from the Flinders Health and Medical Research Institute (FHMRI) at Flinders University and Freemasons Centre for Male Health and Wellbeing (FCMHW) says the study provides important insights into how prostate tumors change their metabolism to enable rapid growth and resistance to therapies.

"Prostate cancer cells are very different to normal prostate cells in many ways but one of the most striking differences is how tumors use sugars and fats for energy production and to rapidly grow. In this study, we found that a protein called 6PGD can support the survival of prostate cancer cells when they are being challenged with a hormonal therapy that is currently used in the clinic".

The study found that switching on 6PGD enables the cancer cells to use glucose for the generation of antioxidants and to make the building blocks for growth.

"We think this is a significant finding because it potentially represents a new mechanism by which prostate cancer cells can become resistant to hormonal therapies, which are the standard-of-care treatment for men with advanced and metastatic disease."

Luke Selth, Associate Professor, Flinders Health and Medical Research Institute (FHMRI)

Professor Lisa Butler from the University of Adelaide and South Australian Health and Medical Research Institute (SAHMRI) and co-senior author of the study, says the results are a step forward in our understanding of the unique metabolism of prostate tumors.

"Using the latest technologies, we generated an incredibly detailed view of how 6PGD influences prostate cancer metabolism. Importantly, our work has pinpointed some clinical agents that may be able to shut down this pathway, so it is possible that our findings could eventually be used to develop a new targeted therapy for this common disease", says Butler.

Indeed, the study showed that 6PGD inhibitors could kill cancer cells grown in lab dishes and even in real tumors taken directly from Adelaide cancer patients, and these inhibitors were more effective when combined with a hormonal therapy.

Source:

Flinders University Journal reference: Gillis, J.L., *et al.* (2021) A feedback loop between the androgen receptor and 6-phosphogluconate dehydrogenase (6PGD) drives prostate cancer growth. *eLife*.doi.org/10.7554/eLife.62592

Diagnostic Accuracy of Prostate Specific Membrane Antigen 18F-DCFPyL PET/CT in PCa

Source: https://www.practiceupdate.com/content/diagnostic-accuracy-of-prostate-specific-membrane-antigen-18f-dcfpyl-petct-in-prostate-cancer-patients/119929/12/3/1

PURPOSE

Prostate specific membrane antigen-targeted positron emission tomography/computerized tomography has the potential to improve the detection and localization of prostate cancer. OSPREY was a prospective trial designed to determine the diagnostic performance of ^{18}F-DCFPyL-positron emission tomography/computerized tomography for detecting sites of metastatic prostate cancer.

MATERIALS AND METHODS

Two patient populations underwent ^{18}F-DCFPyL-positron emission tomography/computerized tomography. Cohort A enrolled men with high-risk prostate cancer undergoing radical prostatectomy with pelvic lymphadenectomy. Cohort B enrolled patients with suspected recurrent/metastatic prostate cancer on conventional imaging. Three blinded central readers evaluated the ^{18}F-DCFPyL-positron emission tomography/computerized tomography. Diagnostic performance of ^{18}F-DCFPyL-positron emission tomography/computerized tomography was based on imaging results compared to histopathology. In cohort A, detection of pelvic nodal disease (with specificity and sensitivity as co-primary end points) and of extrapelvic metastases were evaluated. In cohort B, sensitivity and positive predictive value for prostate cancer within biopsied lesions were evaluated.

RESULTS

A total of 385 patients were enrolled. In cohort A (252 evaluable patients), ^{18}F-DCFPyL-positron emission tomography/computerized tomography had median specificity of 97.9% (95% CI: 94.5%–99.4%) and median sensitivity of 40.3% (28.1%–52.5%, not meeting prespecified end point) among 3 readers for pelvic nodal involvement; median positive predictive value and negative predictive value were 86.7% (69.7%–95.3%) and 83.2% (78.2%–88.1%), respectively. In cohort B (93 evaluable patients, median prostate specific antigen 11.3 ng/ml), median sensitivity and positive predictive value for extraprostatic lesions were 95.8% (87.8%–99.0%) and 81.9% (73.7%–90.2%), respectively.

CONCLUSIONS

The primary end point for specificity was met while the primary end point for sensitivity was not. The high positive predictive value observed in both cohorts indicates that ^{18}F-DCFPyL-positive lesions are likely to represent disease, supporting the potential utility of ^{18}F-DCFPyL-positron emission tomography/computerized tomography to stage men with high-risk prostate cancer for nodal or distant metastases, and reliably detect sites of disease in men with suspected metastatic prostate cancer.

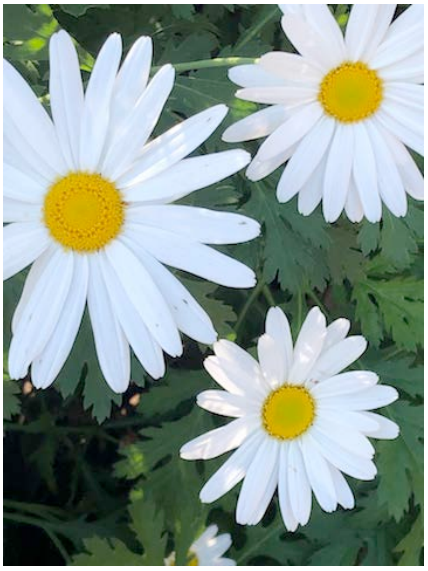
COMMENT

Written by Prof Mark Frydenberg MBBS, FRACS, GAICD

The article adds to the growing body of evidence regarding the utility of PET PSMA scanning (in this study using ^{18}F-DCFPyL) both in the preoperative assessment of high-risk cancers as well as evaluating PSA recurrence post radical prostatectomy. It highlights the relatively high incidence of occult nodal and distant disease with extremely high specificity; namely that, if identified, cancer recurrence is likely. However, due to the inability of PET tracers to reliably identify lesions <5mm, many micrometastases can be missed; hence, why the endpoints regarding sensitivity were not met. As such, although this finding is highly specific, one cannot rely on a negative PET PSMA to rule out microscopic, advanced disease; however, the technology surpasses standard imaging and improves staging and restaging information so that urologists and their multidisciplinary teams can make more personalized decisions about patient management.

Professor Mark Frydenberg graduated from the University of Melbourne, School of Medicine in1982 and was awarded his Fellow of the Royal Australasian College of Surgeons in Urology in1990. He then went to do sub-specialty training in urological cancer surgery as the UrologicalOncology Fellow at the Mayo Clinic, Rochester Minnesota in the years 1991-1992. After returning to Australia he was appointed an Associate Professor in the Department of Surgery at Monash University in1997 and at the same time as the Chairman of the Department of Urology at Monash Health, a position held for twenty years until 2017.

He continues to have very strong academic relationships with basic scientists and also allied health professionals such as psychologists and physiotherapists to ensure that all patients obtain the best possible care pre- and post- operatively from a survivorship viewpoint.



Risk of Prostate Cancer in Relatives of Prostate Cancer Patients in Sweden: A Nationwide Cohort Study

Source:
1June 2021
https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1003616

ABSTRACT

BACKGROUND

Evidence-based guidance for starting ages of screening for first-degree relatives (FDRs) of patients with prostate cancer (PCa) to prevent stage III/IV or fatal PCa is lacking in current PCa screening guidelines. We aimed to provide evidence for risk-adapted starting age of screening for relatives of patients with PCa.

METHODS & FINDINGS

In this register-based nationwide cohort study, all men (aged 0 to 96 years at baseline) residing in Sweden who were born after 1931 along with their fathers were included. During the follow-up (1958 to 2015) of 6,343,727 men, 88,999 were diagnosed with stage III/IV PCa or died of PCa. The outcomes were defined as the diagnosis of stage III/IV PCa or death due to PCa, stratified by age at diagnosis. Using 10-year cumulative risk curves, we calculated risk-adapted starting ages of screening for men with different constellations of family history of PCa. The 10-year cumulative risk of stage III/IV or fatal PCa in men at age 50 in the general population (a common recommended starting age of screening) was 0.2%. Men with ≥2 FDRs diagnosed with PCa reached this screening level at age 41 (95% confidence interval (CI): 39 to 44), i.e., 9 years earlier, when the youngest one was diagnosed before age 60; at age 43 (41 to 47), i.e., 7 years earlier, when ≥2 FDRs were diagnosed after age 59, which was similar to that of men with 1 FDR diagnosed before age 60 (41 to 45); and at age 45 (44 to 46), when 1 FDR was diagnosed at age 60 to 69 and 47 (46 to 47), when 1 FDR was diagnosed after age 69. We also calculated risk-adapted starting ages for other benchmark screening ages, such as 45, 55, and 60 years, and compared our findings with those in the guidelines. Study limitations include the lack of genetic data, information on lifestyle, and external validation.

CONCLUSIONS.

Study provides practical information for risk-tailored starting ages of PCa screening based on nationwide cancer data with valid genealogical information. Our clinically relevant findings could be used for evidence-based personalized PCa screening guidance and supplement current PCa screening guidelines for relatives of patients with PCa.

AUTHOR SUMMARY

WHY WAS THIS STUDY DONE?

- Family history is the strongest known risk factor for prostate cancer (PCa), and current guidelines concur that an earlier screening for men with a family history of PCa is necessary.
- However, limited evidence-based guidance is available on at what age actually this early screening should start.
- This study was conducted to provide precise recommendations about at what age should relatives of PCa patients start screening based on the number of affected relatives and the age at onset of PCa in the family.

WHAT DID THE RESEARCHERS DO & FIND?

- In this nationwide study on 6,343,727 men, the risk of stage III/IV or fatal PCa in close family members of patients with PCa was estimated.
- It was observed that men with family history of PCa reach the screening risk threshold up to 12 years earlier than the general population.
- This study found that age, age at diagnosis of PCa in relative/s, and number of affected first-degree relatives (FDRs) are important elements in increased risk of stage III/IV or fatal PCa, and these factors accordingly resulted in different risk-adapted starting ages of PCa screening.
- Comparison between our evidence-based risk-adapted starting age of screening and recommended age of PCa screening by different guidelines showed a difference ranging from −2 to 11 years.

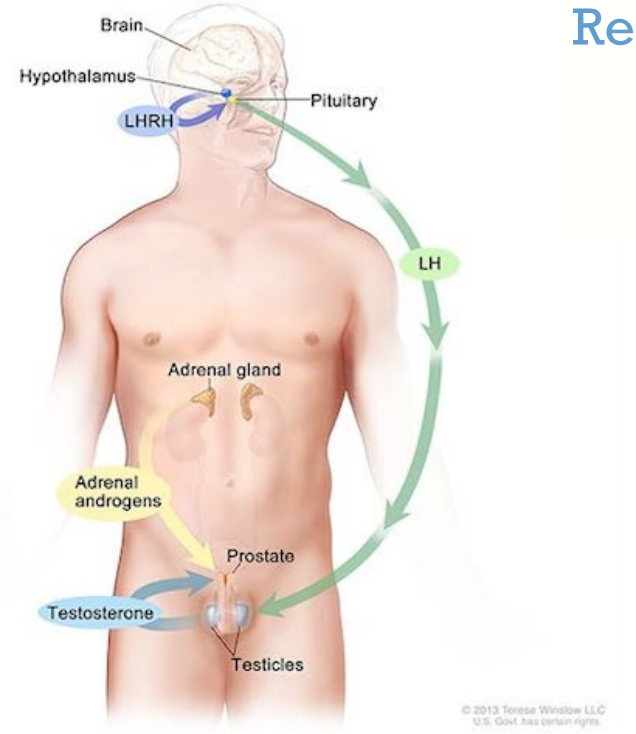
WHAT DO THESE FINDINGS MEAN?

- This study made use of the largest dataset available, to our knowledge, to identify the optimal age for starting PCa screening in relatives of patients with PCa.
- This study took into account not only the number of relatives but also age at onset of PCa in the family members, which is an additional important piece of information for the guidelines.
- The results may contribute to a more evidence-based personalized PCa screening guidance in real-world settings, and clinicians could inform patients with PCa about this possibility and encourage individualized counseling for their relatives.

Relugolix Approval Expected to Alter Treatment for Advanced Prostate Cancer

But NOT in Australia… Yet!

Source: https://www.cancer.gov/news-events/cancer-currents-blog/2021/fda-relugolix-prostate-cancer-androgen-deprivation-therapy



Androgen production in men. The drawing shows that testosterone production is regulated by luteinizing hormone (LH) and luteinizing hormone-releasing hormone (KHRH). The hypothalamus releases LHRH, which stimulates the release of LH rom the pituitary gland. LH acts on specific cells in the testes to produce the majority of testosterone in the body. Most of the remaining androgens are produced by the adrenal glands. Androgens are taken up by prostate cells, where they either bind to the androgen receptor directly or are converted to dihydrotestosterone (DHT), which has a greater binding affinity for the androgen receptor than testosterone.

January 26, 2021, by NCI Staff

A new drug approved by the Food and Drug Administration (FDA) is expected to immediately affect the treatment of some men with prostate cancer. In a large clinical trial, the drug, relugolix (Orgovyx), was shown to be more effective at reducing testosterone levels in men with advanced prostate cancer than another commonly used treatment, leuprolide (Lupron).

Treatments that block the production of the hormone testosterone by the testes have been the cornerstone of advanced prostate cancer treatment for several decades. Known as androgen deprivation therapy (ADT), these treatments are akin to putting a stopper in a car's gas tank: robbing prostate tumors of the fuel they need to grow and spread.

In the clinical trial, relugolix was also much less likely than leuprolide to cause serious heart issues, said Neal Shore, M.D., of the Carolina Urologic Research Center, who led the clinical trial on which the approval was based, called HERO. That's important, Dr. Shore said, because leuprolide and other ADT drugs have been linked with an increased risk of cardiac events, including heart attacks and heart failure.

"For me, this [approval] is significant," Dr. Shore said. "Many of the patients we start on testosterone suppression are at risk of having a cardiac complication."

Given its superior ability to reduce testosterone and safety with regard to heart-related effects, Dr. Shore said, "it's perfectly arguable" that relugolix should be the preferred choice for ADT in men with advanced prostate cancer.

Alicia Morgans, M.D., who specializes in treating prostate cancer at the Robert H. Lurie Cancer Center of Northwestern University, generally agreed.

"I believe this is a new standard of care for men with [advanced] prostate cancer," Dr. Morgans said. "It meaningfully and effectively lowered testosterone levels, which is what we manipulate to try to control prostate cancer."

It may not "necessarily replace every [ADT] option for every patient, but it's definitely a new standard that appears safe and effective," she continued, especially for men concerned about any potential heart-related risks.

Going After Testosterone

Prostate cancer that is confined to the prostate is typically treated with surgery or radiation therapy. Once it advances beyond the prostate, either to nearby tissues or to other parts of the body (e.g., bones, liver), ADT is typically used.

Although several drugs for ADT are available, in the United States leuprolide is the most commonly used option. Known as an LHRH agonist (also called a GnRH agonist), leuprolide acts on the pituitary gland—a tiny organ within the brain that is responsible for producing a hormone that eventually decreases the production of testosterone by the testicles. It is given to patients as an injection into muscle, typically every few months.

Reducing the production of testosterone to very low levels with

(continued 12)

drugs is often called medical (or chemical) castration, because it achieves the same results as surgical removal of the testes.

Relugolix is known as a GnRH (or LHRH) antagonist. It also acts on the pituitary gland, but in a way that more directly and rapidly blocks testosterone production in the testes. In addition, it is a pill that patients take every day.

Testosterone's Trail

Testosterone's production in the prostate begins with the release of a hormone called GnRH by the hypothalamus in the brain. The GnRH then binds to the pituitary gland, via a special receptor, causing the pituitary to produce two other hormones, LH and FSH. In men, these hormones cause the testicles to make testosterone, and in women they cause the ovaries to make estrogen and progesterone.

ADT "wasn't necessarily something we thought would be improved upon, because ... we've had good strategies to lower testosterone with good medications for decades," Dr. Morgans said. The development of drugs like relugolix is important, she added, because it "took something we've been doing forever and tried to make it better."

Improved Testosterone Suppression, Lower Cardiac Risks

More than 900 men with advanced prostate cancer whose tumors still relied on testosterone (known as hormone-sensitive prostate cancer) were enrolled in the HERO trial, which was funded by Myovant Sciences, the manufacturer of relugolix.

Participants were assigned at random to take relugolix daily for 48 weeks or to receive leuprolide injections every 3 months for the same length of time.

Approximately 97% of men treated with relugolix reached and maintained very low testosterone levels through 48 weeks, compared with 89% of men who received leuprolide. In addition, men in the relugolix group also did substantially better on several other measures, including being able to return to normal testosterone levels within a few months of stopping therapy.

The latter finding is "very important," Dr. Shore said. Suppressing testosterone for long periods can lead to significant side effects, he explained, including fatigue, hot flashes, and bone problems. And in clinical practice, ADT might only be used for short periods, such as when it's being given along with radiation therapy.

"So if your testosterone level returns to normal values faster after stopping ADT, that to me is a real positive," he said.

Side effects were generally similar in both treatment groups, although diarrhea was more common in men treated with relugolix. The biggest difference, though, was the effect on the heart: Twice as many men in the leuprolide group than in the relugolix group (6.2% versus 2.9%) had a "major adverse cardiovascular event," which included nonfatal heart attack or a stroke.

When the HERO trial investigators looked specifically at men who had a history of heart problems, the difference in the frequency of these cardiac side effects was even more stark: 17.8% in the leuprolide group versus 3.6% in the relugolix group.

The potential heart risks associated with long-term ADT with LHRH agonists such as leuprolide have come into sharper focus over the past decade, Dr. Shore said. In discussions with colleagues who specialize in studying and treating the cardiac effects of cancer treatments, he continued, "they've told me that the likelihood of a typical man undergoing ADT having a major cardiac event is upwards of 30% to 40%."

Impact on Everyday Care

Fatima Karzai, M.D., of the Genitourinary Malignancies Branch in NCI's Center for Cancer Research, called relugolix "an exciting option" for men with advanced prostate cancer. Its most obvious role will be in men with advanced prostate cancer who also have cardiovascular disease, Dr. Karzai said.

Although trial participants who received relugolix had a more than 50% lower risk of serious cardiac events, she said it's unclear exactly why it poses less of a threat to the heart. Some studies have suggested, she noted, that the difference in how the two drugs work may also influence how they affect plaque deposits in the cardiovascular system.

Relugolix is not the first GnRH antagonist to be approved by FDA to treat men with advanced prostate cancer. Degarelix (Firmagon) was approved more than a decade ago. However, degarelix is given as a monthly injection, and the injections can cause intense pain at the injection site, greatly limiting its use.

Dr. Karzai noted that there are still questions about using relugolix in patient care. For example, there might be problems with men's ability to take a pill every day, as opposed to only having to get an injection of leuprolide or related drugs every few months.

Dr. Morgans agreed that this could be a concern but noted that men with more advanced forms of prostate cancer also receive other drugs that are taken as pills and have been generally good about using them as prescribed.

The ability to take a pill at home rather than having to travel to the doctor's office for an injection definitely offers an upside, Dr. Morgans said. "It's nice for patients to have that control."

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.

Whole-pelvic Radiation Therapy for High-Risk Patients

Source:
16 August 2021
https://www.prostatecancer.news/2021/08/whole-pelvic-radiation-therapy-for-high.html

The decision about whether or not to treat the entire pelvic lymph node area along with the prostate (called whole pelvic radiation therapy (WPRT)) or to treat just the prostate with a margin around it (called prostate-only radiation therapy (PORT)) has long been a matter of judgment. Now we have proof of its benefit in most high-risk patients.

Murthy et al. reported the results of "POP-RT," a randomized clinical trial conducted among 224 high-risk and very high-risk patients treated at the Tata Memorial Hospital in Mumbai, India between 2011 to 2017. What sets this trial apart from previous trials that had equivocal results (like RTOG 9413 and GETUG-01) are the rigorous patient selection criteria and the now-proven treatments they received.

80% of patients were screened using PSMA PET/CT to rule out those with already-detectable lymph node or distant metastases. The rest were staged using bone scan/CT. Patients had to have a probability of microscopic lymph node metastases of greater than 20% using the Roach formula:

Probability of pelvic lymph nodes = (⅔ x PSA) + (10 x (Gleason score - 6))

This meant that high-risk patients had to have the following risk characteristics:

- If Gleason Score 8-10: Any PSA, T1- T3a N0 M0
- If Gleason Score 7: PSA > 15, T1-T3a N0 M0
- If Gleason Score 6: PSA > 30, T1-T3a N0 M0
- Also, any other "Very High Risk" including T3b-T4 N0 M0, with any Gleason Score, any PSA

Treatment consisted of dose-escalated IMRT and 2 years of adjuvant androgen deprivation therapy (ADT):

- Prostate dose= 68 Gy in 25 fractions or treatments (equivalent to about 81 Gy in 40 treatments)
- Pelvic lymph node dose = 50 Gy in 25 treatments
- Pelvic lymph nodes up to the aortic bifurcation were treated, which conforms to current RTOG specs.
- ADT was started 2 months before IMRT and continued for a total of 2 years
- Note: this trial began before ASCENDE-RT proved the superiority of brachy boost therapy, but used a higher IMRT dose and longer ADT. This high-dose IMRT/long-term ADT treatment was proven effective by the DART 01/03 GICOR trial.

After median follow-up of 68 months, the oncological results were:

- 5-year biochemical failure-free survival was 95% for the WPRT group vs. 81% for the PORT group.
- 5-year disease-free survival, which means they had no PSA progression *and* no radiographic progression, was 90% for WPRT (15 recurrences) vs 77% for PORT (36 recurrences).
- 5-year metastasis-free survival, which is a good surrogate endpoint for overall survival, was 95% for WPRT vs 88% for PORT
- Younger patients (< 66) derived more benefit from WPRT
- Among those with recurrences, most (52%) of the recurrences in the PORT arm were in pelvic lymph nodes, whereas few (12.5%) were nodal recurrences in the WPRT arm.

Murthy et al. also reported on toxicity and patient-reported quality of life outcomes comparing the two treatments.

- Acute grade 2 or greater GI toxicity was 33% for WPRT vs 25% for PORT (not statistically different)
- Acute grade 2 or greater GU toxicity was 33% for WPRT vs 24% for PORT (not statistically different)
- Late-term grade 2 or greater GI toxicity was 8.2% for WPRT vs 4.5% for PORT (not statistically different)
- Late-term grade 2 or greater GU toxicity was 20.0% for WPRT vs 8.9% for PORT (statistically different)
- Very few patients in either arm suffered serious (grade 3) toxicity. There was no grade 4 toxicity.
- While higher rectal radiation doses were *not* associated with higher bowel toxicity, higher bladder doses were associated with higher urinary toxicity.
- Patient-reported outcomes were not significantly difference for urinary, bowel or sexual adverse effects.
- A quarter of patients had a previous TURP

Given the relatively mild side effect profile with no clinically significant difference to patients, WPRT should be the standard of care for high-risk patients at high risk of pelvic lymph node involvement. In 2027, we will have the results of a much larger, multi-institutional randomized trial (RTOG 0924) of WPRT vs PORT.

Howard Wolinsky is a Chicago-based freelance medical writer. He worked as a medical and science reporter for The Chicago Sun-Times and writes the "A Patient's Journey" blog for MedPageToday.com. His original article has been edited for length.

A Common Biopsy Is Putting Lives at Risk. It's Time to Retire It

Many physicians are abandoning the transrectal biopsy due to its risks of deadly infection

Source:
By Howard Wolinsky
29 July 2021
https://undark.org/2021/07/29/common-biopsy-is-putting-lives-at-risk/

IN LATE 2010, I underwent a biopsy without much of a thought. My internist had recommended the procedure after suspecting, based on blood tests, that I was at elevated risk for prostate cancer. Off I went to my neighborhood urologist, who had me change into a robe, hop on an exam table, and lie on my side as he delivered numbing local anesthetic in my prostate gland, the walnut-sized organ situated between the bladder and the penis. Over the next 10 minutes, he propelled a hollow needle from a biopsy gun through my rectum 12 times, collecting minuscule samples of my prostate with each plunge.

The procedure, known as a transrectal biopsy, has been considered the gold standard for diagnosing prostate cancer, a condition that affects roughly one in eight men during their lifetimes. But transrectal biopsies are also risky: They can cause infections and, on rare occasions, a life-threatening condition known as sepsis. I started writing about these risks in 2018 after a friend, a facial plastic surgeon, nearly died from a transrectal procedure at the hands of his urologist.

Concerns over these risks have led a growing number of physicians around the world to abandon the procedure, in favor of safer methods. Because prostate cancer is typically slow growing more than a third of patients diagnosed with the condition don't undergo surgery or radiation therapy but are instead placed on active surveillance, a regimen of blood tests, digital exams, MRIs, and biopsies aimed at tracking the cancer's growth and providing an early warning should the cancer advance.

Compared with surgery, a transrectal biopsy may seem like a harmless option. It isn't. The rectal lining is ridden with potentially infectious bacteria, and 5 to 7 percent of patients who undergo prostate biopsies — the vast majority of which are transrectal — develop infections, according to the American Urological Association, or AUA. In up to 3 percent of transrectal biopsy cases, the infections trigger potentially life-threatening and disabling sepsis.

No one knows for sure how many people die from transrectal biopsies. But in 2019, Truls E. Bjerklund Johansen, a consultant urologist and professor emeritus at the University of Oslo, and Per-Henrik Zahl, a senior scientist at the Norwegian Institute of Public Health in Oslo, looked into the question after one of Bjerklund Johansen's biopsy patients died from a brain clot, likely triggered by sepsis. The researchers concluded, based on a national patient registry, that one in every 1,000 Norwegian men who underwent a transrectal biopsy died within 30 days of the procedure.

Transrectal biopsy patients are commonly given powerful antibiotics in preemptive attempts to ward off infection, but such protections aren't foolproof, and they are likely contributing to a rising plague of antibiotic resistant infections,

Bjerklund Johansen is among a growing contingent of doctors who have decided that the safest way to collect prostate tissue is not through the rectum but through the perineum, the skin between the testicles and anus. Unlike the rectum, the perineum can be easily disinfected, and also has another major advantage: It can provide a clearer pathway to the anterior prostate, a region that is harder to reach with transrectal biopsies. The anterior section, the "ceiling" of the organ, is the site of 20 to 35 percent of prostate cancers.

If the transperineal biopsy is so great, why don't all urologists switch?

One reason may be urologists underestimating the risk of transrectal biopsies. An old maxim holds that doctors bury their mistakes, and in the case of transrectal biopsies, mistakes may be hidden behind a misleading cause of death listed on death certificates. Urologists might not link a death from septic shock to transrectal biopsy, even if a biopsy was performed just days earlier. When individual doctors acknowledge the risk of post-biopsy infection, they may believe that infection rates among their own patients are low.

Perhaps more crucially, there's little financial incentive for urologists to make the switch in the U.S. To adopt the technique, they may need to invest large sums of money in new equipment and will need to undergo training to learn a procedure that — at least initially — will be slightly more time-consuming to perform than its transrectal counterpart.

Although the relative merits of the transperineal biopsy continue to be debated, momentum for the procedure has been growing in Europe, China, Australia, and elsewhere. In Australia, the national health plan now offers a higher reimbursement amount for transperineal procedures in an effort to make them the new standard of care. In 2017, Guy's Hospital, a National Health Service facility in London, stopped doing transrectal biopsies altogether. By March 2019, all six of the hospitals in the South East London Cancer Network had followed suit. In January 2021, the European Association of Urology stated in a position paper that "available evidence highlights that it is time for the urological community to switch from a transrectal to a transperineal [prostate biopsy] approach despite any possible logistical challenges." Bjerklund Johansen said that transrectal procedures have been abandoned in most of Norway.

The U.S. has been slower to come around. Bjerklund Johansen said U.S. urologists were skeptical of his research when he presented at the 2019 annual meeting of the AUA. Matthew Allaway, a urologist who invented a device used to position the biopsy needle in transperineal procedures, estimates that only 5 percent of prostate biopsies in the U.S. are performed transperineally, though that number may be even lower. Anecdotally, he estimates that about 60 percent of urologists have switched to the transperineal approach in Britain, and that anywhere from 5 to 30 percent of them have abandoned the transrectal approach across the European Union.

The latest and best review on ADT and Cognitive Function

Source:
16 August 2021
http://www.lifeonadt.com/life-on-adt-blog

One of the most worrisome concerns about the side effects of ADT relates to potential cognitive effects. It is understandably scary for patients and those who live with them to hear that androgen deprivation might affect patients' ability to remember and think.

In this new comprehensive review, the authors examined 31 previous studies and note that half of them failed to find evidence that ADT negatively affects cognitive functioning. However, they also found 11 reports documenting negative effects on cognitive function and that was enough for them to conclude that the concern is real and warrants more research. The primary cognitive effects they found were on memory, most frequently followed by effects on spatial processing ability.

The authors reached two conclusions. The first one is really not new and has been in the literature for close to 20 years. It is that, when patients are discussing with their clinicians whether to start ADT, the "clinician should discuss...potential [cognitive] side effect[s]".

The researchers' second major point was about future research. They argue that future studies should be randomized and use: 1) "a neuropsychological test battery" along with 2) "innovative techniques to examine brain function, structure and metabolism". The concern about test batteries comes from the challenges they had in making sense of all the data because previous researchers have used a wildly diverse set of cognitive tests, making it difficult to extract consistent findings.

The reference to "innovative techniques" is built upon the fact that there are now a variety of ways, such as using PET and MRI scanners, to visualize changes in the brain that can then be correlated with changes in cognitive function. The authors review the few studies that have been done that way. Their call for more research along those lines is, we believe, well justified. Future studies can go beyond just showing that ADT affects men's brains. We know that already. Using, however, the newer imaging techniques will help us understand how, when, and where ADT influences cognitive function. Combining rigorous cognitive testing with modern imaging will help us know exactly how androgen deprivation affects the brain and can document interventions that are most effective in limiting the negative cognitive effects of ADT.

To read the study abstract, see: https://pubmed.ncbi.nlm.nih.gov/34128263/

Marital Status and PCa Incidence: a Pooled Analysis of 12 Case–control Studies from the PRACTICAL Consortium

Social environment is a key factor in the risk of developing prostate cancer. PhD student Charlotte Salmon and Professor Marie-Élise Parent of the Institut National de la Recherche Scientifique (INRS) have shown that widowers are more likely to be diagnosed with advanced prostate cancer. Their research results have been published in the European Journal of Epidemiology.

The link was first identified following analysis of 12 studies from the international consortium PRACTICAL comparing 14,000 men newly diagnosed with prostate cancer and 12,000 healthy men. "This large group of subjects showed us that widowers were at risk of being diagnosed later than married men or men in relationships. As a result, when the diagnosis is made, the disease has often metastasized elsewhere in the body," said doctoral student Salmon, whose thesis focuses on social isolation and the incidence of prostate cancer.

Screening and lifestyle

Numerous studies suggest that the link to marital status exists because living with a partner promotes a "healthier" lifestyle. "Without a spouse's encouragement to see a doctor or get screened if there are symptoms, cancers remain undetected longer and may be diagnosed at a more advanced stage. This makes the prognosis bleaker," Salmon noted. To stay healthy, widowers should seek support from family and friends and more regular medical follow-up.

Other hypotheses to explain these findings include lifestyle factors such as alcohol consumption and the emotional impact of bereavement. In a 2020 study, Professor Parent and researcher Karine Trudeau showed diet could also be a risk factor.

Future studies will provide a better understanding of why widowhood is associated with greater risk and help develop appropriate public health strategies.

Salmon will study not just men's marital status but also the number of people living with them (family members), family structure, living environment (disadvantaged neighbourhood or not), and other social factors.

MONTRÉAL and LAVAL, QC, Aug. 12, 2021

https://www.ustoo.org/News-Page/r9UeGQ7rGs-n-H9YPTSK2xtC2-tZZjZMdCohgzSRn6cwe_wmqM10mybtmCuEWt0q

Prostate Heidelberg Cancer Support Group Meetings

Guest Speakers:

Tues 19 October 10:30am

Nikolajs Zeps

'What will the treatment of Prostate Cancer be like in 10 years time?'

Covid 'Passports'

For those members who don't use a smart phone and need to show evidence that they are double vaccinated – Services Australia 1800 653 809 will send you a 'Covid Vaccination Status' in the mail if you contact them with your Medicare Number

Thank you to the member at Bayside-Kingston for researching this information.

PCa Clinical Trials

For Further information on current and recruiting trials visit:

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

ENZA-p

Enzalutamide With Lu PSMA-617 Versus Enzalutamide Alone in Men With Metastatic Castration-resistant Prostate Cancer (ENZA-p)

https://clinicaltrials.gov/ct2/show/NCT04419402

This is an open label, randomised, stratified, 2-arm, multicentre phase 2 clinical trial recruiting 160 participants over 12 months and followed until 150 events occurred (approximately another 18 months). Participants will be randomised to enzalutamide or enzalutamide and Lu-PSMA in a 1:1 ratio. A minimisation approach will be used to minimise chance imbalances across the following stratification factors: study site, volume of disease (>20 versus ≤20 sites of disease measured on 68Ga-PSMA PET/CT), prior treatment with early docetaxel for castration- sensitive disease (yes vs no), and prior treatment with early abiraterone for castration-sensitive disease (yes vs no).

Locations

- NSW St Vincents, Sydney
  Calvary Mater Newcastle
  Northern Cancer Institute
- QLD Royal Brisbane & Women's,
- SA Royal Adelaide
- VIC Peter Mac, Melbourne
  Austin Health, Heidelberg
- WA Fiona Stanley Hospital

UpFront PSMA

In Men With Metastatic Prostate Cancer, What is the Safety and Benefit of Lutetium-177 PSMA Radionuclide Treatment in Addition to Chemotherapy

This phase 2 randomised clinical trial will compare the effectiveness of Lu-PSMA therapy followed by docetaxel chemotherapy versus docetaxel chemotherapy on its own in patients with newly-diagnosed high-volume metastatic hormone-naive prostate cancer (mHNPC).

Locations

- NSW St Vincents, Sydney
- QLD Royal Brisbane & Women's,
- SA Royal Adelaide
- VIC Peter Mac, Melbourne
  Austin Health, Heidelberg

BroSupPORT

At our August meeting, Ben Shemesh from Monash University gave a presentation of the development of the BroSupPORT portal.

The portal supports men living with prostate cancer by helping them to understand how the side effects they might be experiencing compare with men of similar age and risk profile who have received the same treatment.

The portal includes information on issues that have a big impact on a man's quality of life, like urinary incontinence, sexual and bowel function. The program is sponsored by the Victorian Agency for Health Information (VAHI) and has been developed in collaboration with Monash University as the managers of the Prostate Cancer Outcome Registry-Victoria (PCOR-Vic); Movember as funders of PCOR-Vic; and Alfred Health as the nominated lead Victorian public health service . BroSupPORT uses Patient Reported Outcomes (PROs) data from approximately 11,000 men, collected 12 months after their treatment. It allows men to access the portal after they complete a routine follow-up PROs survey, to see how their results compare with other men like them.

Following a three-month pilot period, the results from the evaluation are being used to inform improvements to BroSupPORT by Monash University and Movember and to provide the basis for sustained funding for program.

https://programs.movember.com/brosupport/

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.*

Your medical bills: Out-of-pocket costs, hidden fees and who's to blame

Four Corners

By Brigid Andersen and Dr Norman Swan
Posted 28 May 2018

The hidden fees
Alarmingly, Four Corners investigators saw several bills, that showed that patients had been charged a booking or administration fee, which medical bodies say are not legal.
Many surgeons receive higher rebates from health funds if they've signed a contract agreeing not to charge a gap fee. So-called booking fees are a way of cheating that arrangement.
The highest booking fee Four Corners saw was more than $6,000.
"Booking fees or other fees beyond the surgical fee are in fact illegal and should not exist and that is unethical to be charging," Royal Australasian College of Surgeons president John Batten told Four Corners.
Four Corners has been told that patients should report it if they are charged a booking fee.
"If a patient sees a fee like that appearing on a statement, they need to ask their doctor what it was for and what the clinical or medical relevance of that is, and if they don't get a satisfactory answer, they should not pay that fee and they should discuss it with their health fund," Private Healthcare Australia chief executive officer Rachel David said.

Who's to blame?
Almost all of the people we spoke to didn't want to blame their surgeons for out-of-pocket costs, however health policy experts say that's exactly who we should be looking at.
Terry Barnes is a policy consultant who's been an adviser to two health ministers, including Tony Abbott. He says health insurers are an easy target.
"They've got partly a PR problem in terms of they're always seen as the bad guys, and they're convenient bad guys, because the product that they sell is highly unpopular. It's about as popular as a fart in a lift," he said.
"Medical providers are always seen as above reproach. They're saints in white coats."
Grattan Institute director of health Stephen Duckett says some surgeons are submitting "outrageous" bills.
"The doctors are able to charge whatever they like. It's almost impossible for insurance companies to set a premium that covers whatever some doctor charges and those fees may be an order of magnitude above what the schedule fee is," he said.
One of the problems is that in the 1940s, a constitutional amendment was made that forbids conscripting doctors to charge regulated fees.

So what can you do?
Discuss with your GP what he or she knows about the charging practices of the specialists they refer to.
There is no relationship between the size of a doctor's fee and how good they are, so ask to be referred to a surgeon who participates in a no gap or known gap scheme.
If the specialist wants you to have a test that isn't reimbursed by Medicare, then ask what difference that test will make to your care.
When in front of the specialist and after the course of care has been discussed, insist on talking about costs.
Be unembarrassed about querying any items you don't understand and tell them if you think you can't afford the fees suggested.
Most surgeons will tailor their fees if they know patients will have trouble paying.
Surgeons are running a business and fees are the way they make their money, so a discussion about how much they're charging is just a business transaction.
Refuse to pay a booking, administration or nursing fee and refer any such bill to your health fund, who will take it up with the surgeon directly.
And seek second opinions. They are your right.

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.

PHCSG Correspondence

Prostate Heidelberg
POB 241 Ivanhoe Vic 3079
prostateheidelberg@gmail.com
prostateheidelberg.info

PHCSG Correspondence

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

PHCSG Meetings 2021 10am – 12:30pm

Tues 16 Feb
Tues 16 March
Tues 20 April
Tues 18 May
Tues 15 June
Tues 20 July
Tues 17 August
Tues 21 September
Tues 19 October
Tues 16 November
Tues 14 December (including Xmas lunch – (subject to COVID)

Please note that all face-to-face meetings have been cancelled until further notice. Please check your email regularly for updates from the PHSCG Committee.

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
- 11/12 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

2020 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

March 2020
- PCFA Consumer Advisory- Coronavirus and Cancer

April 2020
- Telehealth & Delayed Hospital Treatments due to COVID-19
- Fexapotide Triflutate (FT) injection – a new kind of focal treatment to extend time on active surveillance

Prostate Cancer Trials
- DASL-HiCaP Trial
- Evaluation of a mainstream model of genetic testing for men with prostate cancer

May 2020
- ADT May Offer Some Protection From COVID-19 in Men with Prostate Cancer
- TULSA – Novel MRI-guided ultrasound treatment destroys prostate cancer
- Whack-a-Mole A Treatment of Oligometastasis
- Long-term adjuvant ADT improves results of brachy boost therapy in unfavorable-risk prostate cancer patients
- Harnessing the immune system to control prostate cancer spread to the bone

Prostate Cancer Trials
- A study to see whether PET scans using a chemical called Exendin can detect metastatic PC
- Evaluation of a mainstream model of genetic testing for men with prostate cancer

June 2020
- Evaluating the Outcomes of AS in Gleason Grade 2 Prostate Cancer
- Advancing precision medicine for metastatic prostate cancer
- Impact of Primary Prostate Cancer Treatment with Subsequent Metastatic Disease
- Comparative Analysis & Survival Outcomes in a Real-World Practice Setting
- Fexapotide Triflutate (FT) injection – a new kind of focal treatment to extend time on AS

Prostate Cancer Trials
- Impact of 18F-DCFPyL PET scanning in patients undergoing post-prostatectomy Radiotherapy

July 2020
- Testosterone Therapy does not Increase the Risks of PCR or Death after Definitive Treatment for Localised Disease
- Association of Pre-Salvage Radiotherapy PSA Levels after Prostatectomy with Outcomes of Long-term Antiandrogen Therapy in Men with Prostate Cancer
- Testosterone Replacement in the treatment of Advanced Prostate Cancer
- Memorial Sloan Kettering Cancer Center PCa nomograms Prediction Tools

August 2020
- Advanced Prostate Cancer Algorithm
- Blood Test Predicts Response to PC Treatment (liquid biopsy)
- The Perils and Pitfalls of Treating PSA in PCa
- Reprogramming Immune Cells could Switch Defence into Attack in PCa
- Maintenance of Sexual Activity Following ADT

September 2020
- ProtecT Trial showing patient outcomes after AM, RP & EBRT
- Changes in Penile Length after RP
- Active Surveillance for PC – is it right for you?
- The final part of The Perils and Pitfalls of "Treating PSA" in Advanced Prostate Cancer
- Managing Erectile Dysfunction – A Patient Guide

Prostate Cancer Trials
- Efficacy and Safety of Pembrolizumab (MK-3475) Plus Enzalutamide Plus Androgen Deprivation Therapy (ADT) Versus Placebo Plus Enzalutamide Plus ADT in Participants with (mHSPC)
- Navigate: An online treatment decision aid

October 2020
- World Osteoporosis Day
- Lifestyle Factors and Chronic Disease
- Hormone Therapy for PC
- Early ADT for Recurrent PC Challenged
- Unexpected aPC weakness can be targeted by drugs
- Hijacking an Epigenetic Program
- New PC Research: Immunotherapy; Gut Microbiome
- Veyonda New Research on Survival Rates

Prostate Cancer Trials
- MIndonline - mindfulness

November 2020
- Life insurance & Genetic Testing
- World First Surgery in NZ
- Melatonin increases survival
- SBRT disease control
- Public vs Private Hospitals
- Early ADT for Recurrent PC challenged
- Enzamet trial results

Prostate Cancer Trials
- Randomised Phase 2 of sequential 177Lu-PSMA & Docetaxel
- Exercise for Heart Health

December 2020
- ACTA Trial Award
- Rethinking Metastasis
- ESMO Phase 1 AMG160
- Five Ways to Get it Right
- Immunotherapy Offers Hope
- SBRT Doubles Pain Response
- Elevated Streess Hormone Levels

Prostate Cancer Trials