THE WALNUT

APRIL 2018

Newsletter of the Prostate Cancer Support Group—ACT Region

Affiliated with the Prostate Cancer Foundation of Australia (PCFA)
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Next monthly meeting

Our next monthly meeting will be on **Wednesday 18 March 2018**.

There will be no speaker at this month's meeting.

All are welcome to attend our regular monthly meetings and coffee mornings, including partners and carers. No notice is required – simply come along and introduce yourself, or contact one of the people listed on page 2 of this newsletter.

Meetings of our support group are held on the third Wednesday of the month (except in December) at 6:30 pm for 7:00 pm. The usual location is Room 22, Building 1, Pearce Community Centre, Collett Place, Pearce, ACT 2607. See our website here for details and map showing the location: http://tinyurl.com/8gkhysb.

Next coffee morning

10:00 am, Tuesday, 8 May, Canberra Southern Cross Club, Woden.

Coffee mornings are held at 10:00 am on the second Tuesday of each month and alternate between the Woden and Jamison venues of the Canberra Southern Cross Club.

President's Message

I would like to thank the John Curtin School of Medical Research for hosting our event in March. They made us feel very welcome.

Dr Kate Hannan, Research Fellow, stood in at the last minute for her husband, Prof Ross Hannan, who was sick. As she did when she last addressed our meeting in 2017, Kate provided an excellent summary of what the school is working on, and it is inspiring to know that there is such a great world class research facility here in Canberra.

I would also like to thank the other members of the School's staff and students who facilitated our visit and tour of the laboratories. They all helped to make the occasion very special for those who attended and it was fascinating to see what the researchers are doing.

The School is certainly making great strides in understanding the main forms of cancer, including prostate cancer, and in researching better ways of treating them.

Unfortunately, we have been unable to arrange for a speaker for our meeting in April. It has proven to be a very busy time for all the potential speakers we approached. So, we will be using the occasion to share member experiences.

I would also like to thank those members who participated in our outreach events at the Seniors Week Expo on 15 March and the Royalla Country Fair on 18 March. The Seniors Week event went off well and we will participate in that event again in 2019. The weather for the Royalla Country Fair was awful and we, along with most other stall holders, called it a day around lunchtime.

We are now examining what we might do to help mark Men's Health Week in June.

John McWilliam
President

Our March Meeting

Our March meeting was held at the John Curtin School of Medical Research at the ANU.

We started our visit with a presentation from Dr Kate Hannan, Research Fellow at the School on the topic of *The Future of Cancer Research* in Canberra. Dr Hannan answered questions during her talk . After the presentation, three PhD students guided our members through the labs ,explaining their studies and the usefulness of the scientific equipment.

Some of the points made by Dr Hannan during her presentation are as follows:

- The School has around 70 members of staff, organised into four departments – the ACRF Department of Cancer biology and Therapeutics; the Eccles Institute of Neuroscience; .Genome Sciences; and Immunology and Infectious Disease. It currently has seven research laboratories and another laboratory will be added in 2019.
- The School has received $15.4m in grants and in 2016-17 published 63 peer-reviewed papers in scientific/medical journals. In addition to full-time academic staff there are currently 18 students enrolled for a PhD level and 12 for an Hons/MSc.
- The Director, Professor Ross Hannan, also holds the 'Centenary Chair' and is Director of ACT Health Research for the ACT Government.
- The School studies cancer cells in general to understand their initiation, growth, and demise and ultimately understanding factors controlling their survival.
- The Gardiner Group laboratory is studying the mechanics of thrombosis and cancer. Emerging research shows that platelets orchestrate the complex interplay between haemostasis, thrombosis, inflammation, and cancer. The Group is examining thrombosis associated with cancer and things such as deep vein thrombosis and thrombocytopenia (low blood platelet counts resulting in bleeding).
- Closely related to the Gardiner Centre is the National Platelet Research and Referral Centre at the ANU, which seeks to improve the understanding of, treatment for, and quality of life for individuals with platelet disorders. Clinical trials are in progress from phases 1 – 3 to understand cancer biology and develop new techniques relating to platelet attachment to cancer cells.

Appreciation

The Group recognises and expresses its appreciation for the support provided by: the PCFA, SHOUT staff, the Canberra Southern Cross Club, Holy Family School Gowrie, ACT Veterans' Hockey Association Inc, Paddywack Promotional Products, the Naval Association of Australia, German Auto Day and the many individuals who have assisted in our fund-raising activities.

Personal support

For general information, please call SHOUT (Self Help Organisations United Together) during normal office hours on (02) 6290 1984, and their staff will arrange for someone to contact you. After hours, please call 0490 784 151.

If you would like immediate advice, support or assistance, please contact one of the following two people:

President: John McWilliam
Phone: 0416 008 299
Email: president@prostate-cancer-support-act.net

Secretary: David Hennessy
Phone: (02) 6154 4274
Email: secretary@prostate-cancer-support-act.net

SHOUT stalls at shopping centres

SHOUT is planning to stage four stalls at shopping centres each year to promote its members' issues, including those of the PCSG. If you are willing to help out at these events, please email Carol at admin@shourt.org.au. The next event will be held in June.

Dr Kate Hannan who gave the presentation

A robot that the School uses in its research

- Dr Leonie Quinn heads up a group in the Australian Cancer Research Fund (ACRF) Department of Cancer Biology and Therapeutics, which is examining cancer models. Using flies, this Group is using novel approaches to better understand cancer initiation and progression. Dr Quinn has won won an innovation grant from the Cure Brain Cancer Foundation to help understand how brain cancer occurs and ultimately develop new treatments.

- The School has now combined with the ACRF Laboratory (within the School), Canberra Hospital, Calvary Hospital and University of Canberra to integrate study on cancer cell function. The School is working to establish a better collaboration between researchers and clinicians and to provide the opportunity for clinicians also to undertake some research. It is doing this by 'embedding' researchers into clinical units to foster better communication and direction. Ultimately, the aim is to have an outpatients unit at the School. This might also help the School to access a wider range of tissue samples.

- The School considers that there is a need for:
  - more clinical scientists;
  - better engagement between clinicians at the Canberra Hospital and PhD students; and
  - an endowment to help fund clinicians' participation in research.

- Two current studies showing promise were highlighted by Dr Hannan. CX-5461 is a drug found to disaggregate ribosome in prostate cancer (ribosomes are proteins made by cancer cells). Combining CX-5461 with a drug called CX-6258, a transcription inhibitor, is showing promising signs of largely reversing the growth of the cancer in mice.

- The second study indicates that, when cancer cells are viewed under electron microscopes, after application with PMR-116, a single-drug, they appear normal; i.e. a 'conversion' to normality. Further work may involve grafting human tissue into mice to help determine how effective the drugs are in treating cancer in humans.

April Executive Committee Meeting

The Executive Committee met on 4 April. The Committee, among other things:

- reviewed the recent outreach events and agreed that we would attend the Seniors Expo again in 2019, as we received many enquiries at this event. We would not attend the Royalla Country Fair again;

- noted that we had been invited to speak about prostate health awareness at a lunchtime function in the Department of Human Services and agreed on arrangements for this. The event will be held on 22 May 2018; and

- discussed possible speakers for future meetings, and agreed to invite Michael Milton, a paralympian who has recently sought to promote awareness of prostate cancer, to speak at a future meeting.

Rise Above — Capital Region Cancer Relief

The Cancer Support Group-ACT Eden Monaro's Own. It has changed its name to *Rise Above – Capital Region Cancer Relief*.

Rise Above provides financial assistance and support to cancer patients and family residing with them within the ACT, Queanbeyan and surrounds. So, if you are experiencing financial hardship in meeting your treatment costs, you can contact Rise Above. It is located at 21 Cooma Street, Queanbeyan and its phone number is (02) 6297 1261.

A charitable organisation, Rise Above relies on fundraising, community partners, the generosity of businesses and the local community, to meet the needs of the increasing number of families that require our assistance. So, it is also a good cause for your generosity.

Stay up-to-date

Stay up-to-date by joining the PCFA Online Community. The PCFA Online Community is open to everyone who has been impacted by prostate cancer to share their experiences and connect with others. Through the Research Blog, PCFA Online Community members can also learn more about the latest prostate cancer research developments and findings.

It is free and easy to become a member of the PCFA Online Community. You can sign up at: http://onlinecommunity.pcfa.org.au .

Borrowing items from the library

You can borrow items from the Group's library. There is a wide range of materials, from books to videos. Those who are interested in borrowing items from the library or finding out more about our collection can contact U.N. Bhati, email: librarian@prostate-cancer-support-act.net

Articles and reports of interest

The following articles which have appeared recently on web sites or other sources may be of interest to some members. Any opinions or conclusions expressed are those of the authors. See Disclaimer below. With thanks to Don Bradfield and Mike Boesen for their assistance with this segment.

MRI-based prediction model for prostate biopsy risk stratification

S Mehralivand, JH Shih, S Rais-Bahrami, A Oto, S Bednarova, JW Nix, JV Thomas, JB Gordetsky, S Gaur, SA Harmon, MM Siddiqui, MJ Merino, HL Parnes, BJ Wood, PA Pinto, PL Choyke, B Turkbey,, *A Magnetic Resonance Imaging-Based Prediction Model for Prostate Biopsy Risk Stratification*, JAMA Oncology, 2018 Feb 22;[EPub Ahead of Print], reported on in *Practice Update*, http://tinyurl.com/ycdlswa3.

Multiparametric magnetic resonance imaging (MRI) in conjunction with MRI-transrectal ultrasound (TRUS) fusion-guided biopsies have improved the detection of prostate cancer. It is unclear whether MRI itself adds additional value to multivariable prediction models based on clinical parameters.

In this cohort study, a prediction model based on clinical and magnetic resonance imaging parameters was first developed in 400 patients and subsequently validated in two independent populations of 251 patients. Patients underwent MRI, MRI-TRUS fusion-guided biopsy, and 12-core systematic biopsy in one session. The MRI model included MRI-derived parameters in addition to clinical variables.

The model reduced the number of unnecessary prostate biopsies, while still detecting most clinically significant prostate cancers.

Overall, 193 (48.3%) of the 400 patients in the development cohort (mean [SD] age at biopsy, 64.3 [7.1] years) and 96 (38.2%) of the 251 patients in the validation cohort (mean [SD] age at biopsy, 64.9 [7.2] years) had clinically significant prostate cancer, defined as a Gleason score greater than or equal to 3 + 4. By applying the model to the external validation cohort, the area under the curve increased from 64% to 84% compared with the baseline model (P < .001).

At a risk threshold of 20%, the MRI model had a lower false-positive rate than the baseline model (46% [95% CI, 32%-66%] vs 92% [95% CI, 70%-100%]), with only a small reduction in the true-positive rate (89% [95% CI, 85%-96%] vs 99% [95% CI, 89%-100%]). Eighteen of 100 fewer biopsies could have been performed, with no increase in the number of patients with missed clinically significant prostate cancers.

Advanced prostate cancer: a look ahead —hormone sensitive metastatic disease

Wallis, JD, Klaassen, Z, Bhindi, B, et al, *Comparison of abiraterone acetate and docetaxel with androgen deprivation therapy in high-risk and metastatic hormone-naïve prostate cancer – a systematic review and network meta-analysis*, European Urology, October 2017, https://tinyurl.com/y859wrf3, reported in *Practice Update*, February 2018.

The recent publication of several large phase III trials has changed the community standard of care for men presenting with hormone-naïve metastatic prostate cancer. Although this entity was historically reported as 5% of all new diagnoses, the under-utilisation of PSA since changes in screening guidelines were implemented has led to an increase in men presenting with advanced disease. As a result, the ideal therapy and sequencing of agents for men with more advanced disease has been in the spotlight.

In 2015, data from two large trials, CHAARTED and STAMPEDE, changed the treatment of newly diagnosed metastatic prostate cancer to include concomitant docetaxel. Urologists and medical oncologists alike have begun to embrace this new regimen, especially in men with higher-volume metastatic disease, as that was the subset that seemed to garner the greatest benefit.

Again in 2017, two more studies were released that challenged that new, albeit short-lived, standard. LATITUDE and an update of STAMPEDE explored the alternative combination of abiraterone with standard ADT. LATITUDE was limited to men with metastatic disease and included a truly a high-risk cohort of patients having either Gleason >8 and/or more than three bone/visceral metastases. STAMPEDE, on the other hand, had 48% of its cohort comprised of non-metastatic patients – locally advanced disease (PSA >40, and/or T3/4 or Gleason 8–10) or node-positive men. The results were overwhelming; in both men with metastatic and men with nonmetastatic disease, there was significant benefit to adding abiraterone. Specifically, abiraterone with standard ADT in metastatic men improved overall survival, time to pain progression, time to chemotherapy and PSA progression compared with ADT alone. The men with localised disease also had an improvement in failure-free survival, but overall survival data were not mature or significant, likely given the prolonged timeline for nonmetastatic patients.

The abiraterone trials did not have a docetaxel control arm, so direct comparison of the two agents is difficult. Based on almost identical hazard ratios across studies, the magnitude of benefit appears to be very similar between abiraterone and docetaxel in this patient population.

Obvious benefits of abiraterone over chemotherapy include the morbidity profile and replacement of a short-term intravenous therapy with a longer-term oral therapy. This may benefit an older, more debilitated population. Furthermore, the favourable results in non-metastatic patients in STAMPEDE may mean abiraterone is a less volume-dependent agent compared with chemotherapy.

Universal use of abiraterone in men with advanced disease can be problematic as well. Cost, long-term endocrine side effects, and the potential of changing the hormonal milieu of CRPC such that it may become resistant to other therapies upon progression are all valid concerns. Tissue typing and androgen receptor characterisation (eg, AR V-7 status) will likely be important biological classifiers to determine therapy and sequencing.

Trying to personalise treatment based on disease and performance status appears to be the best strategy at this point. Younger men with higher-volume disease may still be great candidates for upfront chemotherapy, whereas frailer patients may be ideal for abiraterone therapy.

Digital rectal examination for prostate cancer screening in primary care: a systematic review and meta-analysis

Leen Naji, MD, Harkanwal Randhawa, BHSc, Zahra Sohani, MSc, PhD, Brittany Dennis, BA, PhD, Deanna Lautenbach, PA, Owen Kavanagh, BHSc, MD, Monica Bawor, BSc, PhD, Laura Banfield, MLIS and Jason Profetto, MD, CCFP, *Digital Rectal Examination for Prostate Cancer Screening in Primary Care: A Systematic Review and Meta-Analysis*, Annals of Family Medicine, March/April 2018, Vol 16, No 2, https://tinyurl.com/y9vmjzso.

Results from a large meta-analysis support the Royal Australian College of General Practitioners' (RACGP) view that routine digital rectal examination (DRE) for prostate cancer screening should be avoided.

The research notes a distinct lack of evidence supporting its use in a primary care setting.

The analysis of seven studies included more than 9000 men who underwent both DRE and biopsy.

The research, conducted by a team from Canada's McMaster University, shows a high risk of bias, with the overall quality of evidence rated as 'very low'.

Given the findings, the authors recommend against routine screening using DRE 'to minimise unnecessary diagnostic testing, overdiagnosis, and overtreatment'.

The results support the RACGP's latest guidance , which states: "DRE is no longer recommended as it is insufficiently sensitive to detect prostate cancers early enough."

Note: A caution offered is that a small number of patients with prostate cancer have an abnormal DRE in the presence of a normal PSA and those patients may therefore possibly not be detected.

PSA screening for asymptomatic men

Hugo Wilcken, PSA screening for asymptomatic men: is the jury in yet? MJA InSight, Doctor's Portal, Issue 10, 19 March 2018, http://tinyurl.com/yc2wylmt

In this article Hugh Wilcken points out that the highly contentious issue of screening for prostate cancer is back in the news after the publication of a large study looking at the effects of prostate-specific antigen (PSA) testing on disease-related mortality rates.

The CAP Trial – involving almost 600 GP practices across the United Kingdom and around 400 000 asymptomatic men aged 50–69 years – compared the outcomes of patients who were invited to have a one-off PSA test with a control group who were not. Around 40% of the men in the intervention arm took up the offer of a test.

After 10 years of follow-up, more cases of prostate cancer were diagnosed in the screened group (4.3% v 3.6%), but there was no difference between the two groups in the number of men who died from prostate cancer. The reason, the researchers say, is that most of the extra cancers picked up in the screened group were of low grade (Gleason Grade 6 or lower) and were therefore unlikely to lead to death. The study findings mirror those of other large trials of PSA screening, which have reported rates of over-diagnosis (detection of disease that would not affect a man in his lifetime) of around 50%.

In an interview on Radio National's Health Report, lead author Richard Martin, a professor of Clinical Epidemiology at the University of Bristol in the

UK, described PSA testing as 'a blunt tool'. He said that what was really needed was 'a better method of identifying aggressive tumours that will harm men'.

Shomik Sengupta, a professor of Surgery at Monash University and USANZ's UroOncology Advisory Group Leader, says the results of the latest study aren't particularly surprising.

"It's reinforcing what's already been found, which is if you do PSA screening you turn up a lot of low grade cancers, and that's not the group you necessarily need to treat. Nowadays, we would put these men in a surveillance program. The truth is PSA testing is happening, it's out there, and inappropriate testing does occur. But we do have well developed guidelines in Australia, which suggest that it can be done in men aged 50–70 years, if the patient wishes it and if he has been appropriately informed by his GP of the potential benefits and harms."

Professor Sengupta says that one promising development is the increasing use of magnetic resonance imaging (MRI) as a tool for identifying which cancers need treatment.

Ultimately, Professor Sengupta says, the way to minimise harms and maximise benefits is to perform PSA testing appropriately, with the appropriate safeguards, and do the follow-up.

From the editor

If you are aware of news, products, publications, web sites, services or events that may be of interest to members of the group I'd like to be informed of them.

If you have received this newsletter indirectly and would like to be emailed a copy direct, or if you would like to add any of your friends or carers, or if you no longer wish to receive copies of the newsletter, please send us an email through the form here:

http://tinyurl.com/ybkxnlg4.

Disclaimer

From time to time in our newsletters we provide information about developments in the diagnosis and treatment of prostate cancer, research articles, documents, audiovisual products, presentations and other interesting materials. However, the Group's Executive and the editor of this newsletter do not have the medical expertise required to make an informed evaluation of the conclusions and recommendations presented in such materials, and we have not verified such conclusions and recommendations through appropriately qualified medical professionals. The information presented in this newsletter must not be interpreted as being endorsed or recommended by the Executive or the editor. Any recommendations made in such materials may not be applicable in your case. Before implementing any recommendations made in the materials that are reported, it is essential that you obtain advice from appropriately qualified medical professionals. The view of the Group's Executive is that no two prostate cancer cases are alike and that no single treatment option is better than any other in all cases. While the information in this newsletter should be of interest, there is no substitute for getting informed medical advice from your own GP, specialists and other medical professionals.