How to Attend our Virtual Meetings

For the Group Meeting at 10am on Tuesday 16 June:
Please advise attendance by Monday 15 June.

Email:
prosateheidelberg@gmail.com
Subject heading:
Zoom Meeting

To join the meeting copy and paste the following Hyperlink into your web browser:
https://us02web.zoom.us/j/84105334090?pwd=Yy9wSWVMb3g2eXlGUk5WVE9iRkpGZz09

If you no longer wish to receive copies of the *PHCSG Newsletter*, please send an email to:
prosateheidelberg@gmail.com

If your membership has lapsed we hope you will consider rejoining and support the continuing work of the group.

Prostate Heidelberg Cancer Support Group

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

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

Prostate Heidelberg

June 2020 Issue 195

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 MEETING: Tuesday 16 June 2020 (Via ZOOM)
10am – 12:30pm

PHCSG Meeting - 19 May

A small group logged into our second Zoom meeting on 19 May intended to put our sessions back on to standard schedule of the third Tuesday of the month. It was great to welcome Max Shub back to share his deep knowledge and experience with the PHCSG. As usual, we shared views, experiences and progress with treatment etc. In terms of future sessions, the Uniting Church are yet to decide on the possible timing of a re-opening of their meeting facilities but do not anticipate the re-opening of our venue in the immediate future. We will therefore continue with Zoom sessions until the position is clarified.

In this month's newsletter we hightlight two articles for members on Active Surveilance (AS), plus information on PARP inhibitors and a comparative analysis of primary PC treatments. On page 4 you will also find an invitation to a PCFA Webinar on Wed 17 June.

Our virtual meeting on Tues 16 June will be with an invited speaker: **Professor Grant McArthur**, CEO of the Victorian Comprehensive Cancer Centre who will present on *'Research at VCCC from a Patient Perspective'*. Zoom invitations will be issued shortly.

Mike 0438 616 240

Source:
auajournals.org
Surveillance II (PD62)
1 Apr 2020

Evaluating the Outcomes of AS in Gleason Grade 2 Prostate Cancer

Prospective Results from the Canary-Pass Cohort

Abstract

INTRODUCTION AND OBJECTIVE:

The safety of Active Surveillance (AS) for grade group 2 (GG2) patients is debated. We sought to compare clinical outcomes of men with GG1 and GG2 prostate cancer undergoing AS in the Canary Prostate Cancer Active Surveillance Study (PASS) cohort.

METHODS:

Participants were prospectively enrolled in an AS study on protocol-directed follow-up at 10 centers nationwide. We included those who had GG1 or GG2 at diagnosis and at least one confirmatory biopsy. Patients were stratified according to GG at diagnosis and whether they were reclassified from initial biopsy. Time from diagnosis to treatment and time from definitive treatment to biochemical recurrence (BCR) were evaluated using Kaplan-Meier method; adverse pathology (AP) at Radical Prostatectomy (RP), defined as GG ≥3, ≥pT3a, or pN1, was analyzed as interval censored data using Weibull regression.

RESULTS:

Between August 2008 and February 2019, 1574 patients met the eligibility criteria. At diagnosis, 1440 (91%) patients had GG1 and 134 (9%) had GG2, out of which 102 (76%) presented with single core of GG2. Patients with GG2 were older (66 vs 62 years) and had shorter median follow-up (5.4 vs 6.9 years) compared to GG1 patients. Reclassification rate at 5 years occurred in 36% of GG2 and 38% of GG1 patients. Overall, patients with GG2 had shorter time to treatment compared to patients with GG1 (median: 4.3 vs. 10.3 years p<0.0001). Among those who were not reclassified, patients with GG2 had shorter time to treatment compared to GG1 (median: 4.55 vs not reached), but had longer time to treatment compared to GG1 and GG2 who got reclassified. The risk of AP at RP was slightly higher for GG2 than for GG1 (hazard ratio: 1.37; 95% CI: 0.73 – 2.54). BCR within 3 years of treatment among those treated with surgery or radiation for GG2 was 10% and for GG1 was 13% (p=0.50).

CONCLUSIONS:

Most GG2 patients enrolled in this AS protocol had low volume GG2 disease. Adverse pathology after RP and BCR after definitive treatment are similar in low volume GG2 patients compared to GG1 patients. Our results show that AS patients with low volume GG2 will have a shorter time to treatment, and limited follow-up post-treatment suggest equal oncologic outcomes.

US FDA approves new PARP inhibitors

prostate.org.au

Advancing precision medicine for metastatic prostate cancer

By Dr Jacqueline Schmitt – Manager, Research Programs for PCFA

In one giant leap for advanced prostate cancer, the US Food and Drug Administration (FDA) has this week approved two new PARP inhibitors for the treatment of metastatic castrate resistant prostate cancers which have specific genetic mutations.

What is precision medicine?
Precision medicine, which is also sometimes called personalised medicine, is a way of selecting the best treatment for a cancer patient based on their unique genetic changes. Currently, men diagnosed with prostate cancer are treated according to their cancer type and stage. But not all men respond the same way to the treatments and a treatment that works for one man with metastatic castrate resistant prostate cancer (mCRPC) may not work so well for another man with the same diagnosis.

Some of the differences seen in how a person responds to a treatment could be due to minor differences that are not seen by imaging scans or by the pathological analysis of tumour biopsy samples. These differences or genetic mutations occur at the DNA level. Two men diagnosed with mCRPC might have very different genetic mutations in the cells of their tumours that could influence the way they will react to different treatments. We wrote in detail about precision medicine in our December 2019 blog.

What are PARP inhibitors?
PARP inhibitors are a group of drugs which block the activity of a family of proteins called poly ADP ribose polymerases (PARP). PARPs are enzymes that have several roles in the cell including repairing damaged DNA. This is an important function because if the DNA of a cell becomes too damaged, the cell will die.

In treating cancer, we want the cancer cells to die and potentially we help this happen by using a PARP inhibitor to block the DNA repair actions of PARP. But cells are very clever, they have more then one way of repairing damaged DNA and often a PARP inhibitor alone is not enough to cause cell death. However, cancer cells often have DNA mutations and scientists have found that PARP inhibitors are more effective at killing cells which already have certain mutations.

There are several different PARP inhibitors currently available in Australia, Olaparib, Niraparib and Talazoparib. These are only available for use in one or more types of cancers of the breasts, ovaries, fallopian tubes or peritoneum. They have been found to be most effective in patients who have mutations in the breast cancer susceptibility genes (BRCA1 and/or BRCA2).

(continued)

PARP inhibitors and prostate cancer

Even though PARP inhibitors are available in Australia, they cannot be used for men with prostate cancer until extensive clinical trials have been completed to show they are safe and effective for men.

In our December blog, we wrote about the results of a phase II multicentre randomised clinical trial called TOPARP-B which was the first study to ask whether a genetic test could identify a group of men with metastatic castration resistant prostate cancer (mCRPC) who would benefit from olaparib treatment. Men in the study were given a genetic test. Those who tested positive for mutations in one or more of the following DNA repair genes, BRCA1, BRCA2, ATM or CDK12 were then treated with olaparib. This study found that olaparib showed anti-tumour activity against mCRPC tumours with mutations in DNA repair genes. It was particularly effective in tumours which had BRCA1 and/or BRCA2 mutations.

Further encouragement for the use of olaparib for men with mCRPC has come from the ongoing Profound phase III multicentre randomised clinical trial. This study is looking at the effects of olaparib on men with DNA repair mutations whose cancers have progressed after hormone therapy with new hormone therapy drugs like enzalutamide and abiraterone. So far, the study suggests that olaparib treatment significantly improves both progression-free survival and overall survival in men with BRCA1/2 or ATM gene mutations. In a press release in April this year, José Baselga, Executive Vice President, Oncology R&D at AstraZeneca, said: "Overall survival in metastatic castration-resistant prostate cancer has remained extremely challenging to achieve. We are thrilled by these results for Lynparza (trade name for Olaparib) and we are working with regulatory authorities to bring this medicine to patients as soon as possible."

Promising results for treating mCRPC have also been seen with the PARP inhibitor rucaparib in the TRITON2 clinical trial. In this study, the researchers wanted to know if mutations in DNA repair genes other than the BRCA genes would also make a cancer cell more susceptible to being killed by a PARP inhibitor. The study recruited 78 men with mCRPC who had defects in DNA repair genes but not in the BRCA genes. They found a limited response to rucaparib in tumours with mutations in the ATM, CDK12, or CHEK2 DNA repair genes as determined radiographically or by PSA levels. But they found a more significant response to rucaparib by tumours which had defects in the FANCA, PALB2, BRIP1, or RAD51B DNA repair genes. The researchers concluded that in men with mCRPC who do not have BRCA mutations, PARP inhibitor treatment might be helpful if they have deletions in other DNA repair genes.

PARP inhibitors approved by FDA

The US Food and Drug Administration (FDA) have approved the use of Olaparib and Rucaparib for the treatment of prostate cancer based on the TOPARP-B, Profound and TRITON2 clinical trials. This is exciting news which carries the promise that precision medicine treatments for men with mCRPC are around the corner. Potentially, a simple genetic test would help clinicians decide who would benefit from PARP inhibitor treatments and who would not.

PARP inhibitors in Australia

These latest developments bode well for universal acceptance of PARP inhibitors as an effective treatment to combat metastatic prostate cancer, with clinical trials currently underway in a number of countries. Locally, we know that researchers, pharmaceutical companies, and federal authorities are in ongoing discussions about the use of olaparib for prostate cancer treatment here, with the drug already approved by Australia's Therapeutic Goods Administration (TGA) for use in treating some female cancers. Stay posted for more information as news comes to hand.

Webinar Registration - https://onlinecommunity.pcfa.org.au

Wed 17 June 2020: 7pm in Canberra, Melbourne, Sydney

Join PCFA CEO Professor Jeff Dunn AO in conversation with Professors Michael Hofman & Declan Murphy

Personalised prostate cancer treatment of the future: Bringing together imaging, diagnostics, and therapy to stop cancer's spread

"Research is transforming the way we manage and treat prostate cancer, providing men around the world with much greater hope of combatting the disease effectively. Today we are one step closer to our vision of a future where no man dies of prostate cancer – standing on the shoulders of Australian research leaders." Professor Jeff Dunn AO

Impact of Primary Prostate Cancer Treatment with Subsequent Metastatic Disease

Comparative Analysis & Survival Outcomes in a Real-World Practice Setting

Abstract

INTRODUCTION AND OBJECTIVE:

Treatment options for clinically localized prostate cancer have included either radical prostatectomy (RP) or several different modalities of radiation therapy. There is conflicting evidence about the relative impact of the primary treatment on the time to develop castrate-resistant prostate cancer, although recent small studies have suggested a possible benefit for those undergoing RP compared to radiation therapy. The objective of this study is to compare the impact of previous local treatment modalities on progression to castrate-resistant state, and overall survival in men with newly diagnosed metastatic prostate cancer via utilization of real-world registry data.

METHODS:

We conducted a retrospective analysis using the Flatiron Health electronic health record-derived database, a nationwide database comprised of de-identified patient-level structured and unstructured data, curated via technology-enabled abstraction between 2010 and 2018. Eligible patients had received previous radiation therapy or surgery for their local disease and had progressed into metastatic disease. We used the date of metastasis diagnosis as the index date. Kaplan-Meier estimates were used to measure overall survival. Cox proportional hazards regression models were used to test the association between prior local treatment and progression to castrate-resistant state, as well as, overall survival; models were adjusted for age, race, Prostate specific antigen (PSA), Gleason score, Castrate-resistant state, administration of androgen deprivation before metastasis, and treatment year.

RESULTS:

Of 664 identified patients meeting the inclusion criteria, 310 (47%) initially underwent radical prostatectomy with or without adjuvant radiation and 354 (53%) received radiation alone. Median follow up from the date of metastasis for RP group, and radiation group was 30 months (17.5,42.4), and 29.4 months (18.6,45.4), respectively. Unadjusted cause-specific hazard regression showed that patients who received radiation therapy had 45% higher risk of developing castrate-resistant state compared to RP group [HR:1.45, CI:1.2-1.74, P<0.001]. This association remained significant upon adjusting for patient and disease-specific parameters [HR: 1.326, CI: 1.035-1.7, P= 0.0259] On multivariable analysis, after developing metastatic disease men who received radiation alone had 77% higher overall mortality [HR:1.77, CI:1.25-2.5, P= 0.0013] compared to men who underwent RP.

CONCLUSIONS:

Among patients with metastatic prostate cancer treated in routine clinical practice, those who had undergone prior RP had a lower risk of developing castrate-resistant state and improved overall survival from the date of metastasis compared to patients with metastatic disease who had received prior local radiation therapy. Notwithstanding the inherent selection bias at the time of choosing the type of local treatment because of unmeasured confounding variables, the results from this study add to the growing evidence that support the benefit of extirpation of the primary disease might confer improved overall survival after developing metastatic disease.

Source:
auajournals.org
Advanced (incuding Drug Terapy) I PD10
1 Apr 2020

Source:
pcnrv.blogspot.com
April 12 2020

Fexapotide Triflutate (FT) injection – a new kind of focal treatment to extend time on AS

A new medicine may be able to help men on active surveillance stay on it longer. The medicine, called Fexapotide Triflutate (FT), is administered just once with a thin (#22 gauge), reportedly non-painful, needle, in the prostate quadrant where GS6 cancer has been detected. It causes prostate cells, both benign and cancerous, to undergo "apoptosis" (programmed cell death). It only kills prostate tissue and not blood vessels or nerves, does not leak outside of the prostate into systemic circulation, and does not affect adjacent tissues of the rectum, bladder, urethra, or periprostatic tissue.

Shore et al. reported the results of a Phase 2 randomized clinical trial in 148 patients at 28 sites. They were randomized to get low-dose FT (2.5 mg), high dose FT (15 mg), or active surveillance (AS). Patients and investigational staff were blinded as to FT dose, with no sham injections for AS patients. The FT patients received a **single** injection only into the quadrant with the cancerous core. Patients were all excellent candidates for active surveillance:

- Gleason score 6
- Stage T1c (nothing felt on DRE)
- Only 1 core with cancer
- ≤ 50% cancer in the core

They were all followed using the same protocol:

- Follow-up biopsy on Day 45 and at 18 months, 36 months, and 48 months
- PSAs every 6 months
- After the first biopsy, 18 of the 49 AS patients were allowed to opt for FT injections
  After 4 years of follow-up:
- 42% of AS patients progressed, and 39% were treated for progression
- 19% of high-dose FT patients progressed, and 11% were treated for progression
- 37% of low-dose FT patients progressed, and 21% were treated for progression.
- Median biopsied tumor grade was Gleason 3+4 among those assigned to AS or low-dose FT vs Gleason 3+3 among those who received high-dose FT. At 18 months, the median tumor grade for the high-dose group was **benign** (no cancer detected) vs GS 3+3 in the other two groups.
- At 18 months, estimated tumor volume in the quadrant with cancer *increased* by 69% for AS vs *decreased* by 59% for FT.
- The effect of high-dose FT was greatest at 18 months, and still had an effect at 48 months.

- The effect of low-dose FT was greatest at 18 months, but was insignificant at 48 months.
- PSA reduction was maintained in both FT groups (-21%)
- There were very few and transient side effects attributable to the injections (blood in urine, sperm or stool), diarrhea or nausea from antibiotic.
- There were no serious adverse effects - no increase in urinary symptoms
- There were no significant sexual problems associated with FT treatment

It is entirely possible that injections across the entire prostate might have improved results.

For comparison, at 5 years after AS, Johns Hopkins (which had similar stringent requirements) reported progression in only half as many patients (21%), about the same percent as in the high-dose FT group. It is unclear why progression among the AS control group was so much higher in the Shore trial.

Comparison to 5αri therapy

Dutasteride has also been used in an effort to slow progression among men on AS. Fleshner et al. reported that after 3 years, 38% of treated patients and 48% of their more liberally-assigned AS patients progressed or were treated. In the Shore trial at 3 years, 10% of high-dose FT-treated patients and 30% of the AS patients progressed and were treated. It's hard to compare these trials because the AS criteria were so different.

At one year after 5αri therapy (finasteride or dutasteride) for BPH in very-low-risk men on AS for prostate cancer, Shelton et al.reported that no cancer was found on biopsy in over half (54%) of the treated men, similar to the finding of the high-dose FT group at 18 months. Only 5% progressed to Gleason 7, similar to the high-dose FT group (6%) at 18 months.

- **5αris** are known to have sexual side effects in 20-25% of men taking them. Sexual side effects may include reduced libido, difficulty in having an erection or orgasm, or gynecomastia.
- Hair growth is a beneficial side effect for many men.
- They have to be taken every day.
- They shrink benign prostate tissue, and may cut PSA in half if the PSA is due to enlargement of the entire prostate. However, in men who have BPH due to enlargement of the transition zone-only (with normal-sized prostates), their effect on BPH and PSA is unclear. Whereas PSA as a biomarker for active surveillance is already problematic, using 5αris may increase confusion and anxiety.
- **FT**, on the other hand, has no sexual side effects
- works well for transition zone tumors, and
- has a smaller effect on PSA (-21%)
- is a pain-free, "one and done" treatment.
- It is unknown what the relative costs will be.

Other potential therapies

In a retrospective study at Cleveland Clinic, statin use was not associated with reduction of progression among men on active surveillance.

There are other medicines in ongoing clinical trials to delay progression in men on AS:

- 2-hydroxyflutamide (intra-tumoral injection)
- apalutamide
- green tea catechins
- curcumin
- Prostatak
- Provenge
- Proscavax

Patients are cautioned against using supplements that may be masking their true PSA in the hope of prolonging AS. "Treating PSA" rather than treating the underlying cancer can lead to mismanagement.

This small study suggests that FT injections can delay progression for men on AS, without any side effects. This is different from focal ablation therapy. There must still be periodic biopsies, although their frequency may be safely reduced. The cost and whether insurance will cover that cost may be a consideration. If it gets approved for BPH (see below), and considering that many men with prostate cancer also have symptomatic BPH, this may be available "off-label" within the next couple of years.

BE YOUR OWN ADVOCATE

Remember that you need to be your own advocate and take the time to learn as much as you can about treatment options available to you. Understand as much as you can so that you are in a position to ask your doctors all the relevant questions. With study and determination you can find the best treatment for your situation.

Prostate Heidelberg Cancer Support Group Meetings

While we are having to distance ourselves and unable to hold face to face group meetings we hope to engage speakers via video conferencing

Guest speaker scheduled for June:

16 June
Professor Grant McArthur
Executive Director of the Victorian Comprehensive Cancer Centre
"Research at VCCC from a patient perspective"
Prof Grant McArthur's research interests include discovery of drug targets in cancer, targeting oncogenes, immunological effect of targeted therapies, clinical trials of targeted therapeutics, personalized medicine, melanoma, cell cycle control, metabolism and protein synthesis in cancer.

Prostate Cancer Trials

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

Australian New Zealand Clinical Trials Registry [anzctr.org.au]
Status: Recruiting
Trial ID: ACTRN12618001530213
Recruitment date: 01/06/2018

Contact: Ms Nicole Haberman
GenesisCare
Cancer Care Research
Level 5, 126 Wellington Parade
East Melbourne Vic 3022
0408 737 216

18FDCPyL is an investigational radioactive diagnostic imaging agent indicated for positron emissiontomography (PET) in patients with cancer with knowledge of the distribution of Prostate Specific Membrane Antigen (PSMA) throughout the body.

To assess the role and impact of a new imaging scan, 18FDCPyLPET in patients referred for salvage radiotherapy (radiation treatment when prostate cancer has recurred) following radical prostatectomy for prostate cancer. 18FDCPy:PET/CT has previously shown to provide high resolution imagery in targeted areas.

Participants will have an 18FDCPyLPET/CT scan, in which the results will determine what management pathway best suits them.

Participants will be required to have 1 PET/CT scan, this scan will take approximately 2 hours. The PET imaging will be performed in the imaging department by qualified Nuclear Medicine Specialists

250 MBq +/50 MBq, depending on patient weight and activity provided on day of scan.

Primary Outcome [1]

The impact of PET/CT will be based on change in treatment intent compared to 1] intent prior to any imaging performed and 2] intent based on the diagnostic CT result.

Grading will be similar to the system reported by van Leeuwen et al: (28) ~ 1] None, 2] Moderate and 3] Major, with an addition of classification of 'Ignored'.

Timepoint [1]

36 Months post enrolment

Secondary outcome [1]

To compare the detection of disease using 18F-DCFPyL PET/CT compared to diagnostic computer tomography specially in pelvic nodal (N) or metastatic disease (M) Kaplin Meier time to event actuarial curves will be constructed to examine disease progression or nodal/distant failure.

Timepoint [1]

36 Months post enrolment

Clinical trials may enable you to receive leading edge treatment, but you must also be fully informed of the risks, costs and safety issues of participating.

Internet Resources

Members have found the following websites useful

Prostate Cancer Foundation of Australia for guides & help
www.PCFA.org.au

Australian Cancer Trials
Information on clinical trials
www.australiancancertrials.gov.au

USA Prostate Cancer Foundation (Guide) PDF guide for men newly diagnosed with PC
www.PCF.org/guid

Us TOO International PCa Education (USA) USA PC support groups' information & newsletter
www.UsToo.org

Cancer Council Victoria for general support services
www.CancerVic.org.au

ExMed Cancer Program
Melbourne based 'best practice' exercise medicine program
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

Australian Advanced Prostate Cancer Support Group for men diagnosed with advanced metastatic PC
www.JimJimJimJim.com

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

PAACT Newsletter (USA) Patient Advocates for Advanced Cancer Treatments
www.paact.help/newsletter/

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 Correspondance

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

PHCSG Meetings 2020 10am – 12:30pm

Tues 18 Feb (guest speaker)
Tues 17 March
Tues 21 April (guest speaker)
Tues 19 May
Tues 16 June (guest speaker)
Tues 21 July
Tues 18 August
Tues 15 September
Tues 20 October
Tues 17 November
Tues 15 December (including Xmas lunch)

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.