The Melbourne Consensus Statement on Prostate Cancer Screening

Summary: There is some confusion with respect to the use of PSA testing for prostate cancer detection. Despite robust evidence of PSA screening as a predictor of risk, the US Preventive Services Taskforce called for the abandonment of routine PSA testing. In contrast, the American Urological Association, National Comprehensive Cancer Network and European Association of Urology continue to support PSA screening, but their recommendations are somewhat conflicting, while most guidelines endorse a shared decision-making process for men considering PSA testing. Leading prostate cancer experts from around the world generated a set of consensus statements at the 2013 Prostate Cancer World Congress in Melbourne to clarify existing guidelines and provide reasonable and rational guidance for the early detection of prostate cancer.

Consensus statements:
1. For men aged 50–69, level 1 evidence demonstrates that PSA testing reduces prostate cancer-specific mortality and the incidence of metastatic prostate cancer
2. Prostate cancer diagnosis must be uncoupled from prostate cancer intervention
3. PSA testing should not be considered on its own, but rather as part of a multivariable approach to early prostate cancer detection
4. Baseline PSA testing for men in their 40s is useful for predicting the future risk of prostate cancer
5. Older men in good health with over ten year life expectancy should not be denied PSA testing on the basis of their age.

Comment: A summary statement for the data supporting each statement is presented on the website listed below.

I like this consensus because I think it takes a balanced approach to analysing the data, taking advantage of the benefits of PSA testing while accepting its frailties. PSA testing should be considered a risk-stratifying test by patients and clinicians rather than a diagnostic test; the diagnostic test is the subsequent biopsy. The biopsy then needs to be interpreted with caution, understanding the associated risk of overtreatment and morbidity that has occurred in the past. We should not “throw the baby out with the bathwater” as currently we do not have a better test to detect the disease at its curable stages.

Commercialisation of discovery research

Presenter: Martin Gleave

Summary/Comment: Professor Gleave is a surgeon-scientist with a large clinical practice in prostate cancer as well as a large research lab focused on drug development in prostate cancer. He gave a talk highlighting the issues surrounding the commercialisation of research. His experience in the field is highlighted by the success of his unit, which has over $50 million in research grants and 25 salaried scientists and multiple PhD students. For most this would be enough of a challenge, but he and his team have gone on to found a biotech company, Oncodeix Technologies, which is NASDAQ listed. His research characterises the molecular mechanisms that mediate treatment resistance in cancer, focusing on stress-activated adaptive responses, and the development of prostate cancer therapies, which use combination approaches targeting multiple pathways. He confronted the dogma that medical interaction proof of principle, through ‘in man’ trials to marketing. The challenge is to validate in pre-clinical models, through ‘in vitro’ animal studies to identify the right patient population, and the correct biomarker, and the right route of administration. Much of this work has gone on to found a biotech company, OncoGenx and this biotech company is NASDAQ listed. His research commercialisation has been highlighted by the success of his unit, which is NASDAQ listed. His research commercialisation has been a consistent annual rate of 3%. What we have found is quite large variations in incidence of post-TRUS infections month-to-month, which defy quite intense investigation. However, these variations have always averaged out to a consistent annual rate of 3%

Anxiety in men with prostate cancer treated by active surveillance

Authors: Anderson J et al

Summary: This single centre study describes the anxieties of 104 men with low-risk prostate cancer active surveillance (AS), and anxieties that predicted health-related quality of life. Anxiety was not demonstrable on the Hospital and Anxiety Depression scale in 91% of the patients, while the memorial anxiety scale for prostate cancer (MAX-PC) indicated that 98% had low levels of PSA anxiety and 87% low levels of prostate cancer anxiety. However, MAX-PC also indicated higher levels of anxiety regarding fear of recurrence in 81% of men. Illness-specific prostate cancer and fear of recurrence were associated with general (state/trait) anxieties and younger age. Overall, 92% of men were satisfied with the information regarding prostate cancer and AS that they received from their urologist.

Comment: One of the concerns with AS has been the psychological burden of living with the disease “untreated”. Probably a better title for the paper would have been “Anxiety in men with prostate cancer managed by active surveillance”. Unfortunately, although the paper shows only a small level of anxiety associated with AS it does need to be remembered that this is a self-selected group. Clearly, men who choose AS as their management strategy do so on the basis that they are most comfortable with this option.

Abstract# 22842

Post-TRUS sepsis: targeted use of prophylactic ertapenem for high-risk patients

Authors: Losco G and Studd R

Summary: This prospective, comparative, single-centre cohort study, examined the use of ertapenem prophylaxis in patients classified as low risk or high risk for post-TRUS sepsis based on established risk factors (previous TRUS or urosepsis, recent ciprofloxacin use, immunocompromise or overseas travel). In the 15 months prior to the introduction of ertapenem prophylaxis 11 of 333 (3.3%) biopsy patients experienced post-TRUS sepsis. Since then, 6 of 124 (4.8%) patients have developed post-TRUS sepsis: 6 of 62 (9.6%) in the low-risk group and 0 of 62 in the high-risk group (p = 0.03). Samples from three patients grew ciprofloxacin-resistant organisms and one grew a ciprofloxacin-sensitive organism, two had no growth. A cost-effectiveness model indicated a per episode cost of routine ertapenem prophylaxis of $161.53 versus $249.77 per episode when using a rectal-swab targeted protocol.

Comment: Great to see a New Zealand paper at the meeting. The topic of post-TRUS biopsy sepsis has been a hot one in the urological literature over the past 24 months or so. The conclusion of the paper is that “Ertapenem for all patients is likely to be the least morbid and most cost effective strategy”. My concern about this is the clear issue of developing resistance with the wholesale use of one of our last resort antibiotics. In our unit we have had a very robust audit running over the last 5 years. What we have found is quite large variations in incidence of post-TRUS infections month-to-month, which defy quite intense investigation. However, these variations have always averaged out to a consistent annual rate of 3%.

Abstract# 24462

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Long-term safety and efficacy analysis of abiraterone acetate (AA) plus prednisone (P) in study COU-AA-302 for metastatic castration-resistant prostate cancer

Authors: de Souza P et al

Summary: A post-hoc analysis (after a median follow-up of 27.1 months) was conducted on patients from study COU-AA-302 (n = 1088; randomised 1:1 to abiraterone acetate 1000 mg plus oral prednisone 5 mg twice daily vs placebo + prednisone) to consider the safety and tolerability of abiraterone acetate during long-term treatment (≥24 months). The HRs for radiographic progression-free survival (0.52; 95% CI 0.45–0.62; p < 0.0001) and OS (0.79; 95% CI 0.66–0.96; p = 0.0151) were improved in patients receiving abiraterone acetate plus prednisone over those receiving prednisone alone, although OS did not reach a pre-specified efficacy threshold (p = 0.0035).

Survival disparities between Māori and non-Māori men with non-localised prostate cancer in New Zealand

Authors: Obertova Z et al

Summary: Differences in survival rates between New Zealand Māori and non-Māori men aged 40–69 years with non-localised prostate cancer were investigated in this study. Of 20,719 men diagnosed with prostate cancer between 1996 and 2010 and registered on the NZ Cancer Registry, 2078 (10%) were recorded as having non-localised prostate cancer at diagnosis of whom 681 have died. Kaplan-Meier analysis revealed that the probability of surviving three years was significantly lower for Māori compared to non-Māori men, regardless of diagnosis years. After adjusting for age, deprivation and diagnosis years, Māori men were more likely to die of any cause and of prostate cancer compared with non-Māori men; HRs 2.79 (95% CI 2.23–3.48) and 2.95 (95% CI 2.31–3.77), respectively. It was also found that Māori men were more likely have diagnosis of metastatic prostate cancer, which the authors suggest may be in great part due to significantly lower screening rates in Māori compared to non-Māori men in NZ.

Abstract# 24842

Abstract# 24850

Independent commentary by Dr Nick Buchan

Dr Nick Buchan is a urologist at Christchurch Public Hospital and at Urology Associates. He is also managing director of Canterbury Urology Research Trust. He returned to Christchurch from Vancouver in Canada, where he undertook a Fellowship in uro-oncology and robotic surgery at the Prostate Centre based at Vancouver General Hospital and affiliated with the University of British Columbia. He has a particular interest in uro-oncology, especially prostate cancer, and has been extensively trained in open and robotic surgery.

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**Radium–223 (Ra-223) safety and efficacy in prostate cancer with bone metastases: Phase 3 ALSYMPCA study findings stratified by age**

**Authors:** Sartor O et al

**Summary:** This poster presented an age group analyses of OS and safety data from the Phase 3 ALSYMPCA trial of placebo (n = 307) or six radium-223 doses (Ra-223; n = 614) 50 kBq/kg IV injections (administered every 4 weeks) in patients with progressive, symptomatic castration-resistant prostate cancer with ≥2 bone metastases and no known visceral metastases. Median OS was significantly longer in the Ra-223 treated <65 year (16.9 vs 11.4 months; p = 0.002; HR 0.567 [95% CI 0.391-0.832]) and 65–74 year (15.0 vs 12.4 months; p = 0.027; HR 0.738 [0.563, 0.967]) age groups, than in placebo recipients, but not in the 75–84 year (12.2 vs 10.8 months) and ≥85 year (14.0 vs 9.5 months) age groups. Adverse event incidence in the various age groups was similar to that of the overall population and as observed in the overall population, vomiting, diarrhea, neutropenia and thrombocytopenia were seen more frequently with Ra-223 versus placebo across age groups.

**Comment:** Radium 223 is a radiopharmaceutical that in this sub-analysis of the ALSYMPCA trial shows a 3.6 month improvement in OS in this select group of men with symptomatic bone metastases without visceral metastases. Radiopharmaceuticals, for reasons I personally do not understand, have been an underdeveloped therapeutic category in prostate cancer. This is an exciting paper that implies the benefit in OS applies in the older age groups as well as younger men. A group that is an exciting paper that implies the benefit in OS applies in the underdeveloped therapeutic category in prostate cancer. This is an exciting paper that implies the benefit in OS applies in the older age groups as well as younger men. A group that traditionally in NZ practice would be less likely to receive chemotherapy.

**Abstract# 24966**

**Impact of a uro- oncology multi-disciplinary meeting on clinical decision making in prostate cancer**

**Authors:** Rao K et al

**Summary:** This presentation prospectively examined the influence on prostate cancer management decisions of uro-oncology multidisciplinary meetings. Over a 3-month period, 120 discussions on 107 patients were considered including 46 (38.3%) patients with prostate cancer. The multidisciplinary meetings made substantive changes to the original management plan in 32 (26.7%) cases, including those of 12 (26%) prostate cancer patients. Metastatic, but not T-stage disease, was associated with more high impact changes (6 of 13 metastatic prostate cancer patients). In addition to treatment decisions, primary cross discipline referrals occurred in 40 (33.3%) cases (12 of 46 [26%] prostate cancer cases), compared with 66.7% in testicular cancers and 42% in bladder cancers (p < 0.02).

**Comment:** This is an interesting paper that highlights the impact of multidisciplinary meetings meetings in oncology. One of the lingering questions for me is whether the changes in management plans for the patients that were discussed ultimately benefited the patients. A future study could perhaps audit the multidisciplinary team management decisions against “best practice” guidelines. Good multidisciplinary teams that work well are dependent on the chairman of the meeting not allowing strong personalities in the meeting to adversely influence decisions.

**Abstract# 25378**

**Phase II study of neo-adjuvant ‘supercastration’ in men with high risk non-metastatic prostate cancer**

**Authors:** Corcoran N

**Summary:** This ongoing open-label, non-randomised, Phase II study aims to determine if neo-adjuvant ‘supercastration’ with a combination of degarelix 240/80 mg once every month, abiraterone 1000mg once daily, bicalutamide 50mg once daily and prednisolone 5mg once daily for 24 weeks improved the pT0 response rate, in comparison with historical controls, in men with clinically localised high-risk prostate cancer. The two stage trial requires at least one pT0 response in the first nine patients to proceed to a second phase with a final sample size of 12–17 patients. After the first phase, combination treatment appears well tolerated, with the most commonly reported side effects being hot flushes and fatigue. Abiraterone dose was reduced in two patients with asymptomatic liver transaminases elevation.

**Comment:** It will be interesting to see the outcome of larger studies in this area as the combination has theoretical advantages over the use of luteinising-hormone-releasing hormone (LHRH) agonists in the neo-adjuvant setting. Use of LHRH agonists alone in this setting have been shown in well constructed randomised controlled trials to reduce positive margin rates, but not biochemical recurrence. Supercastration should prevent the endogenous production of testosterone within prostate cancer cells, which may be the reason these previous studies have not shown a benefit.

**Abstract# 25654**

**Are transrectal prostate biopsies routinely indicated in patients with incidentally diagnosed prostate cancer following TURP for benign disease**

**Authors:** Norris B et al

**Summary:** This multi-institutional analysis of cancer registries in the UK and Australia was aimed at determining the indication for routine trans-rectal ultrasound-guided biopsy (TRUSbx) of the prostate gland in patients with incidental cancer diagnosis after trans-urethral resection of the prostate for benign prostatic hyperplasia. Of 63 patients identified between 2001 and 2010, 22 underwent a TRUSbx, and rates for Gleason score concordance (32%), upgrading (14%) and downgrading (54%) were observed (Spearman correlation coefficient 0.20). TRUSbx did not give additional Gleason score information in 86% of patients. In those who underwent radical prostatectomy (n = 41), rates were 61%, 22% and 17%, respectively (Spearman correlation coefficient 0.15).

**Comment:** This is a question that has always perplexed me. Why is it dogma that we rebiopsy men with the incidental finding of prostate cancer on TURP? I can understand an argument for it in the setting that you are considering active surveillance; however, if active treatment is planned it would seem unwarranted based on this paper, although the numbers are small.

**Abstract# 25774**

**Transperineal template biopsy of the prostate: a review of the impact at Alfred Health**

**Authors:** Huang S et al

**Summary:** This retrospective review of transperineal biopsy (TPB) evaluated detection/grading rates, treatment outcomes and complications in 110 patients undergoing 111 TPBs at a single institution between 2009 and 2013. TPB led to disease upgrade in 37.5% of active surveillance patients, 35% of previous-negative TRUS patients and 58.8% of patients receiving TPB for other reasons. Among patients with disease-upgrading, 77% underwent curative treatment. Acute urinary retention (6.3%) and of clot retention (2.7%) were observed, but urosepsis did not occur.

**Comment:** This was one of many papers purporting the benefits of transperineal biopsy over the transrectal approach. More worryingly, the authors suggest that it should be standard practice in all patients. The economic impact of a change in practice like this in New Zealand, where the majority of biopsies are performed under local anaesthetic, would be profound. Close analysis of the cost and benefit of this approach would be required before making any such change.

**Abstract# 25778**