The New Wave of Immunotherapy Cancer Medicines – The Untapped Potential for Australians

October 2017
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## Acknowledgements

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## Acknowledgements

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## Glossary

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<td>Chimeric antigen receptor</td>
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<td>Epidermal growth factor receptor</td>
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<td>European Medicines Agency</td>
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<td>General practitioner</td>
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<td>Merck Sharp &amp; Dohme (Australia) Pty Ltd</td>
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Immunotherapies represent transformative advances in cancer medicines. How will Australia respond?

The advent of immunotherapies signals the onset of a new paradigm in cancer treatment. With innovations and new applications revealing themselves at unprecedented speed, it is harder than ever for health systems, clinicians, patients and the public to keep pace.

Deloitte Access Economics has developed this point-in-time review for the community to describe the shift to a new wave of cancer medicines and the potential they are showing in the fight against cancer.
Executive summary
The New Wave of Immunotherapy Cancer Medicines

Cancer is a huge problem in Australia
As the leading cause of disease burden for patients, families and the health system, cancer is a significant public health issue in Australia. An estimated 134,174 new cancer cases will be diagnosed in 2017, while 47,753 people are estimated to die due to cancer in the same year.1

Immunotherapies can help significantly in the fight against cancer
Checkpoint inhibitor therapy has the potential to generate an immune response, and hence benefits, for some but not all patients.

Establishing the characteristics and size of the pool of patients who could potentially benefit is an emerging field of research, and to-date there has been no systematic approach to capturing this information. However, a collation of the available evidence from a variety of manuscripts and conference abstracts indicates that up to 7,500 Australians with cancer may benefit from checkpoint inhibitor immunotherapy, where “benefit” is defined as a greater than 30% reduction in tumour size.2,3

More needs to be done to get immunotherapies to the patients who need them
Currently in Australia, checkpoint inhibitor immunotherapies are TGA approved for five cancer types.4 This falls short of the 11 cancer types approved by the FDA in the USA and the six approved by the EMA in Europe.5,6

However, of these five cancer types approved by the TGA, only three are listed on the PBS.7 Since being listed in 2015/16, as of September 2017 a total of 28,080 prescriptions for these immunotherapies have been funded under the PBS.8 With fewer than 1,500 patients currently receiving immunotherapy, it does appear that not as many people are receiving immunotherapy compared to those who might benefit. While needing to set realistic expectations on those who might be helped, it is important to identify these people and ensure they can access immunotherapy early in their disease journey.

Purpose of this report
This review explores the rise of immunotherapies in cancer treatment and the huge potential these medicines are showing in the fight against cancer.

The research provides an account of the patient experience within this new treatment environment, including specific barriers to awareness about and access to the new therapies.

The overarching objective is to catalyse a public discussion of what immunotherapies mean to Australia, and how we now respond to the rising wave of immunotherapies visible on the cancer treatment landscape.

Methodology
In total, 24 stakeholders were interviewed in the development of this research, including patients, government agencies, clinicians, academics, international researchers and health consumer organisations – also known as patient groups or patient advocacy groups.

Interviews were conducted in a semi-structured format. Interviewees were provided a briefing note outlining the intent of the consultation.

Depending on the stakeholder, questions ranged from asking the interviewee to share their experience with cancer immunotherapies, or to discuss their perspectives on awareness and access to these therapies.

The findings are a reflection of the views and stories they provided – supplemented by desktop research regarding the evidence base. Interviews and report development took place independently of the project sponsor, MSD. Stakeholders – including patients – have not been limited to those with experience of MSD products.

Findings – a focus on the future
This report has largely focused on how Australia prepares for a future of cancer care that is more prominently defined by immunotherapies, and improving access beyond the fewer than 2% of the 411,000 Australian cancer patients who are currently accessing immunotherapy treatments.

Awareness of the coming wave
Cancer is increasingly becoming a chronic illness characterised by survivorship. The flow on effects of this shift cannot be ignored. Patients and their families require tailored support, counselling and return to work programs to address their changing needs.

The healthcare system and its processes needs to adapt accordingly to ensure Australia does not lose its place as a leader in cancer care.
Executive summary
The New Wave of Immunotherapy Cancer Medicines

Importantly, silos need to be avoided and, instead, partnerships and democratisation of cancer treatments adopted.

Reputable and evidence-based information must be available to improve the awareness of patients, clinicians and the general public of these new medicines, clinical trials, and special access schemes. There also needs to be a greater level of awareness and understanding around the use of biomarkers to aid in treatment decisions where this is appropriate. It is essential that this awareness is built on a realistic understanding of the promise of these new medicines.

Availability via a tumour agnostic approach
Cancer classification is changing to reflect the molecular characteristics of the cancer as opposed to its organ of origin.

Regulatory and reimbursement processes should change to ensure patients in need can access the biomarker tests and immunotherapies they are likely to benefit from, regardless of where their cancer originated. Clinical trial design could also be adjusted to better reflect the changing nature of the understanding of cancer, and the fast-track processes from TGA reforms implemented in order to expedite channels to treatment for more eligible patients.

Affordability by incorporating comprehensive, real world evidence in the review process
This new wave of cancer medicines is improving the lives of patients, their families and Australian society more broadly.

Investing in the collection of real world evidence of patient outcomes and corresponding indirect outcomes is essential in ensuring the true value of these medicines is captured.

Concurrent funding reforms are also required. A further review of innovative approaches to funding mechanisms is needed.

To improve awareness requires:
- changing the language to one of survivorship and immunotherapy as a potentially transformative alternative for many patients, where appropriate;
- communicating the role that standard treatments – like chemotherapy – will play in cancer treatment for patients now and into the future;
- ensuring patients have access to reputable and evidence-based information, setting out what immunotherapies are available in Australia for whom, and how to access them, as they are emerging through the pipeline; and
- removing sectoral silos and develop partnerships between research, industry and academia, with patients in the middle, to help ensure patients and clinicians can navigate information channels effectively providing further support to survivors who face financial constraints, such as counselling services and return to work programs.

To improve availability requires:
- systemic change along the lines of what has recently been demonstrated by the FDA, adopting a tumour agnostic approach;
- increased investment and coordination in availability of biomarker and screening tests, to better target therapies towards mutations that are likely to respond;
- faster implementation of the new mechanisms available since the TGA Review; and
- greater awareness among oncologists of the TGA’s provisions for special access.

To improve affordability requires:
- capacity constraints in PBAC processes need to be overcome to ensure that listing of new medicines is not delayed as increasingly more fill the pipeline, since the speed of listing is critically important, and because Medicine Australia’s benchmarking has identified that cancer is already the slowest therapeutic area to be reimbursed;
- reimbursement decisions in PBAC need to link with TGA tumour agnostic assessments across a range of therapeutic outcomes, with serious consideration of new models for funding immunotherapies;
- recognising the substantial cost of innovative biological molecules, affordability considerations should include life-saving and compassionate access to trials; and
- the entirety of benefits from newer medicines need to be valued including not just health system, longevity and quality of life impacts, but also productivity and other impacts on patients, carers and society. Data should be captured in trials.

Data should be captured in trials.
I don’t want things to change just for me. My cancer is a genetic cancer and I have other family members including two adult children to think about.

Therese, patient
Cancer in Australia
Cancer in Australia
A point in time review

Cancer is a huge problem in Australia – every four minutes someone is diagnosed, every 11 minutes someone dies.

Almost all Australians will be touched by cancer at some stage – through their own experience or that of close family or friends.

According to the AIHW’s Cancer in Australia 2017 report, 410,530 Australians were living with cancer in 2012. This number is set to increase to 654,124 by 2022.

An estimated 134,174 new cancer cases will be diagnosed in 2017 – that’s one new diagnosis every four minutes. One in three Australian men will be diagnosed with cancer before the age of 75 years. The risk for Australian women is one in four.

By the age of 85, the risk increases to one in two people – male or female – being diagnosed with cancer.

Cancer remains among the leading causes of death in Australia with 47,753 people estimated to die from cancer in 2017 – equating to a death every 11 minutes. In 2014, cancer was responsible for three out of ten deaths.

With over $4.5 billion in direct healthcare costs, cancer represents a significant economic burden. However, this does not include indirect costs, such as lost productivity, or intangible costs from loss of life and health for individuals with cancer and their carers.

Improvements in treatments have increased survival from one in two in the 1980s to two in three today, but side effects can be severe.

Through the latter part of the 20th century, surgery, chemotherapy and radiotherapy formed the staples of cancer therapy. Despite significant improvements in these standard treatments, their debilitating side effect profiles meant the pursuit for new cancer treatments has continued.

The Australian Government has progressively invested in cancer treatment through access to healthcare and contributions to research. Indeed, the five year survival rate from all cancers combined in Australia has improved from 48% in 1984–1988 to 68% in 2009–2013. Unfortunately, such improvements have not been consistent across all cancers. For example, the five year survival rate for an Australian with lung cancer is still less than 14%.

Immunotherapies can offer greater survival prospects with fewer side effects than chemotherapy.

The past decade has seen accelerating scientific advances that have led to the development of a range of increasingly tailored therapies, that can target cancers at a molecular level. This is changing the way doctors look at cancer and heralding a new paradigm of cancer medicines.

Among the new therapies, immunotherapies have a key role by improving the ability of the body’s immune response mechanisms to stop the growth and spread of cancer.

Evidence shows these new cancer medicines are driving improved patient outcomes including better tolerance, reduced treatment burden and improved survival for many people.

Immunotherapy has the potential to change the disease path of cancer from one which is terminal to one characterised by survival, in addition to better quality of life due to the different spectrum (lower toxicity) of side effects.

How will we respond?

How do we value the benefits of immunotherapies from different perspectives – patient experience and clinical outcomes? How will the public, patients and clinicians access information about cutting edge technologies such that access is equitable and expectations are aligned? Do we need to rethink how we conceptualise cancers – that is, at a molecular level rather than the tissue or organ of origin? If so, what impact does this have on reimbursement considerations?

The advent of immunotherapy signals the onset of a new paradigm in cancer treatment that is emerging at unprecedented speed.

The volume and potential impact of the oncoming wave of new treatments is unparalleled.
Cancer in Australia

Historical and emerging therapies

Continual evolution across all cancer therapies is creating the potential for innovative therapy combinations from the old paradigm and the new. In truth, it is harder than ever for health systems, clinicians, patients and the public to keep pace.

We are only at the beginning of this new paradigm and it is ripe with possibilities.

Figure 1: Historical and emerging therapies

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The new wave of cancer medicines
Soon after starting immunotherapy, I was able to return to work and live an almost normal life again. My kids got their mother back. My youngest child is starting primary school next year and I have no doubt that if it wasn’t for immunotherapy, I wouldn’t be there for his first day of prep.

Melissa, patient
The new wave of cancer medicines
Immunotherapies – how they work and help in the fight against cancer

“There wasn’t this level of hope before” – Sue Hegarty, Ovarian Cancer Australia

The advent of immunotherapies in cancer treatment represents a paradigm shift in the cancer therapy landscape.

What are immunotherapies?
Immunotherapies are biologic medicines that work to improve the ability of the body’s immune system to fight cancerous cells. Immunotherapies work differently from chemotherapy and other standard treatments to enhance patient quality of life due to lower toxicity.

Immunotherapies differ from chemotherapy and other standard treatments by using molecular medicine to target the very basis of what makes a cell cancerous, stimulating the body’s immune system in a tailored manner. However, some immunotherapies are more tailored than others.

This has corresponding implications for the quality of life experienced by patients undergoing immunotherapy as a result of the reduced toxicity of side effects.

“Immunotherapy treatment for metastatic melanoma have offered real hope for survival, when 5 years ago there was very little” – Fiona Bennett, Melanoma Patients Australia

How do immunotherapies work?
There are many different types of immunotherapies, each with a different mechanism of action. Some immunotherapies may include a combination of actions. These may include:

- tailoring the immune system’s detection of cancerous cells;
- removing barriers which inhibit an immune response;
- signalling an enhanced immune response;
- blocking specific cell processes;
- providing medicines to promote cell death; and
- delivering tailored immune cells to supplement an immune response.3,17,18

Just as immunotherapies differ in their mechanism of action, cancer cells vary in how they operate within the body.

This has implications for the effectiveness of immunotherapies in treating different types of cancers.

In some cancers, a biomarker test may be appropriate to aid the treatment decision.

What is a biomarker?
A biomarker – or biological marker – can be thought of as an element in our body that can be measured to determine whether a certain bodily process has – or is likely to – occur.

For instance, if a doctor wanted to prescribe their patient a medicine – but it is known that medicine is only effective in patients with a certain biomarker – they may test to see if this biomarker is present.19

“Having equitable and cost effective access to immunotherapy treatments has changed the future for more than half of those diagnosed with metastatic melanoma” – Fiona Bennett, Melanoma Patients Australia
The new wave of cancer medicines

Immunotherapies – potential benefits to be realised

"There aren’t as many winners [yet], but the winners get bigger prizes" – A/Prof Matthew Peters, Concord Hospital

Immunotherapies can improve cancer survival

Checkpoint inhibitor immunotherapy has the potential to generate an immune response, and hence benefits, for some but not all patients. Establishing the characteristics and size of the pool of patients who could potentially benefit is an emerging field of research, and to-date there has been no systematic approach to capturing this information.

However, a collation of the available evidence from a variety of manuscripts and conference abstracts indicates that up to 7,500* Australians with cancer could benefit from checkpoint inhibitor immunotherapy, where “benefit” is defined as a greater than 30% reduction in tumour size. This is shown in Figure 2, which charts the proportion of people, by cancer type, who could potentially benefit from checkpoint inhibitor immunotherapy.

Other types will also extend life and reduce cancer mortality, although it is still too early to quantify the exact magnitude of the combined benefits.

Clinical trials are currently underway for immunotherapies across more than 30 different cancer types, but immunotherapies are only available for three cancer types through the PBS for patients with advanced melanoma, lung and kidney cancer.

However, currently immunotherapy is only available once first line treatments are determined to be ineffective in lung cancer.

This means lung cancer patients must go through standard treatments before they are eligible for PBS reimbursement for immunotherapies, and can die before being able to access them. This process could be improved by better ways of identifying those likely to be refractive to standard treatment, where it may cost less and deliver better outcomes if immunotherapy were available as a first line option.

To some patients, immunotherapies result in no evidence of disease. However, as their tailored mechanism of actions would suggest, these medicines are not a one-size fits all approach. As a result, existing treatments will continue playing a role in cancer treatment, but should no longer be seen as “standard”.

Figure 2: An indicative view of the potential of checkpoint inhibitor immunotherapy in Australia in 2017

Immunotherapies can improve cancer survival.

*This figure was calculated using AIHW cancer mortality forecasts and the percentage of people experiencing a greater than 30% reduction in tumour size as estimated using a collation of the available evidence from a variety of manuscripts and conference abstracts.
Molecular medicine is changing the drug development framework completely.

Prof David Thomas, The Kinghorn Cancer Centre
The new wave of cancer medicines

On the horizon

“\textit{It won’t be long before we’re talking about immunotherapy before chemotherapy... chemotherapy won’t be gone totally but it might take a secondary role}” – Dr Donna Milne, Peter MacCallum Cancer Centre

The wave has only just begun

Patients, clinicians and academics have suggested it may not be long before immunotherapies are used as first line cancer treatments over and above standard therapies.

After all, matching medicines with those who are most likely to benefit is in everyone’s best interest. The government doesn’t want to fund inefficient or ineffective medicines. Pharmaceutical companies want to ensure the integrity of the data collected about their medicines. Clinicians do not want to prescribe medicines that are ineffective, and most importantly, patients do not want to waste valuable time, money and their own lives on medicines which aren’t suited to them or their cancer.

As this new wave of cancer medicines arrives, parallel developments in cancer classification and management are required to ensure they can be accessed by the patients who need them.

Cancer: A molecular disease

The genetic mechanisms underlying cancers are increasingly being discovered and, as a result, their classification is shifting.

At present, cancerous cells are defined by their histology – how they look under the microscope – and their organ of origin. This method of classification is becoming increasingly outdated as researchers discover certain cancers – previously thought to be unrelated – that have common biomarkers or genetic motifs and respond to medicines in similar ways.

Clinicians have said the implications of this shift are already becoming apparent through the breaking down of large traditional cancer groups and the grouping together of smaller groups on the basis of their biomarkers.

The ripple effects of such a change will be felt through multiple domains including clinicians’ ability to screen for and detect cancers at an earlier stage.

To support the continued development of this new wave of cancer medicines, clinicians, academics and patient groups all spoke of the need to ensure the value of these new cancer medicines are captured appropriately and in a manner which keeps pace with shifts in cancer classification. Some suggested that a re-think of the way clinical trials are designed may be required.
Scan results confirmed what we sensed - the tumours had cleared. *The oncologist termed this an “exceptional response”*. We will continue with the immunotherapy treatment. It is truly remarkable. *It is the best outcome I could have wished for*. The body has learnt to successfully fight the cancer.

Ross, patient
The human experience

Left to right: Wendy, Peter, Ross, Mary, Kathy, Igor, Steven, Melissa
It felt like it was all over. I had it all through my chest, all over my body. And then I started on immunotherapies. *Yesterday was my one year anniversary of treatment you know. The reductions – they are remarkable. You can't call it anything else – it's just remarkable.*

Ross, patient
The human experience
How is immunotherapy affecting patient journeys?

“When you give an immunotherapy it’s not certain to work but if it does work it may very well work for a very long time” – A/Prof Matthew Peters, Concord Hospital

For a growing population of cancer patients, immunotherapies are transforming their experience by providing new treatment pathways.

The increasing emergence of immunotherapies are addressing the vast unmet needs of patients who have not responded to standard therapies or for whom standard therapies are inadequate. Clinicians and patient groups spoke with excitement of many instances where they have observed cancer patients using immunotherapies achieving outcomes previously unseen from standard treatments. However, this message was strongly balanced by recognition that the experiences of patients using immunotherapies is varied and not all of the mechanisms underlying this variation are fully known or understood.

“In some diseases it’s become a panacea”

Patients and the patient groups that represent them spoke of the significant quality of life improvements experienced by patients using immunotherapies. Their discussion centred around three areas where immunotherapies had the greatest impact on the quality of life for patients, with significant ripple effects extending to their families and society.

Reduced evidence of disease

Patient groups spoke of instances where patients in intensive or palliative care were eventually free from detectable evidence of disease following treatment with immunotherapy.

The flow on effects of such a drastic transformation are immense, with both patients and carers able to resume normal, healthy lives.

Reduced treatment burden

In many cases, patients and patient groups spoke of the reduced treatment burden associated with immunotherapies. This was observed in terms of a reduced number of treatments, reduced time required for each treatment and, in some cases, an improved method of treatment delivery such as via a tablet or injection. Patients were able to live a more normal life, free from the constant reminder that they are sick.

“A new spectrum of side effects”

Clinicians spoke of the different spectrum of side effects associated with immunotherapies compared with the side effects of standard treatments. In some cases patients have experienced much less severe side effects, allowing them and their carers to return to work and relieving much of the financial pressures associated with a cancer diagnosis.

One patient group shared the story of a patient who – after commencing immunotherapy – was shortly able to return to work and resume her usual routine. As a young woman, she valued not having to lose her hair or openly appear sick, and the infrequency of her treatments meant she could continue to live her life relatively uninhibited by her diagnosis or treatment.

Side effects of chemotherapy vs. immunotherapy. What is the difference?

While the side effects of immunotherapy may vary depending on which type of immunotherapy is used – amongst other considerations – stakeholders spoke of instances where patients experienced vast improvements in side effects when moving from chemotherapy to immunotherapy. However, this experience is variable.

One clinician described the side effects of immunotherapies as being closer to allergic and flu-like symptoms, compared with the nausea, vomiting and hair loss often associated with chemotherapy.

For instance, Cancer Council Australia lists the side effects of immunotherapies as including fatigue, skin rash, diarrhoea, abdominal pain, dry eyes and joint pain.13 As immunotherapies directly impact the body’s immune response, immune related adverse effects need to be monitored.

The side effects listed for chemotherapy include nausea and vomiting, diarrhoea or constipation, fatigue, mouth sores or ulcers, increased risk of infection, increased risk of bruising, hair loss, muscle weakness, skin sensitivity to sunlight, dry or tired eyes and loss of appetite.20

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Kathy describes herself as a writer, a creative albeit sometimes reluctant public speaker, a whole-foods foodie, a cancer thriver, an awareness renegade and a patient advocate. **Kathy is fast approaching a two year period of no evidence of disease following a long battle with metastatic melanoma since her initial melanoma diagnosis in 2006.**

Kathy was 23 when she was first diagnosed with melanoma in her forearm. At the time, Kathy had been living and working in London for one and half years and decided to pursue treatment through the UK NHS to avoid having to face further delays upon returning to Australia. Time was not something Kathy wanted to waste. Kathy underwent surgery to remove the lesion and, following a period of rehabilitation, returned home to Australia where she enjoyed a period of seven years “completely free”.

However in May of 2013, it was discovered that Kathy’s cancer had returned. This time the lesions had spread from her lower to upper right arm where they then clustered. Kathy underwent several major surgeries in quick succession, resulting in the removal of muscle, causing extensive nerve damage. Describing the effects of these surgeries and the treatment to follow as “traumatic”, Kathy underwent radiotherapy followed by major rehabilitation and experienced lymphoedema as a side effect. Unfortunately, Kathy soon received the news that her cancer had advanced to a terminal stage with unresectable lesions in her lungs.

Although devastating, Kathy views her progression to a terminal stage as having provided her access to a broader spectrum of treatments, as she was now overseen by a dedicated medical oncologist specialising in melanoma rather than being a “watch and wait” patient monitored by a surgeon.

**However, the timing was not quite right and Kathy missed out on an immunotherapy clinical trial by a matter of four days, only three days before her 33rd birthday.** Determined to keep moving forward, Kathy and her oncologist organised for tissue samples to be sent to the US to determine her cancer’s genetic profile. The results were not promising, with the mutations comprising Kathy’s cancer further limiting the treatment options available to her.

At this stage, Kathy’s options were limited to an immunotherapy treatment which had received PBS approval a few months earlier. Knowing there was a high risk of failure, Kathy commenced the treatment and tolerated it well compared to many other patients considering its particularly harsh side effects. However, upon completion it was discovered Kathy’s lesions had grown significantly.
Kathy’s oncologist advised there were further treatments on the horizon but none that were available now. This was “a bitter pill to swallow” for Kathy and her family who had to “sit on [their] hands and hope [she] would soon gain access to a clinical trial or compassionate access scheme”. However, “waiting wasn’t an option” for Kathy who focussed on regaining control of her health and researching the options available. At one stage, Kathy and her partner were planning to move to the US in the hopes that Kathy could better access treatments there – “When you don’t really have many options you do what you can to live”.

Luckily, Kathy and her partner did not have to leave their family and friends behind in Australia in search of treatments abroad. Instead, Kathy was one of the couple of hundred patients accepted to a compassionate access scheme for an immunotherapy treatment. As she would later discover, this was the very same immunotherapy for which Kathy had missed out on a clinical trial by four days and, as it turns out, the same immunotherapy she was trying to access in the US.

Kathy began treatment with the immunotherapy in June 2014 and knew straight away that it was working. Kathy had a subcutaneous lesion protruding from beneath the skin of her abdomen and within the first month of her treatment, the lesion reduced in size. Finally, Kathy was on the right path. After the first three months, a scan showed a significant reduction in Kathy’s lesions, from approximately 16 to five. The time required to receive the immunotherapy infusions was much less draining than before and, to top it off, Kathy didn’t experience any major side effects.

In October 2015, after less than two full years of compassionate immunotherapy access, Kathy received the news that she had no evidence of disease.

In reflecting on her experience, Kathy acknowledges that time and timing has played an important role in her treatment. Even as early as four years on, Kathy considers the cancer therapy landscape to be completely different to that in 2013 – “Immunotherapy has really changed the landscape of what people with cancer can do…I was told to stop working and access my superannuation, whereas a lot of patients going through immunotherapy now can still work”.

Kathy continues to advocate for access to immunotherapies, particularly with respect to reducing the gap that exists between the TGA and PBAC review period. Because, as Kathy knows, timing is everything.
If you could write the book, this is what you’d write. **You want your body to learn how to fight these things** as opposed to relying on chemotherapy.

Ross, patient
Melissa's story began in July 2013, at the age of 38, when her children were aged one and six. After being itchy for a couple of months and then finding some lumps in her neck, she was diagnosed with stage three Hodgkin’s lymphoma. She was told it was a good cancer and that she’d be cured with six months of chemotherapy. Unfortunately, things didn’t go to plan and she fell into the very small percentage of people who don’t respond to first line treatment. She had primary refractory Hodgkin’s lymphoma, which carries a poor prognosis.

Melissa then underwent two cycles of salvage chemotherapy which involved week long stays in hospital. A subsequent scan showed that she had finally achieved complete remission. "I had waited nine months to hear those words but the relief was short lived. The chemotherapy had made me so immunosuppressed that I developed a severe lung infection that almost claimed my life”. Melissa was in hospital for a month. When she recovered from the chest infection, she underwent a stem cell transplant in June 2014. "Brutal is the best word I can think of to describe that experience. I was in hospital for 25 days and given what is described as a lethal dose of chemotherapy – chemotherapy so strong that it would have killed me if I wasn’t ‘rescued’ by getting my stem cells back“.

Recovery from the transplant was slow and tough. Melissa spent most of her time in bed and would throw up after a simple activity like having a shower. About two months after the transplant, she had a scan and was devastated to learn that not only had it failed, but her lymphoma had progressed. "It was in my neck, chest, lungs, bones – everywhere". She was too weak for further chemotherapy, so she was forced to fundraise to pay nearly $80,000 for a drug that wasn’t PBS listed at the time. This drug worked well for a while, but then sadly, her lymphoma started progressing yet again.

Melissa was rapidly running out of options; chemotherapy didn’t work, the stem cell transplant didn’t work, the new drug had stopped working and she didn’t have a match on the worldwide bone marrow donor registry. It was then that Melissa went to see another haematologist for a second opinion and he suggested that she go on a clinical trial for an immunotherapy drug. It sounded promising but the catch was that she had to wait several months for the trial to start. "In that time, my lymphoma went from being only in my neck and chest to being all over my body again. It was scary, just letting my lymphoma grow and spread, not knowing if the immunotherapy was going to work when I finally started it".
Melissa had her first dose of immunotherapy in July 2015 and the response was nothing short of amazing. “I could literally feel my enlarged lymph nodes melting away and I immediately started feeling better. My energy levels soared and I regained the large amount of weight I had lost going through chemotherapy”. After just four cycles of immunotherapy, a scan showed that she was in remission. “I stayed on immunotherapy for two years and the side effects were minimal. They could have been infusing saline for the way it made me feel. There is just no comparison to chemotherapy”. Melissa has now been off treatment for three months and a scan last week showed that she is still in remission.

“The fact is, chemotherapy nearly killed me and it didn’t do much for my lymphoma. I was unable to work for over two years, and my mum had to move in with me as I was unable to care for my own children. Soon after starting immunotherapy, I was able to return to work and live an almost normal life again. My kids got their mother back. My youngest child is starting primary school next year and I have no doubt that if it wasn’t for immunotherapy, I wouldn’t be there for his first day of prep”.

It seems odd to say that someone who has endured what Melissa has, is lucky, but when it comes to timing, she really does believe that she is lucky. “I am lucky that I was able to gain access to immunotherapy at a time when I had run out of options. I am also lucky to have found a very dedicated and passionate haematologist who has undoubtedly saved my life”. Just recently, Melissa lost a very close friend who was diagnosed with Hodgkin’s lymphoma only one year before her. Immunotherapy wasn’t available at the time he needed it and he underwent further intense treatment. He ultimately died as a result of complications of all the treatment he had endured, not lymphoma. “I am positive he would still be alive today if he had been able to access immunotherapy earlier”.

“I truly believe that oncologists will look back one day and say “I can’t believe we used to put people through such brutal treatment”. Immunotherapy is the way of the future and I sincerely hope that more Australians are able to access it through clinical trials and PBS listing where there is strong evidence that it works”.
"There is still a lot to learn"

While this new spectrum of side effects may provide an improved quality of life for some patients, the potential side effects of immunotherapy are by no means trivial and should not be overlooked. As cancer increasingly becomes a disease characterised by survivorship, these side effects may need to be tolerated for longer periods of time.

In addition, the risk of side effects and the time pattern in which they are likely to occur is yet to be well established. By contrast, the side effects of standard treatments are well described, and comfort may be derived from what is known. If immunotherapies are to overtake standard therapies as the first line of treatment, careful and correct management of their side effects will need to be maintained.

Care must also be taken to acknowledge the varied experiences of patients using immunotherapies. Our discussions with clinicians and patient groups often referenced the existence of four patient groups when considering the varied nature of patient responses to immunotherapies. These groups are characterised by patients who respond to immunotherapies and eventually attain the status of no evidence of disease, patients who respond but require ongoing management and support, followed by patients who respond but for whom the side effects are unbearable, and finally, patients who do not respond at all.
Immunotherapy isn’t easy for everyone. Not everyone is going to take to it with no issues – some might – but not everyone. But ask any one of them – would you do it again? Yes. Yes they would. When you are in this world, you have one goal. Survival.

Susan, patient
The word 'access' is commonly used to refer to funding or regulation. But access refers to much more than money. To have access you need information – good information. You need legal/regulatory frameworks to work in your favour. And finally, you need the financial means – be it through self-funding or a subsidy.

This report considers these three domains of access in relation to immunotherapies in cancer treatment: awareness, availability and affordability.

A comprehensive approach addressing these three domains will allow Australian patients to access these medicines faster.
It’s here. The time to act is now. **We don’t want to miss this wave.** It’s time to start working through the challenges and thinking about the potential of these medicines.

Elizabeth de Somer, Medicines Australia
Accessing new cancer medicines

A focus on the future

More needs to be done to get immunotherapy to the patients who need it

At present, the TGA has approved five cancer types that can be treated by checkpoint inhibitors.\(^4\) This falls short of the 11 cancer types approved by the FDA in the USA and the six approved by the EMA in Europe.\(^5,6\)

However, of these five cancer types approved by the TGA, only three are listed on the PBS.\(^7\) Since listing – and as of September 2017 – a total of 28,080 prescriptions for these immunotherapies have been funded under the PBS. 17,008 of these prescriptions were dispensed in the 2016/17 financial year, equating to approximately 1,417 per month.\(^8\) If we assume the typical patient on immunotherapy has their prescription filled monthly and that patients are using these medicines long term, this monthly figure can be used as a proxy for determining the average number of patients accessing these checkpoint inhibitor immunotherapies.

Fewer Australians who could benefit from immunotherapy are currently accessing it through the PBS

Of the 47,753 people estimated by the AIHW to die from cancer in 2017, the number of people who might benefit from checkpoint inhibitor immunotherapy – based on a collation of the available evidence from a variety of manuscripts and conference abstracts – is approximately 7,500 Australians, where “benefit” is defined as a greater than 30% reduction in tumour size.\(^1,2,3\)

With this ballpark in mind, and with fewer than 1,500 patients currently receiving immunotherapy, it does appear that not as many people are receiving immunotherapy compared to those who might benefit – approximately 20% from this reckoning. This figure – 7,500 patients – is conservative, as there are many more patients with cancer who will not die in 2017, but would benefit from immunotherapy.

While needing to set realistic expectations on those who might be helped, it is important to identify these people and ensure they can access immunotherapy early in their disease journey. This process could be improved by better ways of identifying those likely to be refractive to standard treatment, where it may cost less and deliver better outcomes if immunotherapy were available as a first line option.

Reimbursement delays and capacity constraints are barriers to access

The average time to listing a cancer medicine on the PBS is 597 days. This is, on average, 200 days longer than in other disease areas.\(^21\) Moreover, with the number of new submissions for immunotherapies increasing, the system is facing imminent capacity constraints.

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You hear of people – they sell their house, they cash in their super. They crowd-fund and feel guilty if it doesn’t work. *Us? Well, we couldn’t afford it.* Paying for it just wasn’t an option.

Wayne, patient
**Accessing new cancer medicines**

A strategic approach going forward

**A comprehensive strategic approach to awareness, availability and affordability will allow Australian patients to access these medicines faster**

The word “access” is often used to refer to funding or regulation – but access means much more than money and rules. You need access you need good information. You need legal/regulatory frameworks to work in your favour. And finally, you need the financial means – be it through self-funding, a subsidy or other avenues.

We now consider these three domains of access in relation to immunotherapies in cancer treatment: awareness, availability and affordability.

**Awareness of the coming wave**

Immunotherapies represent a paradigm shift in cancer treatment. For many individuals, it represents a shift from terminal illness to one characterised by survivorship.

The system needs to recognise this shift and adapt its processes accordingly to improve access to these medications for patients who stand to benefit from their use, and to ensure Australia does not lose its place as a leader in cancer care.

Stakeholder consultations have uncovered a number of areas where investment in improving awareness may assist in bringing about this necessary system change:

- building awareness amongst patients, clinicians and the general public regarding the importance of clinical trials as a means for accessing new, cutting edge medicines;
- improving the awareness of clinicians – particularly medical oncologists – of the TGA’s provisions for special access;
- ensuring reputable, evidence-based information on these new cancer medicines is readily available to patients and the general public – a common source of truth; and
- changing the conversation regarding cancer so clinicians, government and the general public think about the survivorship issues of cancer including the need for counselling services and return to work programs to help cancer survivors and their families return to normal life.

**Availability via a tumour agnostic approach**

The genetic mechanisms underlying cancers are increasingly being understood. This means it is becoming less relevant to speak or organise information/services in a language which defines cancer patients in terms of their cancer’s organ of origin. The organisation of clinical and government processes needs to change to reflect this new language.

The FDA’s unprecedented decision in May 2017 to approve a single prescription drug for treatment of solid tumours with a specific genetic signature in any organ – regardless of the tumour’s organ of origin – has paved the way for similar transformations around the world.

This has been labelled the “tumour agnostic approach”.

Clinicians and patient groups also spoke of the need for clinical trials to reflect this approach in the way they design their recruitment criteria.

**Affordability by incorporating comprehensive, real world evidence in the review process**

Cancer is an important problem that is worth investing in, as already evidenced by the 20% improvement in the five year survival rate from all cancers over the past three decades, due to consistent generous investment by the Australian Government in cancer research and access.

However, the government-led assessment of registration and reimbursement of cancer medicines is not amenable to this shifting cancer classification.

These processes need to adapt. Stakeholder consultations have suggested comprehensive, real world data is essential in ensuring decision makers have access to the right information regarding the holistic benefits of these cancer medicines. Concurrent funding reforms are also required. A further review of innovative approaches to funding mechanisms is needed.
Immunotherapy has really changed the landscape of what people with cancer can do...I was told to stop working and access my superannuation, whereas a lot of patients going through immunotherapy now can still work.

Kathy, patient
Awareness of new cancer medicines
There’s lots and lots of information out there, trying to make sense of what could help me is really hard, I’m not a doctor.

Troy, patient
Awareness of new cancer medicines
Issues navigating to find accurate, relevant information – from the patient perspective

“The bigger the choice of available treatments, the greater the chance that you or your loved one will respond and respond favourably”
– Fiona Bennett, Melanoma Patients Australia

Awareness of the presence and potential of immunotherapies varies across the public, patients and even clinicians. Awareness is a function of two elements. First, the existence of evidence-based information. Second, the capacity to navigate that information and discern what is relevant.

Patients and the patient groups which represent them spoke of the challenges they face in navigating through the system to self-educate and identify appropriate immunotherapies.

Equally, patient groups and clinicians spoke of challenges managing the expectations of the public and patients who received incomplete information from the media and inaccurate websites that “peddle hope over evidence”.

Why is awareness important?

In many respects, the Australian health system is consumer driven. Without complete and accurate information, patients are unable to make informed decisions about their health and treatment. As such, awareness of new cancer medicines is essential in driving access for patients. This includes a greater level of awareness and understanding around biomarker testing to aid in treatment decisions where this is appropriate.

Awareness can be facilitated via a number of mechanisms. When it comes to health information, stakeholders have suggested clinicians, the media and the rise of “Dr Google” are playing key roles in informing the Australian public today.

Clinicians and patient groups spoke of the fine line between providing evidence-based hope and setting unrealistic expectations. They noted, with frustration, that they frequently find themselves in situations where low health literacy leads to misconceptions of the promise offered by “breakthrough” discoveries heralded in the media. Often these reports lack mention of the lengthy timeframes required for these discoveries to reach the market, if they reach the market at all, and finer details regarding their target patient population.

The cruelty of unduly raising the hopes of patients and their families is painfully evident through stories shared by patient groups of patients who have chased a therapy – often at extreme cost to themselves, their family and the health system – only to find out that it did not deliver what they hoped.

What is the current state of awareness in Australia?

Patients

Many stakeholders felt that patients quickly develop a good understanding of cancer and cancer therapies, when they have to. With one stakeholder noting “you have to be sick to be aware”. Indeed, when reflecting upon the period after their diagnosis, patients spoke of asking lots of questions and reading a lot of detail to improve their understanding. Those who had scientific backgrounds mentioned the significant advantage this provided during this difficult time.

However, one clinician highlighted the paradox of the situation as patients must quickly come up to speed on sometimes very complex health information at a time in their lives when they are least equipped to do so.

As such, the need for evidence-based information from respected sources in these difficult times is essential in ensuring patient awareness is not inhibited by having to decipher between good and bad information.

Working to improve the availability of accurate, relevant information for patients and clinicians, and the health literacy of the general public, may all assist in increasing the proportion of patients accessing potentially beneficial therapy beyond those who currently do.
Patient story

Troy

“Trying to work out what’s going to have some sort of effect for you and get in touch with someone going through something similar to you is extremely hard”.

In 2013, Troy was diagnosed with urachal bladder cancer after going to his GP numerous times for pain in his groin. Troy underwent immediate surgery but discovered his cancer had returned 18 months later.

Following a second round of surgery and three combinations of chemotherapy, Troy was told “you have to face the fact that this is going to kill you, there’s nothing you can do, go and get your life in order”.

At the age of 49, with three daughters and two grandchildren, this was not a statement Troy was prepared to accept. He was determined to beat this cancer and organised for a referral to another oncologist, in addition to making enquiries with a contact he found on the internet.

Troy was put in touch with a doctor in Japan who had treated this type of cancer before with an immunotherapy. So Troy and his wife packed their things and travelled to Tokyo, where they spent five weeks while Troy underwent treatment. However, upon their return to Australia they discovered Troy’s cancer had spread. But it had not been completely in vain, for Troy had made friends with a fellow patient whom he still keeps in contact with to share information.

Troy then underwent a series of treatments involving infusions, chemotherapy and radiotherapy, with limited success. During one of his treatments, a nurse on duty gave Troy a Rare Cancers Australia cap. As Troy approached what he thought was the end of his available options, he emailed Rare Cancers Australia who suggested he contact the Australian Genomics Health Alliance to organise genetic testing.

Unfortunately, the genetic test revealed the type of immunotherapy Troy trialled in Japan never would have worked for him. However, it also revealed that Troy’s cancer expressed an EGFR mutation. A contact from the Australian Genomics Health Alliance organised for Troy to participate in a CAR-T-cell trial sponsored by a pharmaceutical company in China – a trial that, without his genetic test, Troy would have been ineligible for.

At the time of writing, Troy is preparing to go to China next month.
We need to address health literacy early on so later decisions can be better informed.

Jo Root, Consumers Health Forum of Australia
Awareness of new cancer medicines
Clinician and other inputs towards improved awareness

“When patients are informed about treatment options they have the power to ask more questions” – Sharon Millman, Lymphoma Australia

Clinicians
Cancer therapy is moving faster than it ever has before, and there are certain groups who need to be aware of these developments before patients and the general public. These groups are primarily composed of clinicians, namely the clinicians who are likely to be supporting the patients who take these medicines.

However, some stakeholders commented on the variable knowledge of clinicians. These stakeholders lamented the stories of patients who find themselves moving between clinicians in search of someone who could provide accurate information and access to immunotherapies.

Patient groups in particular stressed the importance of ensuring clinicians were aware of the clinical trials and special access schemes available to patients.

No one clinician can ever know all of the available cancer therapies, however, it was suggested that existing siloes in the cancer treatment sector – comprising clinicians, patient support groups and government – are restricting the conversations that can be had and who they can be had with.

In addition to removing these siloes, patient groups advocated for a two pronged approach with education provided to both clinicians and patients on (1) what these medicines are and (2) correct side effect management.

General public
While the media’s promotion of good news stories is important in raising public awareness of new therapies, clinicians spoke of the risk of warping patients’ perspectives of the effectiveness of these drugs and their expectations that they will not only be accessible and available to them, but that they will save their life. Thus, there is a need to take care in what is communicated to ensure a realistic perspective regarding what these therapies will and will not do.

"The level of awareness in the general public is almost zero...complete shock when they discover a drug is not on the PBS" – Kate Vines, Rare Cancers Australia

Pathways for improving awareness
Because of the difficulty keeping pace with the rapid developments in cancer medicines, it is important that we start thinking through the complexities of how to build awareness.

Many noted that awareness initiatives will need to be patient centric – driven by patient needs and motivated by patient outcomes. “First, we change the language to match the outcome – and the outcome we want is survivorship” advised one patient group. “Next, we change the sector. Bottom up”. Many clinicians and patient groups consider partnerships between research, industry and academia, with patients in the middle, as essential in removing silos in the cancer treatment sector.

Regardless of the system or the changes it may undergo, ensuring patients have access to reputable and evidence-based information – knowing where to find their source of truth – is thought to be crucial in driving access to new medicines.

Further support is required for patients who retire early or who cash in their superannuation early, who then respond well to immunotherapy, leaving them and their families in financial limbo. Support mechanisms could include counselling services and return to work programs.
Patient story

Susan

“I really felt like I was a new explorer...it was a very isolating and lonely journey”

At the time of writing, Susan had been recently diagnosed with metastatic cancer. Having educated herself about Lynch syndrome and its risks of aggressive, early onset cancers following her diagnosis in 2013, Susan knew that following “standard of care” protocol – complex surgery then standard therapies – would quite probably mean serious health complications. She was resolved to access immunotherapy as a first line treatment.

However, Susan faced clinicians who were not well-versed in the possibilities of immunotherapy and tried to direct her treatment down more well-worn paths with immunotherapy only as a final option.

Despite being well informed, Susan felt as if she was at risk of falling through the cracks and described herself as a “new explorer” in a system struggling to catch up with the latest developments in cancer medicines.

Eventually, Susan discovered a clinical trial offering immunotherapy as a first line treatment and was accepted onto it. However, she acknowledges, “there aren’t many people with as much time, knowledge or stubbornness as I had and not too many that would have been able to get access as I did to immunotherapy treatment”.

Describing her journey as “isolating and lonely”, Susan calls for the removal of siloes in cancer care. With many years’ experience in communications, public relations and corporate social responsibility, Susan advocates for changing the conversation to effect systemic change, noting with determination that “in politics, as in business, history has shown that if you succeed in changing the conversation first, systems have to follow to meet the new expectations”.

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Many people may be confused about cancer and other health issues but learn more when they need to. I think that’s okay. My clinicians have helped me understand my disease and its implications.

Therese, patient
Availability of new cancer medicines
We no longer need to define cancer by what tissue you are looking at down a microscope. It’s irrelevant to talk about body parts when you are talking about the future of cancer medicines. Go deeper. Talk about the molecular make-up of a tumour. Talk about what it is that really makes a cancer a cancer.

Prof Ian Olver, Sansom Institute for Health Research
Availability of new cancer medicines

Patients and patient groups reflect on fairness and timeliness

TGA processes, reforms and decision speed

Availability to Australians of emerging therapies is largely determined by the registration process under the purview of the TGA. Among other considerations, the TGA assesses evidence to ensure that medicines meet a threshold of quality, safety and efficacy for sale in Australia. The TGA also determines the sequence in which medicines are to be taken by patients – that is, whether a new medicine will become the first line of treatment or follow unsuccessful administration of existing treatments. Pharmaceuticals are also accessed by Australian patients through eligibility and entrance into clinical trials, and by traveling overseas to access medicines in other countries where they are available.

New medicines – particularly cancer medicines – are coming to market at unprecedented speed. The TGA process has been recently reviewed and reforms continue to adapt to the rapidly evolving medicines landscape. Reforms that have been implemented to date allow the TGA to utilise assessments of medicines undertaken in other countries and to fast-track “novel” and lifesaving medicines.

Despite these reforms, in a number of instances relating to cancer medicines, Australia has still lagged behind the US FDA and the European EMA, which continues to result in lost treatment opportunities for Australian patients.

While patients, patient groups and clinicians applauded the steps taken to modernise Australia’s registration process, most interviewees noted that there is an impetus to continue the process of change, with particular emphasis on:

- faster implementation of the new mechanisms available since the TGA Review; and
- greater awareness amongst oncologists of the TGA’s provisions for special access.

“Why not me?”

To date, immunotherapies for cancer treatment in Australia have continued to be registered on the basis of where in the body the cancer originated. Patients and patient groups reflected on a number of different experiences where this categorisation seemed artificial, either because the origin of the initial tumour was unknown, or because the therapy can work on a variety of cancers but is only currently approved for one originating site.

One patient commented, “I don’t understand why they are talking about body parts when all that the medicines see are the tumours”. Another patient group commented that there is “a huge inequity. Why aren’t these available across the board?”.

Equally, patients and patient groups alike spoke of the frustration and despair they felt when watching people who had equivalent stories to their own accessing treatments simply because of the country they lived in. “It is extremely frustrating” one patient stated “just to know that these drugs are available for patients just like me in other parts of the world”.

“There’s hope, but there’s no time”

Cancer is a time critical disease. Earlier diagnosis and treatment is irrefutably correlated with an increased probability of survival. In response, regulatory systems worldwide have sought to expedite registration processes, moving to list innovative medicines earlier in the trials process.

But still, for many it is not fast enough. Naturally, safety and quality are primary concerns – though a number of stakeholders questioned if there was more that could be done to further speed up the process in line with comparable, developed nations.

One patient group spoke of the registration of an immunotherapy that came too late for a family the patient group was supporting. “It wasn’t an easy time for us” they commented. “On one hand, we had patients who were ecstatic. On the other hand, we comforted a mother whose 28 year old son accessed only one round of treatment. It came much too late”. 

"The impact that technology is having on cancer therapies is moving at a faster rate than the pace of change in the regulatory system. This means timely access to new and improved therapies is an increasing issue for people living with cancer” –  Bill Petch, Leukaemia Foundation
In that time [while I waited several months for the trial to start], my lymphoma went from being only in my neck and chest to being all over my body again. It was scary, just letting my lymphoma grow and spread, not knowing if the immunotherapy was going to work when I finally started it.

Melissa, patient
“I don’t think it is the way of the future. It is the future”

In 2014, Jonathan went to the doctor having discovered a lump under the skin of his chin, which was cut out. He went back and forth with tests only to finally reveal that he had a rare form of skin cancer – Metastatic Merkel Cell Carcinoma.

Jonathan’s cancer behaved in an unpredictable way. “It was a cancer of an unknown primary” Jonathan explains. “No one could find any of it on my skin but it was already in my lymph system”. Soon, another lump was discovered under his armpit and 8 lymph nodes were cut out.

He commenced a round of radiotherapy within a few months of his original diagnosis. This was followed by further surgery in which several lymph nodes were removed as well as a slice of his lip.

Jonathan was quick to find information on the newer therapies that could help him. He determined that chemotherapy would do little more than give him back a few months of life. An economist by profession, Jonathan reasoned “it wasn’t worth it; it would be a few more months… but a few months of horror”.

“I’m a lucky fellow” Jonathan reflects “I am well informed, I come from a well informed family with a lot of clinical knowledge – especially my scientific niece, Leah”.

But awareness alone didn’t help. Jonathan’s diagnosis and the behaviour of his cancer prevented him from accessing the medicine he needed either on the PBS or even through clinical trials. This was despite the therapy being listed on the PBS for melanoma at the time.

Still, Jonathan pursued his therapy of choice rejecting suggestions he should commence chemotherapy or further radiotherapy in the interim.

Finally, his oncologist advised that there was an opportunity for him to self-fund access to the immunotherapy he was seeking. His experience was exceptionally positive. He suffered few side effects and kept up with his work as a consultant through his treatment. His cancer has not reappeared for two years now.
It is the catalyst for a democratisation across cancer groups. Doing the greatest good for the most people no longer bears reference to a body part. It refers to a molecular level commonality. This breaks the big cancer groups down while simultaneously binding the smaller cancer groups together. It will change the equation for listing medicines.

Prof David Thomas, The Kinghorn Cancer Centre
Availability of new cancer medicines
Is it time we applied a new lens?

“Within the next ten years, there will be a revolution in the way we classify cancers – away from where in the body they occur or how the tissue looks down a microscope – to a genomic view. Cancer will be treated as a molecular disease. Systems need to keep up.” – Prof David Thomas, The Kinghorn Cancer Centre

Systemic change and investment in testing

“I teach a module on cancer therapies”, stated Dr Donna Milne, of Cancer Nurses Society of Australia, “and, right now, it’s a class on chemotherapy. At the end, I save a bit of time to talk about immunotherapies. I fully expect that in my career, I am going to see the balance of these topics turned on its head”.

Australia has one of the highest cancer survival rates in the world. In large part, this can be attributed to the progressive attitude the health system has taken to research, registration and reimbursement.

To maintain its position, Australia must keep pace with not only the evolution of treatment but also the evolution of processes adopted in countries around the world.

As the genetic mechanisms of cancer are increasingly discovered, one stakeholder noted that this will force change at the level of the treating clinician and – in turn – at the level of the regulator and funder. Cancer will be reclassified on a molecular basis.

Stakeholders commented that availability would increasingly need to be determined on a molecular level.

This, commented several stakeholders, will require two things:

- first, systemic change along the lines of what has recently been demonstrated by the FDA in bureaucratic decision making processes for pharmaceutical approvals. “Not a bolt on to the existing process” one stakeholder cautioned, but “a rework of the process – fit for purpose and from the bottom up. The current processes were not designed with this molecular level of thinking in mind”; and

- second, to support this move, increased investment and coordination in the development and availability of associated screen tests, to better target therapies towards biomarkers that are likely to respond.

“It is not appropriate to persist with an inflexible methodology” one stakeholder commented, “that is fixated on classifying cancers at the level of organs. We need to think about it at a molecular level”. Indeed, this renewed lens for classifying cancers in registration processes has been reflected in the FDAs latest decisions.

Notably, the Australian Health Minister, the Hon Greg Hunt signalled an interest in encouraging PBAC and the TGA to adopt tumour agnostic assessments in August 2017.

Canada, pCODR
Cancer medications are evaluated separately from other drugs. Patients provide substantial input to broaden the valuation of medicines.

European Union, EMA
The EMA’s Committee for Advanced Therapies (CAT) specialises in providing scientific assessments of advanced medicines, including immunotherapies. The CAT both creates an environment where the development of advanced therapy medicines is encouraged, and provides the EMA with scientific expertise and advice for how it should formulate initiatives relating to the development of innovative medicines and therapies.

England, NICE
Products are assessed by NICE as meeting existing ICER thresholds (noting End of Life Criteria provides a higher threshold if relevant. Then, if agreed that further evidence would address the uncertainty, the product is reimbursed pending a second assessment by NICE where new data – including real world evidence, is made available.

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Case study: FDA Announcement in May 2017

In May 2017, the FDA made an unprecedented decision to approve a single prescription drug for treatment of solid tumours in any organ, dependent only on whether the malignancy bore a specific genetic signature.

The announcement marked an important milestone. It signalled that cancer will no longer be identified, categorised and treated by the organ that it inhabits. In a shift that is already underway, cancers will be known by – and treated for – the genetic mutations which define them.

The FDA’s decision has profound implications for patients, researchers and clinicians alike. Patients may no longer face restrictions in access on account of the original location of their cancer. This will drive change in the clinical treatment industry which has to date been largely siloed in accordance with organs or systems – be it blood, brain, lung or skin. Similarly, clinical trials will need to adapt their recruitment to a new criteria to that which they have used in the past – the genetic signature of tumours.

In August 2017, the FDA followed with a comparable ruling on an immunocellular therapy, signalling its commitment to modernising its processes in alignment with the therapeutic landscape.
Even after chemotherapy and major surgery followed by radiation treatment the doctors found secondary tumours in my lower spine and in soft tissues all over my body. Clearly my outlook was grim and I was advised to ensure my affairs were in good order! After just 12 weeks on immunotherapy the reduction of the soft tissue tumours was noticeable and dramatic. We could feel the tumours diminishing each week.

Ross, patient
It’s in everyone’s interest to think about and administer these treatments from a molecular lens. Patients? They don’t want something that is going to waste their time, raise their hope and ultimately isn’t for them. Neither do clinicians. Poor results don’t help the company and are an inefficient use of already tight Government funds. It’s in everyone’s interest to rethink things from a molecular lens.

Prof Sanchia Aranda, Cancer Council Australia
Affordability of new cancer medicines
The challenges of balancing equity and sustainability of funding

In Australia, medicines are paid for through several pathways including hospitals, private sector contributions (trials and compassionate access schemes), the PBS and out-of-pocket costs.

At present only a small proportion of the potential indications for which immunotherapies are able to be used in cancer treatment receive subsidised funding from the Government. This translates into substantial challenges in access for many patients.

“What is the Government’s role here?”

In the main, medicines accessed within community and outpatient care settings are generally supported by the PBS and by consumer co-payments. For medicines that are not listed on the PBS, outside research pathways patients may be able to self-fund access to medicines for indications listed on the Australian Register of Therapeutic Goods.

Up until the last decade, the PBS was largely able to cope with the speed and cost of new medicines entering into the Australian market through standardised valuation processes and conditions of listing. In more recent years, however, the PBS has been subject to a series of reforms to balance the stability of the fund against increasing demands on access.

The latest innovations in medicines – particularly oncology medicines – raise new challenges which the PBS must work with in order to ensure its capacity to offer Australians timely and equitable access to medicines.

Without consideration of new or novel funding mechanisms, the PBS may fail to meet its core purpose for Australians (timely access) and/or become financially unsustainable.

The challenges stakeholders described can largely be grouped into four categories. First, the substantial cost of innovative cancer medicines such as immunotherapies. These costs, clinicians and academics explained, are driven not only by the process of discovery which sits behind these drugs but also the cost of developing appropriate trials and then subsequently manufacturing biological molecules that are far more complex than chemical agents.

Second, and related to this, stakeholders also spoke about challenges in valuing the true benefits of these medicines. “There needs to be more data, more effort, more rigour put into demonstrating the whole value profile of these medicines” commented Elizabeth de Somer of Medicines Australia. Elizabeth noted that the value which needs to be accounted for should span outside the rigidities of the Federal Health budget. “Evidence needs to be systematically collected on broader benefits – to the patient, to the carer of that patient, to the economy in which these drugs can return patients and carers back to productively participate in. Currently clinical trials are not set up to systematically measure these broader productivity impacts. The time is now”.

Third, stakeholders – including patients – commented on the urgency related to listing for reimbursement. “There is a good reason to take time to list. Every listing reflects a trade-off – the

“This is a moment in history”

— Hon Minister Greg Hunt, Australian Government Minister for Health, at the CanForum in Parliament House, Canberra on 9 August 2017

Fourth, as discussed with respect to availability, many stakeholders commented that current reimbursement decision processes still treated cancers as being siloed in accordance with their primary organ of origin. “It’s immaterial” commented one clinician, “it makes no difference where the tumour started when deciphering whether the investment is a worthy one or not from the Government’s perspective. All that matters is if it works. And the key to it working is a question of molecular properties”.

Indeed, the Federal Government is cognisant of the need to change. Speaking at the CanForum conference recently, Mr Hunt flagged plans to “bring together” TGA and PBAC “pan-tumour” assessments “across a range of therapeutic outcomes”. Though it has not been the focus of this piece of work, it is clear that in thinking through the implications of change, there will need to be serious consideration of new models for funding immunotherapies into the future.
The patient perspective

The impact of self-funded treatment

Wayne

In 2014, Wayne went into the doctor to check the source of a persistent toothache only to stumble upon a far more serious diagnosis of high-grade maxillary adenocarcinoma. The condition is very rare – only 150 Australians would receive a similar diagnosis in any given year with only 4% of this number diagnosed as having adenocarcinoma.

Wayne spoke passionately about the difficulty he has faced finding appropriate treatment. “You are just floundering in an ocean of treatments, trying to grab onto something but you just get lost”.

Wayne has undergone several rounds of surgery – including the removal of a great deal of the bone structure from the right hand side of his face and his right eye. As well as close to 18 rounds of chemotherapy and 37 sessions of radiotherapy.

Immunotherapy for Wayne’s rare condition is not funded under the PBS and Wayne has no ability to pay for it himself. He is now driving his treatment team to complete compliance paper work in order to receive screening which may make him eligible to receive treatment in a clinical trial environment.

“It is the main treatment I have been hoping for” Wayne concludes, “I just need a way in”.

Jonathan

Jonathan self-funded access to his immunotherapy treatment. He considered himself lucky for being able to afford the therapy which was close to $100,000. “It isn’t easy and not everyone could do it. I was paying that for my treatment when the person with melanoma next to me was getting it off the PBS for $37”.

Troy

Troy is self-funding to travel to China this year to participate in a trial that will give him access to immunotherapies. “I have my plans laid out – how will I stay in contact with my wife, what will happen if I need treatment that I can’t get in China?”. “It has been expensive” he reflects “I travelled to Japan for one treatment. My wife and I funded that. But it didn’t work. I’ve been all over really. I’m lucky we worked and held life-insurance for long enough that I can now draw it down to afford it”.

Ross

Ross is self-funding his access to immunotherapy. Having been told to “get your affairs in order” he knew the options were limited. Clinical trials for a new immunotherapy treatment were closed, so self-funding was the only option. “It’s working. It is expensive but it’s my lifeline. Tumours had spread to various parts of my body, but the scans show I am now clear. I’m not coming off it. I feel lucky to have this option – and feel for those who cannot afford this life-saving treatment.”
You just go around in your head – ‘if, if, if’ … IF I had the money. IF I had THAT cancer instead of my cancer. IF I lived THERE instead of here… then I’d have a shot.

Troy, patient
Summary of findings
I’m comfortable saying to patients *had you been in this position 5 or 6 years ago I wouldn’t have been as optimistic.*

Dr Donna Milne, Peter MacCallum Cancer Centre
Summary of findings
A recap of the issues and solutions

Cancer is the greatest health issue facing Australians today, contributing substantially to mortality and disease burden, and with huge financial and social impacts.

While pleasing increases in survival have been achieved through traditional treatments (surgery, chemotherapy and radiotherapy), together with prevention and early intervention, the advent of novel treatments such as immunotherapies drive a new paradigm in the way that cancer is both treated and experienced. Patients, clinicians and other stakeholders note that, for at least a sub-population of patients, immunotherapies are key to reclassifying the disease from one which is terminal to one which may be characterised by survival.

Currently, fewer Australians who could benefit from immunotherapies are currently accessing them. The volume and speed of discovery in this cancer treatment sphere calls for a re-imagination of access pathways, defined across the domains of awareness, availability and affordability.

Awareness of immunotherapies

Awareness is a function of (1) the existence of evidence-based information, and (2) the capacity to discerningly navigate that information to find what is relevant for a patient’s circumstance.

Patients face challenges navigating the current system in order to self-educate on the relevance of new cancer treatments including immunotherapies to their personal condition and the pathways for accessing this treatment. Patients are moving between clinicians to find someone who can provide accurate information and access to cancer immunotherapies.

They worry about the “lottery” they face in accessing accurate, timely information about emerging therapies that may change the trajectory of their disease pathway. At the same time, they need realistic expectations of when and how often such treatments would be appropriate or available for their condition.

The fragmented structure of the cancer treatment sector is also out-dated, as patients need to reorganise themselves in accordance with the molecular characteristics of their tumours, rather than parts of their body.

Important steps to improve awareness include:

- change the language to one of survivorship and immunotherapy as a potentially transformative alternative for many patients, where appropriate;
- ensure patients have access to reputable and evidence-based information, setting out what immunotherapies are available in Australia for whom, and how to access them as they are emerging through the pipeline, including information on biomarker testing where appropriate;
- remove sectoral silos and develop partnerships between research, industry and academia, with patients in the middle, to help ensure patients and clinicians can navigate information channels effectively; and
- provide further support to survivors who face financial constraints, such as counselling services and return to work programs.

Availability of immunotherapies to treat cancer

The availability of emerging pharmaceutical treatments to Australians is largely determined by the registration process under the purview of the TGA. Medicines are also accessed by some patients through clinical trials, personal investments such as travel overseas, and compassionate access.

Registration of cancer therapies in Australia is still closely tied to the organ or system where a patient’s cancer originates, which draws artificial lines and creates inequitable outcomes among patients. Despite recent TGA reforms that enhance fast-tracking and access to life-saving treatments, the regulatory system is no longer aligned to research outputs.

Important steps to improve availability include:

- systemic change similar to what has recently been demonstrated by the FDA, adopting a tumour agnostic approach that recognises molecular level treatment;
- increased investment and coordination in availability of biomarker and screening tests, to better target therapies towards biomarkers that are likely to respond;
- faster implementation of the new mechanisms available since the TGA Review; and
- greater awareness among oncologists of the TGA’s provisions for special access.

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Summary of findings

Recommendations going forward

Affordability of immunotherapies

At present only a small proportion of the potential indications for which immunotherapies are able to be used in cancer treatment receive subsidised funding from the Government. Immunotherapies are an emerging therapy that have high costs of development and production and, as such, are prohibitively expensive for many patients who seek to self-fund.

Australia is a world leader in cancer survivorship following years of public investment in securing access to treatments. However, reimbursement processes – just as with registration processes – have been designed with an entirely different frame of therapies in mind. Challenges exist in holistically valuing the benefit of new therapies – particularly where benefits accrue across portfolios – as well as challenges relating to the speed of development and the urgency in granting timely access to patients.

No jurisdiction in the world has comprehensively solved the challenges that immunotherapies present to current subsidisation processes. Stakeholders called for a fundamental shift in assessment processes, and that these would need to be considered starting from the design of trials, to the conditions of provisional listing (a shift to dependence on real world evidence), and right through to consideration of innovative, ongoing reimbursement models.

Important steps to improve affordability include:

- capacity constraints in PBAC processes need to be overcome to ensure that listing of new medicines is not delayed as increasingly more fill the pipeline, since the speed of listing is critically important and cancer is already the slowest therapeutic area to be reimbursed;
- reimbursement decisions in PBAC need to link with TGA tumour agnostic assessments across a range of therapeutic outcomes, with serious consideration of new models for funding immunotherapies into the future;
- recognising the substantial cost of innovative biological molecules, affordability considerations should include life-saving and compassionate access to trials; and
- the entirety of benefits from newer medicines need to be valued including not just health system, longevity and quality of life impacts, but also productivity and other impacts on patients, carers and society. Data should be captured in trials.

“This is what one of my colleagues would say is a penicillin moment really for drug therapy for cancer”

– A/Prof Georgina Long

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If I was diagnosed tomorrow I would say, I don’t want it cut out. I don’t want chemotherapy and I don’t want radiotherapy. Just put me on first line immunotherapy and if it works then that is the end of my treatment, thank you very much!

Jonathan, patient
References


5. FDA, Drug prescribing information, https://www.accessdata.fda.gov


Consultation Brief | A new wave of cancer medicines

Thank you for agreeing to meet with us to discuss our work considering the new wave of cancer medicines. This consultation brief provides an overview of topics we would like to discuss.

A new wave of cancer medicines

Cancer is an important public health issue—the leading cause of disease burden for patients, families, and the health system in Australia. Over 140,000 new cases are diagnosed every year nationally.

Through the latter part of the 20th century, chemotherapy and radiotherapy have formed the staples of cancer therapy. Despite significant improvements in these standard treatments, their side effect profile has meant the pursuit continues for targeted cancer treatments that act specifically on cancer cells.

Advances in scientific discoveries have revealed therapies that can disable or block specific cancer cell processes. Among these targeted therapies, immunotherapies have become an important part of treating many types of cancer, by using the body’s own immune system.

These new cancer medicines have been reported to drive improved patient outcomes including better tolerance, fewer side effects, decreased risk of recurrence and improved long-term survival.

Objectives of this report

Deloitte Access Economics has been engaged by Merck Sharp & Dohme to explore and broaden the awareness of the new wave of cancer medicines; the potential they show in fighting cancer; and pathways for access.

The work will be informed by consultation with patients, clinicians and other key stakeholders.

Topics for consideration

We like to understand your experience with respect to the following topics.

It is up to you whether you would like to be identified in our report or remain anonymous.

Your story: What has been your experience with these new medicines? How has this compared with your experience with standard treatments?

Awareness: How did you become aware of these new medicines? What sources do you use to keep up to date and/or find out more?

Access: What has been your experience in accessing these new medicines? Have you faced any barriers or challenges?

Potential: Do you have any thoughts on how the current system could be improved? If you are aware of systems in other countries, how do you think Australia compares?

A new wave of cancer medicines

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Through the latter part of the 20th century, chemotherapy and radiotherapy have formed the staples of cancer therapy. Despite significant improvements in these therapies, they have potential harm to healthy tissue and associated undesirable side effects has meant the pursuit continues for targeted cancer treatments that act specifically on cancer cells.

Advances in scientific discoveries have led to therapies that use agents to disable or block the processes that enable cancer cells to grow, divide and spread.

Among these targeted therapies, immunotherapies have become an important part of treating many types of cancer, by using the body’s own immune system. There are two types of targeted therapies which are of greatest relevance to the present work:

- Small-molecule compounds are typically developed for targets that are located inside the cell because such agents are able to enter cells relatively easily.
- Monoclonal antibodies are relatively large and generally cannot enter cells, so they are used for targets that are outside cells or on the cell surface. These innovative targeted cancer medicines have resulted in improved patient outcomes and experiences, better tolerance, fewer side effects, decreased risk of recurrence and improved long-term survival.

Objectives of this report

Deloitte Access Economics has been engaged by Merck Sharp & Dohme to explore and broaden the awareness of the new wave of cancer medicines; the potential they show in fighting cancer; and pathways for access.

The work will be informed by consultation with patients, clinicians, peak bodies, health consumer organisations, academia and government.

Topics for consideration

In our consultation we would like to understand your perspectives with respect to:

- Innovation: What are the recent advances in cancer medicines? How do these compare across indications?
- Value to patients: What benefits do these new cancer medicines offer? How do they compare with alternative treatments?
- Access: What is the current state of access to, and funding of, new cancer medicines in Australia? What barriers or challenges does this present for patients?
- Changes: What changes would need to be made to the current system to ensure cancer patients continue to receive optimal treatment as new medicines are developed?
- Potential: Do you have any thoughts on how the current system could be improved? Do you have a view of how Australia compares with other jurisdictions?