Expert Forum

Prostate Cancer Weekend Forum:
Integrated patient management in advanced prostate cancer

Making Education Easy 2017

In this review:

Welcome to this review of the inaugural Prostate Cancer Weekend Forum held in Auckland on 21-22 May 2016.

The meeting was chaired by Dr Peter Fong, Consultant Medical Oncologist at Auckland Hospital, and featured keynote speaker Professor Charles Ryan from the University of California at San Francisco (UCSF). This meeting was solely sponsored by Janssen under the advice of an independent steering committee to determine and coordinate the scientific content.

PATTERNS OF CARE IN mCRPC IN NEW ZEALAND

Dr Peter Fong, Auckland Hospital

Prostate cancer is the most common cancer in New Zealand men. In 2012, 3129 men were newly diagnosed with prostate cancer and 607 died from metastatic or castration-resistant disease – a mortality rate of around 20%.[1]

There is no one model or pattern of care for metastatic castration-resistant prostate cancer (mCRPC) in New Zealand or indeed internationally. The successful registration of several drugs for CRPC and the recent studies of chemo-hormonal therapy in men with castration-naïve prostate cancer (CNPC) have led to considerable uncertainty as to the best treatment choices, sequence of treatment options and appropriate patient selection.

Surgical orchiectomy aside, Pharmac funding is available for goserelin, leuprorelin, bicalutamide, docetaxel, abiraterone acetate and zoledronic acid. Available but unfunded drugs are enzalutamide, cabazitaxel, and denosumab. Of concern in New Zealand are the patients who should but are not receiving timely treatment for advanced disease. This may be due to geographical factors, non-referral back to appropriate specialists interested in treating advanced prostate cancer and perceived or real resource limitations.

Medical oncology and advanced prostate cancer care at ADHB

In New Zealand, there are nine public medical oncology centres and urology services provided through about 20 hospitals. Dr Fong described the medical oncology service in the Auckland region. It currently consists of 23 medical oncologists who subspecialise in various tumour types, with three predominantly involved in genito-urinary cancer. The number of mCRPC cases referred is growing year-on-year, with around 80-100 new cases referred thus far in 2015-16. However, there are also a growing number of CNPC patients referred for treatment; 20-40 in ADHB thus far in 2015-16.

The majority of patients referred to the ADHB medical oncology service have mCRPC, for which docetaxel and abiraterone acetate treatments are available. Clinical trials are important and seen as an integral part of the service. The PROSPER trial is for patients with early non-metastatic CRPC progressing on androgen deprivation therapy (ADT). Patients with metastatic CNPC can participate in the ENZAMET trial looking at the early use of enzalutamide in addition to docetaxel chemotherapy. Trials in latter stage advanced disease are being set up.

THE EVOLUTION OF TREATMENT FOR mCRPC AND NEW THERAPEUTIC DEVELOPMENTS

Professor Charles Ryan, University of California, San Francisco, CA, USA

It is now well known that for lethal prostate cancer to occur, it must occur in the context of two biological and clinical events happening at the same time: castration resistance, demonstrated by a rise in prostate-specific antigen (PSA) and progression of disease despite a low level of testosterone; and metastasis. Both of these biological functions can be discreetly targeted, and the last six years has seen a sudden increase in the availability of treatments that not only prolong survival but also delay disease progression and complications such as skeletal-related events. One of the issues going forward will be developing second-generation agents and determining combinations and sequencing of treatments that are clinically effective and safe as well as financially feasible.

CHAARTED study

The CHAARTED study,[2] coupled with the STAMPEDE trial,[3] has moved docetaxel into the castration-sensitive setting. In the CHAARTED study, men with metastatic hormone-sensitive prostate cancer (mHSPC) who received docetaxel plus ADT had a median overall survival (OS) improvement of 13.6 months versus ADT alone. However, it is important to interpret these results knowing that CHAARTED was initiated in 2005 at a time when abiraterone acetate, enzalutamide and cabazitaxel were not available.

One of the issues that is emerging around the CHAARTED study is whether extent of disease is relevant. In men with high-volume disease, the treatment effect of docetaxel plus ADT was more pronounced, with an OS benefit of 17 months.

Abiraterone acetate

Post-chemotherapy

Abiraterone acetate is a CYP-17 inhibitor which targets androgen production. Results of the COU-AA-301 study in the post-chemotherapy mCRPC setting demonstrated that OS was significantly prolonged in the abiraterone acetate

plus prednisone group compared with the prednisone-only group[4] (15.8 months [95% CI 14.8–17.0] vs 11.2 months [95% CI 10.4–13.1]; hazard ratio [HR] 0.74, 95% CI 0.64–0.86; p<0·0001).

Pre-chemotherapy

Subsequently, the COU-AA-302 study investigated the use of abiraterone acetate in the pre-chemotherapy mCRPC setting.[5] Radiographic progression-free survival (PFS) was significantly prolonged in the abiraterone acetate plus prednisone group compared with the prednisone-only group (16.5 months vs 8.3 months; HR 0.53; 95% CI 0.45-0.62; p<0.001). Final OS analysis showed that OS was significantly prolonged in the abiraterone acetate plus prednisone group compared with the prednisone-only group (34.7 months vs 30.3 months; HR 0.81; 95% CI 0.70-0.93; p=0.0033).[6]

The abiraterone acetate treatment effect was more pronounced when adjusting for the 44% of prednisone patients who received subsequent abiraterone acetate (HR 0.74). Abiraterone acetate doubled the maximal decline in PSA relative to the prednisone control arm (69% vs 29% of patients achieved a greater than 50% decline in PSA, respectively). Notably, the observation that 29% of patients in the prednisone control arm experienced a decline in PSA by ≥50% suggests that prednisone alone represents an active control therapy.

Can we cure prostate cancer?

The development of new therapies has raised the question of whether prostate cancer can be medically cured and whether early aggressive hormonal therapy, even in the localized tumour setting, can eliminate disease.

Enzalutamide

Post-chemotherapy

Enzalutamide is an androgen-receptor-signaling inhibitor which targets androgen receptor (AR) binding more potently than does bicalutamide. Results of the AFFIRM study in the post-chemotherapy mCRPC setting demonstrated that OS was significantly prolonged in the enzalutamide group compared with the placebo group (18.4 months vs 13.6 months; HR 0.63; 95% CI 0.53-0.75; p<0.001).[7]

Pre-chemotherapy

In the PREVAIL study, patients with chemotherapy-naïve mCRPC received either enzalutamide or placebo.[8] Enzalutamide reduced the risk of radiographic progression or death by 68% (HR 0.32, 95% CI 0.28–0.37; p<0.0001) and the risk of death by 23% (HR 0.77, 95% CI 0.67–0.88; p=0.0002). A total of 626 patients (72%) in the enzalutamide group, versus 532 patients (63%) in the placebo group, were alive at the data cut-off date (HR 0.71; 95% CI 0.60-0.84; p<0.001).

Cabazitaxel

About 12 years ago, the TAX 327 study showed that docetaxel improved OS in mCRPC patients versus mitoxantrone (18.2 months vs 16.4 months; p=0.03).[9] Since then, there have been a number of attempts to improve the OS rate by adding drugs to docetaxel, but none have been successful. Cabazitaxel is a docetaxel derivative with antitumour activity in docetaxel-resistant cancers and has been investigated for use in combination with prednisone or prednisolone in patients with CRPC previously treated with docetaxel. One possibility of why it might work after docetaxel failure is that it is not a substrate for the p-glycoprotein multidrug resistant pump, so is therefore less likely than docetaxel to be effluxed out of cancer cells.

In the randomised TROPIC study of cabazitaxel or mitoxantrone with prednisone in patients with mCRPC previously treated with docetaxel, median OS was 15.1 months in the cabazitaxel group versus 12.7 months in the mitoxantrone group (HR 0.70; 95% CI 0.59-0.83; p<0.0001).[10] A head-to head open-label study (FIRSTANA) comparing cabazitaxel and docetaxel in 1168 chemotherapy-naïve mCRPC patients presented at ASCO 2016 found that cabazitaxel did not demonstrate superiority for OS compared to docetaxel.[11]

Overarching principles of CRPC management

- No standards of care exist on how to manage patients without radiographic evidence of metastases.
- Maintain ADT in all patients (LHRH agonists/antagonist or orchiectomy).
- Allowing asymptomatic mCRPC to go untreated until symptoms develop is no longer advised given the efficacy and tolerability of new agents.
- Consider bone targeted therapy in patients at risk for skeletal combinations.
- Consider that progression can be 'mixed' or in a focal site despite systemic control of disease – focal sites of progression can be treated with radiation therapy.
- Molecularly driven treatment selection is being developed and enrollment in clinical trials that test this is ideal.

MONITORING OF PATIENTS ON ABIRATERONE ACETATE - AN INTEGRATED APPROACH

Part 1: An oncology nurse practitioner's perspective

Kirstin Unahi, Southern DHB

In New Zealand, abiraterone acetate has been available for patients with mCRPC since May 2015. Ms Unahi discussed the systems used by Southern DHB to monitor patients receiving abiraterone acetate and other cancer therapies.

The Southern DHB covers all of Otago and Southland. It is the largest geographical area of any of the New Zealand DHBs, covering over 62,000 km, which in itself can present significant barriers to care in terms of distance and accessibility for its large rural population. But perhaps more significantly in the setting of prostate cancer, it has an aging population who prefer to live in rural areas – the at-risk population is moving away from main treatment centres.

The Oncology Haematology Assessment Unit (OHAU)

The Oncology Haematology Assessment Unit (OHAU) at Southern DHB is a nurse-led virtual clinic which was developed a couple of years ago with a number of aims in mind. These included:

- Improving patient safety and care by monitoring symptoms and side effects of cancer treatment in a timely manner.
- Reducing avoidable treatment delays and dose reductions.
- Standardising the advice given to patients using evidenced based assessment tools.
- Promoting appropriate use of services and resources and supporting the reduction of avoidable hospitalizations.
- Providing a single point of contact for patients throughout the region and appropriate triage of all calls.

A 24-hour 0800 number is given to all patients receiving oncology/haematology therapies. Incoming clinical enquiries to this number are telephone triaged, and patients are given advice over the phone and provided with education, follow up and referral to primary or tertiary services, or on site advanced nursing assessments.

Key to the success of OHAU is that nurses are able to proactively monitor high risk patients on treatment. All patients are contacted after their first cycle of chemotherapy and after subsequent cycles if patients are at high risk of toxicity, have complex co-morbidities or unstable symptoms of disease, are elderly or frail, or have psychosocial issues or a mental health diagnosis.

Southern DHB conducted an audit of OHAU and found it is associated with reductions in hospital admissions, length of stay, and presentations to ED. Patients report high satisfaction and that they love having a nurse at the end of the phone.

MOSAIQ: an electronic monitoring programme

MOSAIQ is a comprehensive electronic information management system used within OHAU. It can be used to review, prescribe, dispense, treat, and document patient data in a single database solution. Customisable electronic records can be viewed online from multiple sites, with integration from external diagnostic laboratories and pharmacies. Appointments can be scheduled, and letters, reports and documents created.

Where does abiraterone acetate fit?

A monitoring schedule is required at the start of abiraterone acetate therapy for hepatic toxicity, hypokalaemia, hypertension and fluid retention due to mineralocorticoid excess. Within Southern DHB a joint decision was made to place the primary use of abiraterone acetate after bicalutamide and before taxanes for those patients who are chemotherapy naïve. Care of these patients is centralised within Radiation Oncology at the Dunedin Cancer Centre

with a preference for managing patients at home in the primary care setting by making use of existing effective monitoring systems (OHAU and MOSAIQ).

Patients are seen in clinic by a consultant, prescribed abiraterone acetate, and then electronic approval of the prescription automatically generates quality check lists (QCL) to OHAU and outpatient nursing staff (**Figure 1**). Consultants perform the tasks in red boxes and nurses perform the tasks in yellow boxes. Once a patient has commenced on medication, that patient is entered into the MOSAIQ schedule for telephone follow-up monitoring. MOSAIQ allows analysis of these patients, such as reasons for terminating therapy, and median survival.

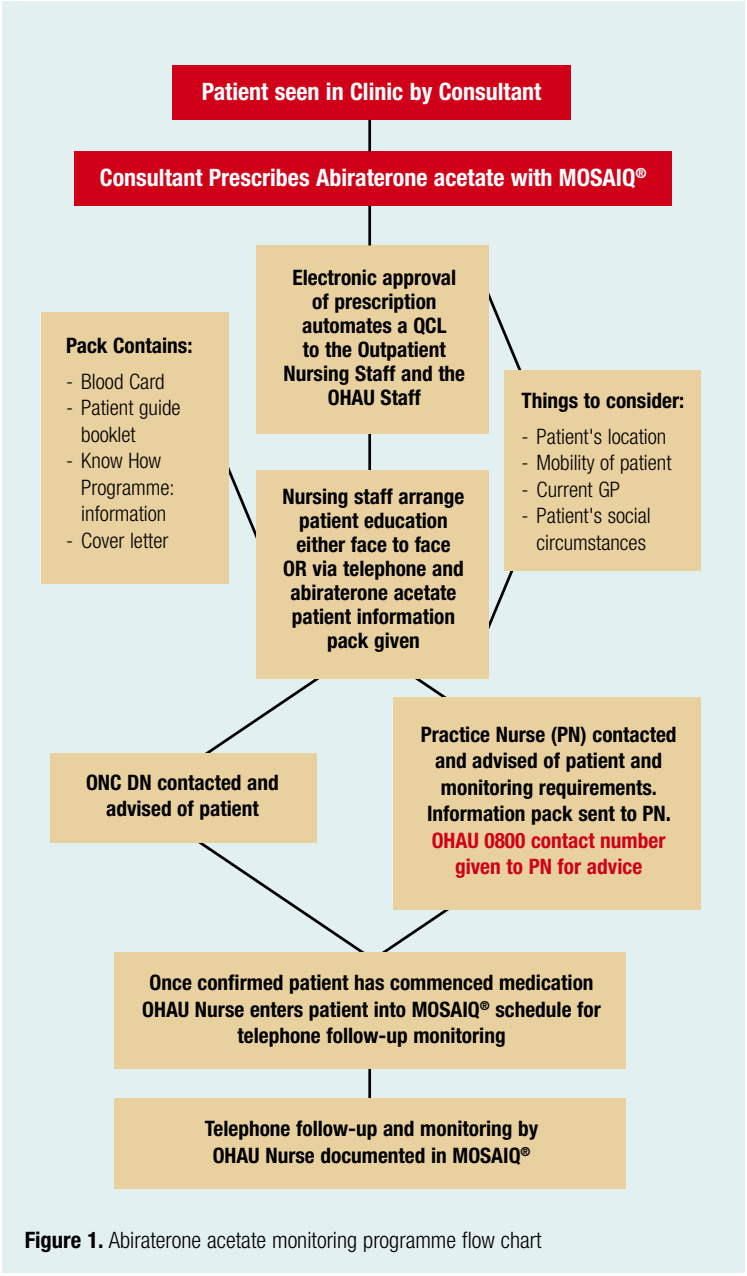

Figure 1. Abiraterone acetate monitoring programme flow chart

Strengths and limitations of the programme

Southern DHB's care package provides cohesive, comprehensive cancer care. Nursing staff are passionate about monitoring side effects of treatment and supporting patients as much as possible; MOSAIQ has made this process all that much easier for nurses. OHAU provides early identification of toxicities and has provided remarkable outcomes in providing supportive care to oncology and haematology patients; patients report that they feel well supported. The monitoring programme is reliant on the team, not an individual, with all patients' notes available electronically with no requirement for hand-over between staff. Limitations include the need for nursing staff to remember to reschedule phone calls into MOSAIQ (only a set number are electronically scheduled), and managing the high volume of patients.

Part 2: A radiation oncologist's perspective

Dr Shaun Costello, Southern DHB

The 2014 Management of Metastatic Prostate Cancer Study explored the national and regional picture of metastatic prostate cancer in New Zealand men. Disturbingly, of 194 patients, 57 received more than four PSA tests over 1 year, but 46 patients (24%) did not receive a single PSA test. Similarly, a high number of patients did not have their testosterone level tested after the initiation of ADT. The study also showed that, compared with international data, a very low proportion of patients were alive at 24 months – really not good enough in 2016.

As discussed by Ms Unahi, the Southern DHB covers a very large rural area which presents significant barriers to care in terms of distance and accessibility. Multiple players are involved in delivering treatment and communication between centres is an issue. Patients also tend to move between multiple services. This led to difficulties in determining when drugs have been given.

The unfavourable picture of mCRPC management in New Zealand along with unique issues within Southern DHB were the background to the development of the monitoring programme.

The next step will be combining the monitoring programmes for leuprorelin and abiraterone acetate (currently, these are two separate programmes). Southern DHB will also attempt to combine urology and oncology services for ADT and look at the feasibility of monitoring patients post radiotherapy or prostatectomy.

KEY POINTS

- Abiraterone acetate therapy can be well managed within a rural population spread over a very large area.
- Minimal co-operation from primary care is involved.
- Minimal physician involvement is required.
- The OHAU virtual clinic is a safe, cost effective and patient-centric model.
- Feedback from patients, staff and primary care is universally positive.

INTERNATIONAL BEST PRACTICE IN MANAGING CRPC PATIENTS

Professor Charles Ryan, University of California, San Francisco, CA, USA

Professor Ryan told delegates that the challenges to best practice in CRPC worldwide are:

- How to treat non-metastatic CRPC.
- How to sequence therapies.
- What to do when therapies no longer work (i.e. resistance).

In patients with non-metastatic CRPC, shorter PSA doubling time (PSADT) (i.e. <6 months) is associated with increased risk of bone metastases or death.[12,13] The preferred therapy (NCCN guidelines) for a patient with non-metastatic CRPC is observation if PSADT is ≥10 months, and clinical trial or secondary hormonal therapy if PSADT is <10 months.

In light of CHAARTED and STAMPEDE data, NCCN guidelines state that patients with mHSPC and high volume M1 disease should be treated with continuous ADT and docetaxel without prednisone for 6 cycles. However, patients with low volume M1 disease have no proven definitive benefit from chemotherapy. This area of high volume versus low volume disease remains in a state of evolution.

Metastatic castration-resistant prostate cancer

The issue with mCRPC guidelines is that proposed treatment algorithms reflect a lack of precision. NCCN guidelines for example state that in such patients, castrate serum levels of testosterone should be maintained and bones should be protected with appropriate drugs. However, beyond that there is really no significant specific clinical guidance. There are many treatment options listed in guidelines, but what should we give and when?

The use of the AR-targeted therapies abiraterone acetate and enzalutamide prior to chemotherapy in mCRPC has been confirmed in two large randomised trials.[5,8] However, questions remain whether patients with or without visceral metastasis benefit, because, the COU-AA-302[5] study did not allow patients with visceral metastasis, whereas the post-chemotherapy study did. Limited experience with visceral metastasis is available from PREVAIL as only 12% of the patients in this study had visceral disease.[8]

Abiraterone acetate and enzalutamide: how should therapy be sequenced?

While abiraterone acetate and enzalutamide are two therapeutic options active in the treatment of advanced or metastatic prostate cancer, the issue of progression remains. How should these two drugs be sequenced for optimal patient benefit? Some patients respond to one drug and not the other and vice versa. This could be for a variety of reasons, including extent of disease. Median survival in abiraterone acetate-treated patients with visceral metastases is 12.9 months but 17.1 months in patients without.[14] Abiraterone acetate therapy after enzalutamide is associated with a very modest PSA response, while enzalutamide after abiraterone acetate is associated with slightly better PSA responses. Hypertension (24%) and fatigue (32%) have been described with abiraterone acetate therapy, however only about 5% of hypertension was grade 3–4.[6] Adverse events are more CNS-driven with enzalutamide therapy; hypertension still occurred (13%) but was probably arterial hypertension rather than fluid overload hypertension.[8] Falls (11.6%) and fatigue (35%) were significant.

Consider abiraterone acetate for patients with:

- Mild baseline pain – steroids may help
- Significant baseline fatigue
- Polypharmacy
- Falls, gait or neurological issues

Consider enzalutamide for patients with:

- Diabetes
- Remote living
- Renal impairment
- Baseline oedema or CHF

When to start secondary AR targeting

In the US, the vast majority of abiraterone acetate and enzalutamide use is in the pre-chemotherapy setting. In Professor Ryan's practice he typically prescribes these drugs: in asymptomatic patients; after ADT (bicalutamide); only in patients with metastases; and for patients with PSA 15-50 ng/mL. Symptomatic patients or patients with liver metastases typically get chemotherapy not abiraterone acetate or enzalutamide.

At the 2015 inaugural Advanced Prostate Cancer Consensus Conference the questions below were posed to an international panel of experts.[15] Their answers are shown in brackets.

1. Do you recommend abiraterone acetate/enzalutamide as first-line therapy for otherwise healthy, asymptomatic or minimally symptomatic mCRPC patients in addition to ADT (i.e. prior to docetaxel)? Yes (88%).
2. Is it appropriate to extrapolate the results of PREVAIL (enzalutamide vs placebo in chemotherapy naïve CRPC patients) and COU-AA-302 (abiraterone acetate + prednisone vs placebo + prednisone in chemotherapy-naïve CRPC patients to certain symptomatic chemotherapy-naïve CRPC patients? Yes (77%).
3. Is it appropriate to extrapolate the results of COU-AA-301 study to certain chemotherapy-naïve patients with visceral metastases? Yes (88%). This may be based on the fact that abiraterone in the post-chemotherapy setting had activity in patients with visceral metastases.
4. What is your preferred first-line choice for survival-prolonging endocrine agents for otherwise healthy mCRPC patients if all options are available? NON CONSENSUS (39% abiraterone acetate, 27% enzalutamide, 33% either one of the two).

KEY POINTS

- AR-directed therapy is the standard of care for mCRPC in much of the world.
- Various factors may drive first-line choice of abiraterone acetate or enzalutamide for mCRPC.
- Guidelines continue to support chemotherapy both early and late.
- Patients with rising PSA may still benefit from ongoing therapy.
- Sequencing strategies requires further research.

NZ MINISTRY OF HEALTH PROSTATE CANCER WORKING GROUP UPDATE

Professor Ross Lawrenson, University of Waikato

The four year Prostate Cancer Awareness and Quality Improvement Programme (AQIP) was launched in 2013 to improve outcomes for New Zealand men with prostate cancer. This work is being supported by the Prostate Cancer Working Group. The Working Group is made up of experts from across the cancer care pathway and includes specialist subgroups covering primary care, equity, pathology, specialist care and advanced cancer.

Primary care subgroup

In 2015, the primary care subgroup developed and published prostate cancer management and referral guidelines for GPs.[16] The group asked the Ministry of Health to identify what could be done towards achieving a nationally consistent pathway for DHBs and PHOs across primary and secondary care. The Ministry of Health has requested DHBs include in their 2016/17 annual plans actions and milestones to "work with PHOs to identify actions to implement the prostate cancer management and referral guidance in 2016/17".

Along with BPAC, the group is developing a mobile optimised web-based tool to assist men and GPs in shared decision making about early detection and treatment of prostate cancer. During this process, BPAC interviewed up to 1000 patients. They found that men have very low knowledge of prostate cancer in general, and do not have active participation in their decision making. Furthermore, Maori often get health messages that are "death messages" about cancer. This frames expectations and puts up a barrier to engaging with Maori.

Pathology subgroup

The pathology subgroup has been evaluating the new prostate cancer grading system to replace the Gleason scoring system.[17] Members of the International group will be visiting Auckland, Hamilton, Wellington, Christchurch and Dunedin over the space of a week in early September to discuss the new grading system.

Specialist subgroup

The specialist subgroup is in the process of developing a national register for men with localised prostate cancer, and has developed guidance on using active surveillance to manage men with low-risk prostate cancer.[18] This Guideline has been distributed to DHBs. The Ministry of Health Cancer Team in 2015/16 quarter 3 Regional Service Plan regional response requested an update on progress regarding the implementation of the Guidance on using active surveillance to manage men with low-risk prostate cancer. The next step will be to bring together a multidisciplinary group including urology, radiation oncology, medical oncology, palliative care and specialist nurses to look at guidance on the management of advanced prostate cancer.

Guidance on using active surveillance to manage men with low-risk prostate cancer[18]

Entry criteria for active surveillance

Men who meet **all** of the following criteria should be considered for active surveillance:

- Life expectancy ≥10 years
- Gleason score 3 + 3 = 6 (ISUP grade 1)
- Localised, low-volume prostate cancer
- PSA <10 µg/L
- Tumour stage is T1 or low-volume T2 (T2a)

Exit criteria for active surveillance

If a man meets **any** of the following criteria for exiting active surveillance, his treatment should be changed to curative treatment or watchful waiting:

- Life expectancy <10 years
- Repeat biopsy shows Gleason score >3 + 3 = 6 (ISUP grades 2-5)
- Higher-volume prostate cancer
- PSA ≥10 µg/L
- Tumour stage is >T1 or low-volume T2 (T2a)

CURRENT AND FUTURE PATHWAYS TO PERSONALIZED MEDICINE IN mCRPC

Professor Charles Ryan, University of California, San Francisco, CA, USA

Clinicians are now getting a clearer idea as to what is behind the lack of decrease in PSA to abiraterone acetate or enzalutamide therapy. AR splice variants (AR-Vs) are variations in how RNA is spliced after it comes off DNA. AR-V7 is the most well-known splice variant, in which the androgen receptor is capable of binding the DNA regions of various genes without the necessity for testosterone. Therefore, presence of AR-V7 could be a biomarker for poor outcomes but needs to be externally validated. A study of 62 CRPC patients showed that AR-V7 was present in only 11.6% of tumours pre-abiraterone acetate or enzalutamide therapy, whereas AR-V7 was present in 25% of tumours after enzalutamide therapy, 51.2% after abiraterone acetate therapy and 66.7% after both therapies.[19] This is known as treatment-mediated selection pressure, leading to a more resistant tumour.

In the COU-AA-301 study,[4] low androgens worsened survival – this raises the question of whether tumours become capable of using other 'fuels' when androgen is blocked. This is an area that needs to continue to be explored. If androgen levels are prognostic, this would be important for refining clinical trial development.

Professor Ryan's group is now studying the genomic differences between abiraterone acetate-susceptible versus resistant tumours. The most important observation so far has been a histological phenotypic change in abiraterone acetate or enzalutamide resistant tumours. Of 124 biopsies, 35% were pure adenocarcinomas, 13% were pure small-cell neuroendocrine carcinomas, 26% were a mixed phenotype and 26% were a new, never-before described histological type called intermediate atypical carcinoma (IAC). Unexpectedly, just as many small-cell neuroendocrine carcinomas occurred in lymph nodes as liver, and just as many liver metastases were adenocarcinoma as small-cell neuroendocrine carcinomas. While advances have been made, biological personalization in mCRPC is not yet at the same level as in breast cancer or NSCLC.

There has been much discussion around dual DNA repair targeting in CRPC. Germline BRCA 1,2 are rare in prostate cancer, present in only 0.33% to 5% of tumours. However, homologous DNA repair defects (HR) are common; germline and somatic inactivating mutations in HR DNA repair genes collectively occur in up to 20% to 25% of prostate cancers. Targeting DNA repair with PARP inhibitors has shown some success in a phase II clinical trial in mCRPC patients.[20]

Going forward, researchers need to think strategically, creatively and efficiently as clinical trials are designed. Much work is needed on biomarkers, standardizing tissue assays and clinical trial endpoints. Non-invasive methods of evaluation such as CTCs and cfDNA need to be validated and standardized. Clinical events, such as primary resistance to AR-V7, need to be linked to actionable findings. Finally, biopsy techniques need to be standardized, with biopsies taken at initiation and at resistance.

KEY POINTS

- Biological personalization in mCRPC is not at the same level as in NSCLC (for example).
- Despite that, heterogeneous treatments can now be applied to this heterogeneous disease.
- Biopsies / CTCs will become standard to evaluate pathways.
- Proactive and risk adapted treatment is personalized medicine for the time being.
- Biological studies will be integrated into this approach.

PSMA–PET IN PROSTATE CANCER MANAGEMENT

Dr Peppe Sasso, Auckland Hospital

PSMA is a type II membrane protein with 100 to 1000-fold overexpression on the surface of prostate cancer cells. Expression levels increase according to the tumour stage, grade and castration resistance. It therefore has potential for imaging, prognosis and therapeutics.

PSMA–PET imaging can add molecular information to multiparametric-MRI and, therefore, delineate suspicious lesions for targeted biopsies, especially in patients whose biopsy samples are tumour-negative. Furthermore, PSMA–PET imaging shows increased specificity and sensitivity compared with current standard imaging (CT, MRI and bone scintigraphy) in patients with primary intermediate-risk or high-risk prostate cancer.

PSMA–PET imaging improves detection of metastatic lesions even at low serum PSA values in biochemically recurrent prostate cancer; detection rates are around 58% at PSA 0.2<0.5 ng/mL and up to 97% at PSA ≥2 ng/mL.[22]

Worldwide, PSMA–PET is increasingly being used to target stereotactic ablative radiation therapy (SABR) to sites of metastatic disease. SABR shows control rates of metastases ranging from 88% to 100% at 6 months to 3 years, and PFS rates of more than 50% in the first 12 months.[21]

Enhanced detection of prostate cancer lesions with PSMA–PET might enable improved patient-tailored therapy planning and, therefore, lead to improved therapy outcomes.

PALLIATIVE CARE IN PROSTATE CANCER

Dr Shamsul Shah, Auckland Hospital

In a traditional disease care model, patients are treated to cure, then referred to palliative care when treatment fails. However, palliative care is applicable early, with therapies to prolong life. Therefore, it is important to move towards a more integrated care model where palliative care begins early with increasing input over the last year of life, enabling the opportunity for advanced care planning (**Figure 2**). In this way, patients can be asked the most difficult questions at an optimal time – i.e. not when they are in a crisis by admission to hospital.

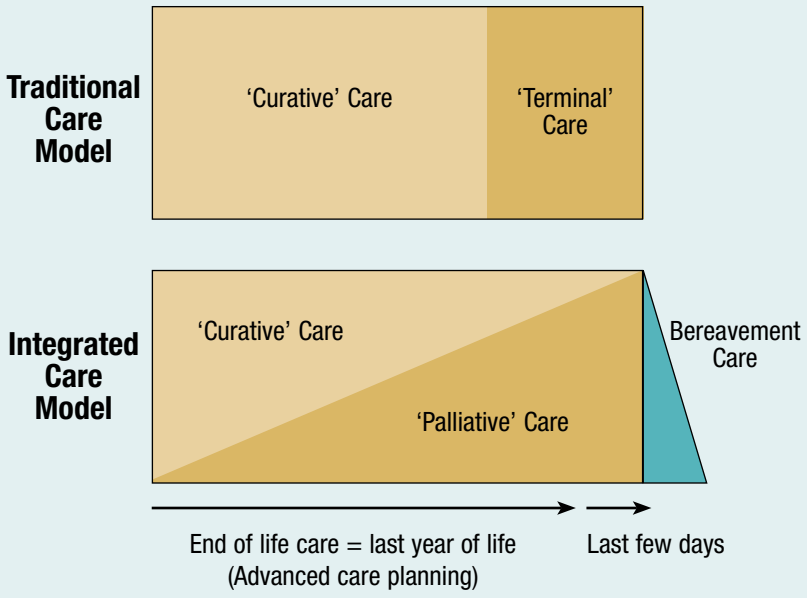

Figure 2. Traditional versus integrated care model

According to Atul Gawande, palliative care is dependent on need, not prognosis. It is not about dying and is all about 'giving people their best possible day, however they might define it under the circumstances.'[23] Early palliative care can have a survival benefit[24] and, while chemotherapy can improve symptoms and QOL, this may not always be the case during the last six months of life.[25]

Common prostate cancer symptoms

A review of prostate cancer and QOL[26] found pain in 70% to 90% of patients and bone disease in 90%. Pain is typically neuropathic and incident in nature. Other symptoms include fatigue, anxiety and depression, anorexia and weight loss, spinal cord compression (1-12%), urinary dysfunction, sexual dysfunction, lymphoedema and delirium.

Sexual dysfunction

Sexual dysfunction is described as being unable to enjoy intimate relations for oneself or partner; however, although patients may lose capacity for sex, it is often not out of mind. Only half of patients potent at diagnosis will have an acceptable level of potency after treatment. Erectile dysfunction is estimated to occur in 60% to 93% of patients following radical prostatectomy and in 67% to 85% of patients following radiotherapy and can be perceived as more distressing than urinary incontinence.

Uncomfortable questions regarding sexual function are often the important ones to ask. Asking men questions about their feelings with regards to their sexual lives and relationships may be beneficial in making informed decisions. In a study of over 27,000 males and females, more than half had at least one sexual concern but only 19% sought medical care. The majority of patients would prefer to have the opportunity to discuss their sexual concerns with a health professional.

Starting the conversation

According to Gawande, useful questions to ask patients to help with decision making include:[23]

- What is your understanding of your condition?
- What are your goals if your health worsens?
- What are your fears?
- What are the trade-offs you are willing to make and not willing to make?

KEY POINTS

- Palliative care is applicable early, with therapies to prolong life.
- A referral to palliative care is based on need and not prognosis. A recent study suggests that early referral to palliative care might have a survival benefit.
- Uncomfortable questions regarding sexual function are often the important ones to ask. Asking men questions about their feelings with regards to their sexual lives and relationships may be beneficial in making informed decisions.
- Starting the conversation can help with decision making including a patient's understanding of their condition, what their goals are if their health worsens, their fears and the trade-offs they are willing to make in having treatments.

STRUCTURE OF MULTIDISCIPLINARY TEAMS IN ONCOLOGY

Dr Mark Sidhom, Liverpool Hospital, Sydney

In advanced prostate cancer, it is important that a multidisciplinary team (MDT) approach is involved in patients' care, including urologists, radiation oncologists, medical oncologists, nurse specialists and palliative care specialists. The benefits of MDTs include increased adherence to guideline-based treatment, reduced time from diagnosis to treatment, improved outcomes, and greater enrolment into clinical trials.

Multidisciplinary care has become incorporated into national and international clinical practice guidelines as a model for best practice in cancer care. MDTs are a formal consultation process that gives rise to a duty of care between the MDT doctors and the patient. Each doctor is responsible and potentially liable for all decisions of the MDT within their area of expertise. However, many doctors do not believe they are responsible for the decisions made in MDTs and to some extent they are not conducted in a way which reflects the responsibility of the participating doctors. In a survey conducted in Australia by Dr Sidhom, 33% of doctors thought that the MDT discussion environment is suboptimal.[27] Even though 85% of doctors have disagreed with the final MDT decision in an important way at some time, 71% did not formally dissent on those occasions.

So, how should MDTs be best structured and conducted? In 2007, a workshop of clinical, legal and ethical experts was held by the Australian National Breast Cancer Centre to develop consensus advice in this area, with the aim of achieving best outcomes for patients while also providing appropriate guidance for health professionals and health services.[28] The consensus recommendations generated at the workshop emphasise the importance of good communication with patients and between team members, improving documentation and ensuring transparency in the processes that support multidisciplinary care.

KEY POINTS

- MDT discussion is likely standard of care in most tumour subsites.
- Adequately resource the MDT to ensure comprehensive consideration of issues.
- Promote an open discussion environment.
- Document discussion, decision and dissent.
- When there is disagreement, all opinions should be discussed with the patient.
- Be aware of patient privacy and consent issues.

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