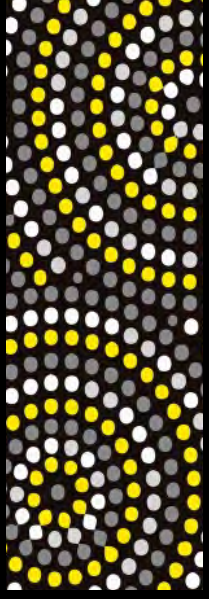
CAR T-cell therapy: Is Australia ready, willing and able?

Making next-generation treatments accessible to Australian patients with multiple myeloma.

evohealth

April 2023



Evohealth acknowledges that we work on the traditional lands of many Aboriginal clans, tribes, and nations.

We commit to working in collaboration with Aboriginal and Torres Strait Islander communities and peoples to improve health, emotional and social well-being outcomes in the spirit of partnership.

About Evohealth

The delivery of healthcare is complex.
Our focus is not.

Better health for all Australians.

Contents

About this white paper

Background

CAR T-Cell Therapy: Is Australia ready, willing and able? is an evidence-based and product-agnostic white paper developed between June 2022 and April 2023. It was independently authored by Evohealth, a specialist health advisory firm, in partnership with a project Advisory Committee of clinicians, patients, patient advocates, policymakers, researchers and delivery/ implementation experts.

This white paper analyses the current state of chimeric antigen receptor (CAR) T-cell therapy in Australia, expected opportunities and our healthcare system's preparedness for delivering CAR T-cell therapy at scale. It also provides results of a rigorous evidence-based economic analysis of the health and societal benefits of CAR T-cell therapy.

Approach

This white paper has a focus on multiple myeloma. Multiple myeloma is the most recent clinical indication for CAR T-cell therapy both in Australia and overseas. It is expected to have a disruptive impact on care due to the relatively large patient population compared with the currently approved indications for CAR T-cell therapy in Australia.

This white paper has been informed by:

- A comprehensive review of published academic literature, grey literature and clinical guidelines;
- Interviews with Australian policymakers, clinicians, patients and patient advocates with involvement in CAR T-cell therapy and/or multiple myeloma care;
- A rigorous and evidence-based economic analysis of the health and societal benefits of CAR T-cell therapy (see Appendix A for methodology); and
- The contributions of our expert project Advisory Committee members

While this project received funding from Janssen Australia, Janssen representatives did not participate in the development of the report to ensure the independence of Evohealth and the project Advisory Committee.

Foreword

This report has been informed by the real stories of lived experience of multiple myeloma patients, as well as the expert perspectives of clinicians, patient advocates and many others who are rather involved in the difficult journey of navigating multiple myeloma. Among those who are closest to the devastating impacts of blood cancer, there is great hope for the promise of CAR T-cell therapy.

> Australia is an international leader in the development of CAR T-cell therapy. CAR T-cell therapy for patients with multiple myeloma is a **transformative technology** - the response rate and duration of response is unprecedented. As we move this technology into earlier lines of therapy, **functional cure may be achievable for a significant proportion of patients**. As a community, we need to ensure we have a prompt and coordinated roll out of CAR T-cell therapy to ensure consistent supply of product, equitable access and high quality delivery of care to all patients across the country who would benefit from this therapy - **HAEMATOLOGIST**

> I might not be here next year and I dare not think too deeply about new treatments because I don't want to be disappointed. With CAR T-cell therapy, I sit in hope for all multiple myeloma patients - that **in the future, they won't have to experience what I've gone through** [with conventional treatments] **- MULTIPLE MYELOMA PATIENT**

> We ask the Government to not only **make this game-changing therapy available to Australians living with myeloma** but to ensure the infrastructure supporting the delivery of CAR T-cell therapy encompasses support in the community. As not all hospitals will be able to facilitate CAR T-cell therapy, **Myeloma Australia's Myeloma Support Nurses are here to fill the gaps.** They are highly experienced haematology nurses available to provide the education and support that doesn't exist in most treating centres. We are here to walk alongside those living with myeloma, their carers and health professionals from diagnosis to end of life **- MYELOMA AUSTRALIA**

Acknowledgements

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We extend our sincere thanks to our multiple myeloma patients, **Geoff Nyssen** and **Nigel Rosen,** for sharing their stories with us.

Executive Summary

Multiple myeloma is a devastating and incurable disease affecting thousands of Australians and their families. Patients endure months or even years of debilitating treatment with harsh medicines and intensive procedures in a hope for survival. There is an immense physical, psychological and financial toll as patients adapt to a 'new normal' defined by their disease [1].

There is hope on the horizon. chimeric antigen receptor (CAR) T-cell therapy is a promising new treatment that harnesses a patient's own immune cells to fight life-threatening cancers. Evidence shows that a single dose of CAR T-cell therapy is safe, effective and offers hope where no comparable treatment is available. CAR T-cell therapy also has the potential to alleviate protracted treatment timeframes and restore quality of life to patients [14, 15].

For Australians to benefit from this innovative treatment, CAR T-cell therapy must be funded and made available to suitable patients in public hospitals. Patients living with multiple myeloma and other blood cancers do not have time to wait.

Too many patients are being left behind

Over the last 50 years, the introduction of combination chemotherapy and immunotherapy, radiation therapy and stem cell transplantations has improved the likelihood of survival for many blood cancers [17]. Despite these advances, thousands of patients each year continue to lose their lives to blood cancer. As a collective, **blood cancer is Australia's second deadliest cancer**, taking 16 lives each day [18, 19].

Multiple myeloma is a rare and incurable blood cancer that causes debilitating bone pain, fatigue and fractures, with **2,625 new diagnoses** in Australia each year [13]. It has one of the poorest prognoses of all blood cancers, with only **55 per cent** of patients living beyond five years of their diagnosis and **27 per cent** of patients living beyond ten years [13, 20]. Multiple myeloma patients will typically undergo years of treatment with cytotoxic chemotherapy medicines to keep symptoms at bay and prolong their survival [21]. Yet, even with the best available treatments, **1,100 Australian families** lose a loved one to this cruel disease each year [10, 13]. These Australians and their families deserve better.

Up to
2,625
Australians are diagnosed with multiple myeloma each year [5].

55%
of patients
with multiple myeloma live for five years beyond their diagnosis [13]

1,100
Australians
die from multiple myeloma each year [10,13].

Fighting back with next-generation treatments

The next generation of therapies offer hope. There is mounting evidence, both from Australian and international experience, that CAR T-cell therapy is a safe, effective and durable treatment [1, 2, 23]. CAR T-cell therapy has the potential to reshape traditional treatment pathways for blood cancer, replacing relentless cycles of chemotherapy and other treatments with a single dose infusion [24-26].

The first CAR T-cell therapies for multiple myeloma have received regulatory approval in the United States and Europe, with the lifesaving treatment now being administered in hospitals to eligible patients. There is compelling evidence from clinical trials that between **72 and 97 per cent** of multiple myeloma patients respond to CAR T-cell therapy [8, 26]. Importantly, the effects of a single dose treatment are durable, with up to **77 per cent** of patients remaining free of disease progression at 12 months [8, 12]. This is a significant gain over what is observed with conventional treatments, particularly for those patients who have already failed several prior therapies.

Up to 97%
of multiple myeloma patients respond to CAR T-cell therapy [8].

77%
of multiple myeloma patients remained progression-free at 12 months [8].

> CAR T-cell therapy has the potential to replace stem cell transplants for multiple myeloma within the next five years.-
> **AUSTRALIAN HAEMATOLOGIST**

To date, Commonwealth and State & Territory Governments in Australia have taken the important step of funding two CAR T-cell therapies (Kymriah® and Yescarta®) for relapsed and refractory forms of certain leukaemias and lymphomas [28, 29]. It is expected that multiple myeloma will be the next indication approved for CAR T-cell therapy in Australia. We must therefore anticipate a future in which CAR T-cell therapy is a mainstay of treatment for blood cancer for much higher volumes of patients.

The introduction of CAR T-cell therapy for multiple myeloma could quadruple the number of patients seeking access to care compared to current levels [6].

Saving lives and reducing the burden of disease

With 40 to 50 CAR T-cell therapies expected to be approved globally by 2030 [30], there will be growing pressure on Governments to fund patient access to these life-saving and transformational therapies. The benefits to patients are compelling: Evohealth has modelled the health and societal benefits of CAR T-cell therapy for patients with multiple myeloma at different stages of their treatment journey, informed by a comparison of published clinical trial results and the current standard of care.

Our analysis shows that CAR T-cell therapy for multiple myeloma can delay disease progression by an average of almost **6 years** versus just 2.4 years for current therapies. Patients receiving CAR T-cell therapy could live for **15 years** from diagnosis, restoring life expectancy to that of the general Australian population based on the median age of diagnosis. For patients with an incurable disease, these additional years of life represent priceless opportunities to spend precious time with family and friends, be part of their communities, experience important milestones and be free of the physical and psychological toll of their disease [31]. While CAR T-cell therapy benefits patients at any point in the treatment pathway, the most promising results are expected with early use – consistent with innovative care in other disease areas.

Patients treated with CAR T-cell therapy can be expected to live longer and with less disease burden than patients receiving conventional treatments.

Evohealth's modelling shows that CAR T-cell therapy as a first-line treatment can achieve:

An average of
15 years
of life from the point of diagnosis

886
fewer patients dying from multiple myeloma

Productivity gains of
$36 million
from patients and carers returning to work

$6.5 million
gained in additional tax revenue due to increased productivity

Our healthcare system must prepare for a new era of blood cancer treatment

The introduction and scaling of novel treatments such as CAR T-cell therapy for larger populations poses complex challenges. Healthcare systems must navigate the negotiation of funding arrangements, equitable access, manufacturing, logistics, accreditation and clinical delivery of specialised products. Countries across Europe, the United Kingdom, Asia and the United States are already taking action to navigate the next wave of therapies with innovative funding agreements, accreditation processes, partnerships, centres of excellence and models of care [32-34]. To avoid being left behind, Australian Governments must act now to ensure our hospitals, clinical workforce and budgets are prepared for a new era in cancer medicine, in which CAR T-cell therapy is the standard of care.

Is Australia ready, willing and able to deliver CAR T-cell therapy?

In 2021, Evohealth published *Cell & Gene Therapies: Rising to the Challenge*. The report examined Australia's preparedness for the arrival of highly specialised therapies such as CAR T-cell therapy and set the tone for the challenges that lay ahead [15]. In this white paper, we investigate if Australia is ready, willing and able to deliver funded access to CAR T-cell therapy for patients at scale.

Our key findings are:

Ready?

Australia is at the start of its journey with CAR T-cell therapy [35]. We identified three key barriers to delivering CAR T-cell therapy at scale:

- The **quantum of Commonwealth and State & Territory Government health funding** available to cover the cost of new therapies;
- The **capacity of our already-stretched healthcare system** to meet patient demand for this highly specialised therapy; and
- The **lead-times required** for treatment sites to be established and accredited for delivery of CAR T-cell therapy.

Willing?

While there is a groundswell of support for funded access to CAR T-cell therapy for suitable patients among clinicians and patient groups, Australian Governments (at all levels) have differing perspectives on supporting investment in CAR T-cell therapies at scale. As more CAR T-cell products receive regulatory approval and more patients become eligible for access, a nationally consistent and equitable approach to reimbursement, referrals and patient support will be critical.

Able?

Eleven treatment sites across Australia have already demonstrated their capability and capacity to deliver CAR T-cell therapy safely to patients through clinical trials and/or commercial use [16]. While this provides a strong foundation for delivery, three barriers threaten Australia's ability to deliver CAR T-cell therapy at scale:

- The **small pool and pipeline of clinical staff** (including haematologists, nurses, lab technicians and ancillary) with domain expertise in CAR T-cell therapy;
- Australia's current **reliance on offshore manufacturing** of CAR T-cells; and
- Sufficient access to **real-world evidence** to inform clinical decision-making and health service planning.

Our healthcare system needs to keep pace. With over **1,000 clinical trials underway globally** for CAR T-cell therapies [36], we must be ready for swift innovation in how these treatments are delivered so patients can have hope for a better future.

Recommendations

There are seven evidence-based recommendations to ensure Australia's healthcare system is ready, willing and able to implement CAR T-cell therapy at scale within the next five years. We have a window of opportunity to change the future for Australians living with, and dying from, blood cancer - including multiple myeloma. Embracing these recommendations will ensure patients in need receive equitable and timely access to lifesaving therapies, positioning Australia as a leader in care.

- Prioritise national reimbursement of CAR T-cell therapy;
- Streamline and, where appropriate, standardise the implementation and delivery of CAR T-cell therapies;
- Invest in training and growing the next generation of CAR T-cell therapy specialists;
- Develop five- and ten-year plans for delivery of CAR T-cell therapy for each State & Territory;
- Increase funding to existing patient support organisations to educate and empower patients about CAR T-cell therapy;
- Build a national real-world evidence base for CAR T-cell therapy; and,
- Establish a collaboration to shape a national plan for onshore cellular manufacturing.

Detailed recommendations

1 Prioritise national reimbursement of CAR T-cell therapy

National reimbursement of safe and effective CAR T-cell therapies for suitable patients is the single greatest barrier to transforming the outlook of blood cancer in Australia. Innovative funding models have been an important pillar of success to date in bringing CAR T-cell therapies to patients. As clinical evidence to support the use of CAR T-cell therapies in earlier treatment lines grows, there will be greater pressure to ensure Australian patients have timely and equitable access to lifesaving treatments.

2 Streamline and, where appropriate, standardise the implementation and delivery of CAR T-cell therapies

Patient access to CAR T-cell therapy is being hampered by fragmented approval and implementation processes for new therapies. With the current landscape, it can take several years from the time a CAR T-cell therapy product is approved to it being available to patients in public hospitals. Even for available therapies, barriers to equitable access and referral mean that eligible patients are missing out on CAR T-cell therapy because of their location or choice of health practitioner. Approval, implementation and delivery of CAR T-cell therapies must be streamlined, simplified and unified.

3 Invest in training and growing the next generation of CAR T-cell therapy specialists

The scaling up of CAR T-cell therapy will intensify demand on specialist healthcare staff (such as haematologists, nurses, intensivists, pharmacists and lab technicians), clinical resources (such as apheresis and infusion clinics, hospital and intensive care beds, laboratories) and specialist manufacturing. With an already strained healthcare workforce, urgent action must be taken to retain Australia's existing CAR T-cell experts and to invest in building a talent pipeline by training the next generation of clinical, research and technical/manufacturing leaders.

4 Develop five- and ten-year plans for delivery of CAR T-cell therapy for each State & Territory

Developments in CAR T-cell therapy are accelerating at pace, with exponential growth occurring in parallel for other highly specialised therapies. With 40-50 CAR T-cell therapies expected to be approved globally by 2030 [30], we must anticipate significant increases in demand on existing and future treatment sites. With States & Territories responsible for the clinical delivery of CAR T-cell therapy, their development of five- and ten-year plans will be instrumental in forward planning for health expenditure, treatment site selection, service and capacity planning, workforce development and overarching clinical governance.

5 Increase funding to patient support organisations to educate and empower patients about CAR T-cell therapy

As a novel therapy, the choice to receive CAR T-cell therapy can be daunting for patients and their families. Patient support organisations play an important role in educating, informing and supporting patients to be in control of their disease journey. The demand for these services will only increase as more CAR T-cell therapies become available. A multi-pronged strategy that harnesses and builds on the expertise and resources already held by patient support organisations in the blood cancer space will go a long way to ensuring every patient is educated, empowered and equipped.

6 Build a national real-world evidence-base for CAR T-cell therapy

Real-world evidence on patient outcomes with CAR T-cell therapy is critical for informing the future treatment landscape. Clinical outcomes data will inform decisions about its place in practice and funding of new and existing therapies. Activity data is instrumental for health service planning, particularly as hospitals ramp up capacity to deliver CAR T-cell therapy at scale in the future. There is an urgent need to invest in a national real-world evidence-base that serves the needs of policy, clinical, delivery and industry stakeholders. Opportunities for industry to co-fund data collection, input and reporting should be explored.

7 Establish a collaboration to shape a national plan for onshore cellular manufacturing

There is an opportunity for Governments to benefit from investing in onshore cellular manufacturing. The ability to produce CAR T-cells onshore will simplify patient access to care, minimise exposure to disruptions in supply chains and support job creation and upskilling for Australian workers. A national approach will ensure that our brightest minds can collaborate, not compete, in advancing CAR T-cell technology here in Australia.

CAR T-cell therapy is an investment in a better future for Australians with multiple myeloma. Together with patients, their families and clinicians, we call on Australian Governments to commit to saving lives with early and equitable access to CAR T-cell therapy.

CAR T-cell therapy: A new weapon in the fight against blood cancer

Each year, 100+ new

clinical trials for CAR T-cell therapies are registered [37].

Six CAR T-cell therapies

are approved and being used around the world today to fight blood cancers [25].

There are 1,000+ clinical trials

underway globally for CAR T-cell therapies [36].

40-50

40-50 CAR T-cell therapies are expected to be approved by 2030 [30].

100+

100+ CAR T-cell therapies are expected to be approved by 2035 [36].

The unmet needs of multiple myeloma patients

There is no cure

for multiple myeloma.

1,100 Australians die each year from multiple myeloma [10, 13].

2,625 Australians are diagnosed with multiple myeloma each year [13].

55% five-year survival

27% ten-year survival

Multiple myeloma has a five-year survival rate of 55 per cent [13] and a 10-year survival rate of just 27 per cent [22].

The benefits of CAR T-cell therapy

Up to 97% of multiple myeloma patients who received a single infusion of CAR T-cell therapy respond to treatment [12].

CAR T-cell therapy will allow more patients with multiple myeloma and their carers to return to work. This could yield productivity benefits of up to $9 million for a cohort of patients diagnosed in 2022 alone.

With early access to CAR T-cell therapy, Evohealth's analysis indicates that...

15 years

Multiple myeloma patients could live for an average of 15 years from diagnosis compared to less than 7 years on current therapies.

6 years

Multiple myeloma patients could live free of disease progression for an average of 6 years from diagnosis

886 deaths avoided

For a cohort of patients diagnosed in 2022, 886 deaths due to multiple myeloma could be avoided.

The future of blood cancer treatment is changing

Blood cancer is Australia's second deadliest cancer, accounting for more than 5,950 deaths each year [18, 19]. Almost 20,000 Australians will be newly diagnosed with a form of blood cancer such as myeloma, leukaemia or lymphoma in 2023, with devastating impacts on their health and quality of life [19]. In addition to managing debilitating symptoms, patients undergo gruelling treatments over months or years - all whilst carrying the psychological burden of an uncertain prognosis [18].

While survival rates have improved over the last 50 years, there is a heavy toll associated with current treatments. Intensive regimens of combination chemotherapy, immunotherapy, targeted therapies, stem cell transplants and radiotherapy are commonly used, with risks and side effects that can affect patients for the rest of their lives [14]. Patients often experience pain, fatigue, nausea, gastrointestinal symptoms, immunocompromise and an array of other symptoms as a result of treatment, with considerable impacts on their quality of life and social participation [14, 38].

Many patients will sadly experience a relapse of blood cancer following an initial remission. Tragically, some will go on to develop refractory disease that stops responding to treatment altogether [14]. Every day, 16 Australians die from blood cancer – many of whom, along with their loved ones, have struggled with the weight of an incurable condition [19].

The rise of highly specialised therapies

Highly specialised therapies (HSTs) are emerging as a powerful new weapon in the fight against blood cancer. Unlike conventional medicines (such as chemotherapy) that use synthetic chemicals to treat disease, HSTs harness a patient's own biology to target pathology at its source, providing a durable therapeutic effect with a single dose [15]. There are two main types of HSTs:

- **Cellular therapies** involve a transfer or modification of live cells into a patient's body, such as in CAR T-cell therapy.
- **Gene therapies** introduce, replace or alter DNA within a patient's cells to correct an underlying cause of disease.

CAR T-cell therapy: a single dose cancer treatment

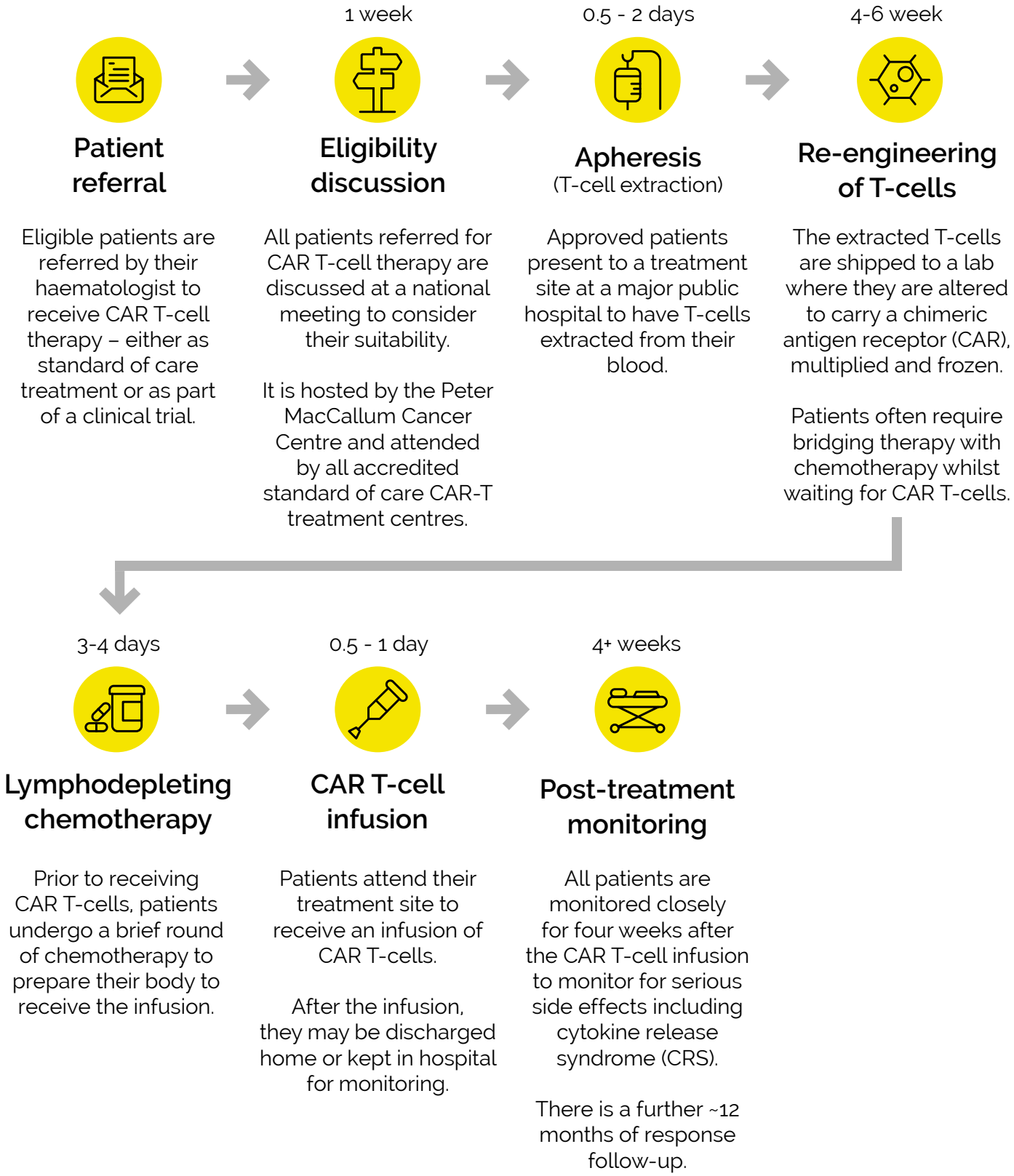
CAR T-cell therapy is a novel HST that has established itself as a frontrunner in fighting blood cancer. This innovative treatment alters a patient's own immune cells to identify and attack cancer cells [39, 40]. Administered in a single infusion, CAR T-cell therapy is emerging as a viable alternative to existing treatments such as chemotherapy in patients with relapsed or refractory leukaemia, lymphoma and, most recently, multiple myeloma [29]. It has been shown to be safe and effective in these indications with remarkable outcomes [14, 15]. For example, CAR T-cell therapy has led to complete remission in 80 per cent of eligible patients with acute lymphoblastic leukaemia (ALL) who had exhausted all alternative treatments [41]. By inducing remissions where other treatments have failed, CAR T-cell therapy offers hope of survival and better quality of life for blood cancer patients [14, 15].

What is CAR T-cell therapy?

CAR T-cell therapy is a highly specialised therapy that is currently used to treat select forms of relapsed or refractory blood cancers, although clinical trials are investigating its use in earlier treatment lines. CAR T-cell therapy works by altering a patient's own T-cells (a type of white blood cell) to carry chimeric antigen receptors (CAR) on their surface, which equips the immune system to identify and attack cancer cells. In this way, CAR T-cell therapy can be thought of as a 'living medicine'. CAR T-cell therapy is given as a single dose, usually as a day procedure at an infusion clinic, followed by around one month of close monitoring and 12 months of follow-up care [1-3]

Unlike chemotherapy which requires repeated treatment cycles, CAR T-cell therapy is a one-time procedure. There are several important steps to prepare for the infusion and strict monitoring requirements in the weeks afterwards (Figure 1) [3].

Figure 1. A typical journey for treatment with CAR T-cell therapy in Australia [3],[16]



Access to CAR T-cell therapy in Australia

CAR T-cell therapy is making its way to Australian shores. At the time of writing, three CAR T-cell products – Kymriah®, Yescarta® and Tecartus® – are approved for use in our public hospitals. Kymriah® and Yescarta® are publicly co-funded by Commonwealth and State & Territory Governments for eligible patients, whereas Tecartus® is only available for self-funded or third-party funded patients (Table 1) [28, 29].

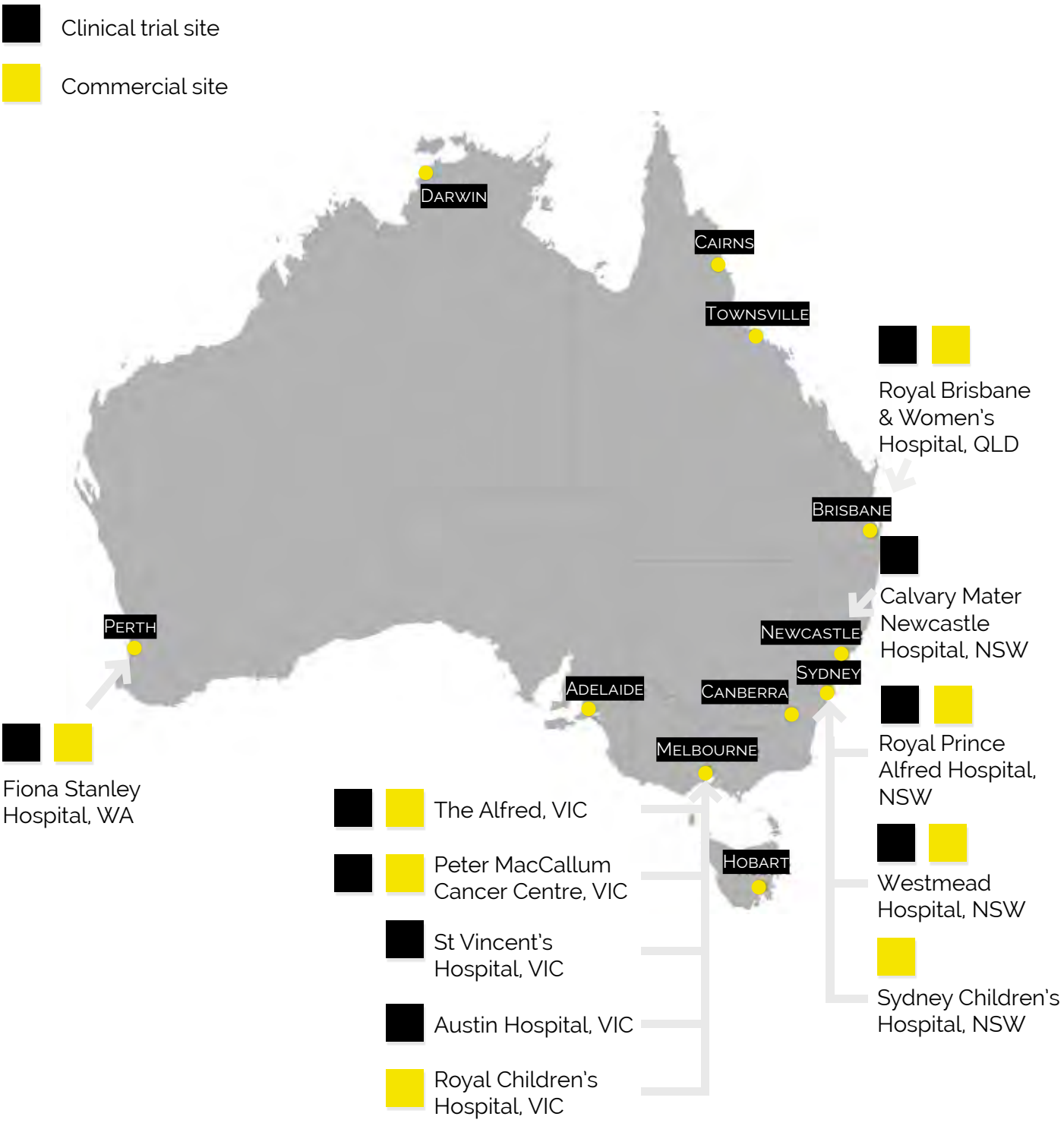
Table 1: CAR T-cell therapies available in Australia [28, 29].

Product	Approved indications
Kymriah® Tisagenlecleucel	Paediatric patients with relapsed or refractory B-cell acute lymphoblastic leukaemia (ALL). Relapsed or refractory adult diffuse large B-cell lymphoma (DLBCL) after two lines of treatment.
Yescarta® Axicabtagene ciloleucel	Relapsed or refractory adult DLBCL, primary mediastinal large B-cell lymphoma (PMBCL), transformed follicular lymphoma (TFL) and high-grade B-cell lymphoma (HGBCL).
Tecartus® Brexucabtagene autoleucel	Relapsed or refractory mantle cell lymphoma (MCL).

As a highly complex and specialised treatment, CAR T-cell therapy is currently restricted to a small number of major public hospitals [16]. At the time of writing, Evohealth has identified 11 hospitals across New South Wales, Victoria, Queensland and Western Australia that administer CAR T-cell therapy to eligible patients [16] (Figure 2). These hospitals treat both local and interstate patients, with cross-border arrangements in place between State & Territory Governments to support access to care for all Australians [42].

CAR T-cell therapy treatment sites

Figure 2. Australian hospitals that administer CAR T-cell therapy [16]



The next wave of CAR T-cell therapy

CAR T-cell therapy is in its infancy in Australia, with use currently restricted to small clinical populations. However, since the first CAR T-cell product was approved by overseas regulators in 2017, research and development has accelerated at pace (Figure 3) [43]. More CAR T-cell therapies are expected to become available to Australian patients in the near future, with at least four already approved by overseas regulators for specified lymphomas (Breyanzi®, Carteyva®) and multiple myeloma (Carvykti®, Abecma®) [24]. Within the next five years, we must be prepared for the cancer treatment landscape to shift dramatically.

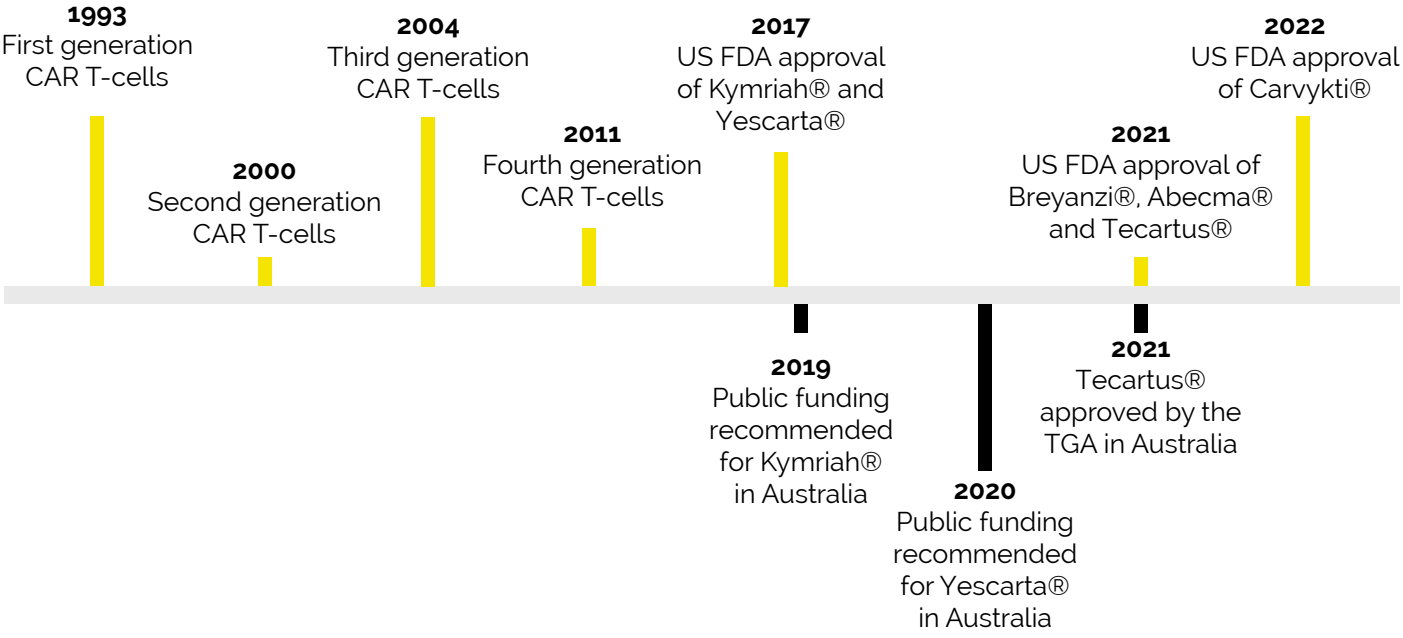


Figure 3. The accelerating pace of CAR T-cell research and development - adapted from Teoh & Chng (2021) [44].

More CAR T-cell therapies for more patients

The future of cancer medicine is changing before our eyes, with HSTs playing an increasingly prominent role. CAR T-cell therapy is gaining strong momentum (Figure 4). There are 1,000+ clinical trials globally for CAR T-cell therapies, with almost 100 new trial registrations each year [36, 45]. In Australia, there are 130 clinical trials underway for regenerative medicines including 15 CAR T-cell therapy trials registered between 2015 and 2021 [46].

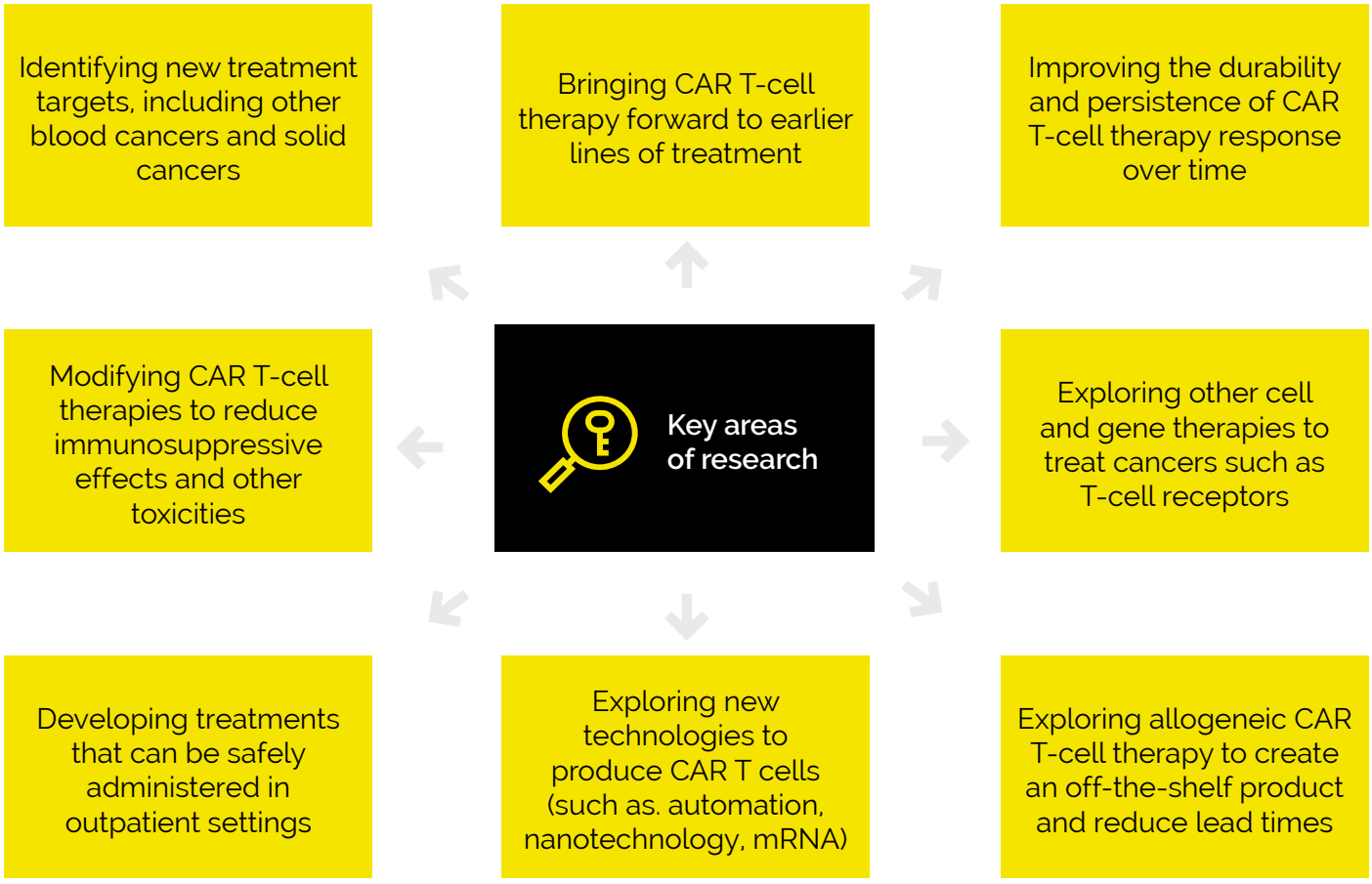
The impact of these advances will soon be felt by our healthcare system. As HSTs usher in a new era of medicine, there is expected to be significant growth in the volume of CAR T-cell products entering the Australian market. It is estimated that 40-50 CAR T-cell therapies will be available globally by 2030, with half of these expected to be for blood cancers [29].

Figure 4. The global landscape for highly specialised therapies [15, 29, 36, 37]

2,000+	1,000+	100+	40-50	100+
cell and gene therapies in clinical trials globally.	clinical trials underway for CAR T-cell therapies in cancer treatment.	new clinical trial registrations each year for CAR T-cell therapies.	CAR T-cell therapies expected to be available by 2030.	CAR T-cell therapies forecast to be approved by 2035.

As research and innovation progresses, future CAR T-cell therapies are expected to look very different from today. Current areas of investigation (Figure 5) are seeking to improve many aspects of the technology, from safety and efficacy to the possibilities of new antigen targets – which would allow CAR T-cell therapy to be used for a wider range of clinical indications.

Figure 5. Key areas of CAR T-cell therapy research worldwide [22, 25, 47, 48].



Gains in CAR T-cell research and development will deliver a range of benefits for Australian patients and the broader healthcare system, including:

More durable responses:

New generation CAR T-cell therapies, combined with a better understanding of the technology, will enable the production of T-cells that persist for longer post-infusion - producing a deeper and more durable treatment response [22, 48].

Faster treatment times:

The possibilities of allogeneic (or off-the-shelf) CAR T-cell therapies, as well as gene-editing technologies that can create CAR T-cells within the body, could shorten manufacturing timeframes to 24 hours or less and treatment timeframes to approximately two hours [22, 47, 49].

Better treatment experience:

Several studies are investigating ways to reduce toxicity and improve management of side effects arising from CAR T-cell therapy, such as cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome. This will improve the treatment experience and health outcomes for patients [47, 48].

Reduced resistance:

Improved engineering and increased specificity of CAR T-cells will enhance the ability to control therapy, reducing the risk of poor outcomes associated with treatment resistance and rejection [50].

Wider scope of treatment:

With new treatment targets being identified, CAR T-cell therapy is expected to become available for more clinical indications with larger patient populations, such as multiple myeloma or even some autoimmune conditions [51]. While research is underway to explore the potential of CAR T-cell therapy for solid tumours, progress in this area has been slower than for haematological B-cell malignancies [47].

Streamlined manufacturing:

As technology and automation improves, a reduction in labour costs for the development of CAR T-cells can be reasonably expected to follow. Manufacturing optimisation can also limit product deviations and reduce batch failures, achieving efficiencies whilst increasing quality and consistency [52, 53].

Multiple myeloma: a catalyst for change

Multiple myeloma is highly anticipated to be the next clinical indication considered for CAR T-cell therapy in Australia [4]. As an incurable condition associated with poor quality of life, funded access to CAR T-cell therapy has the potential to be transformational for thousands of Australians that are newly diagnosed each year and their families [5].

The brutal toll of an incurable disease

Profile of multiple myeloma in Australia

2,625
Australians are diagnosed with multiple myeloma each year [5].

1,100
Australians die from multiple myeloma each year [10, 13].

5,000
By 2035, over 5,000 Australians will be diagnosed with multiple myeloma each year [5, 10].

55%
The five-year survival rate for multiple myeloma is just 55 per cent [13].

Overview of multiple myeloma

Multiple myeloma is a rare and incurable blood cancer that develops from plasma cells, a type of white blood cell found in bone marrow [19]. Plasma cells are a crucial part of a healthy immune system, producing antibodies that help to fight infections. When they become cancerous, abnormal plasma cells spread throughout the bone marrow and reduce space available for healthy blood cells, resulting in abnormal antibodies with no useful function [5].

Multiple myeloma affects areas of the body where bone marrow is found including the spine, skull, shoulders, ribs, hips and pelvis [19]. Patients experience a range of challenging symptoms such as bone pain and fractures, frequent infections, tiredness, shortness of breath, kidney problems and frequent bruising [19]. There are typically periods of relapse (where symptoms are present) and remission (where patients are disease-free and symptom-free) [5].

> Multiple myeloma is not a cancer that you can just cut out. It has a poor prognosis and treatment is complex. - **MULTIPLE MYELOMA PATIENT**

Treatment approach

The current standard of care for multiple myeloma involves several cycles of combination therapy (usually with two or three chemotherapy or immunotherapy drugs used in combination) and, for those who are eligible, an autologous stem cell transplantation (ASCT) (Figure 6). As an incurable disease, the goal of treatment is to alleviate symptoms, achieve periods of remission and prolong survival [20]. Treatment typically commences when disease is active and continues until it is no longer detectable, although many patients now undergo maintenance therapy continuously [20, 35].

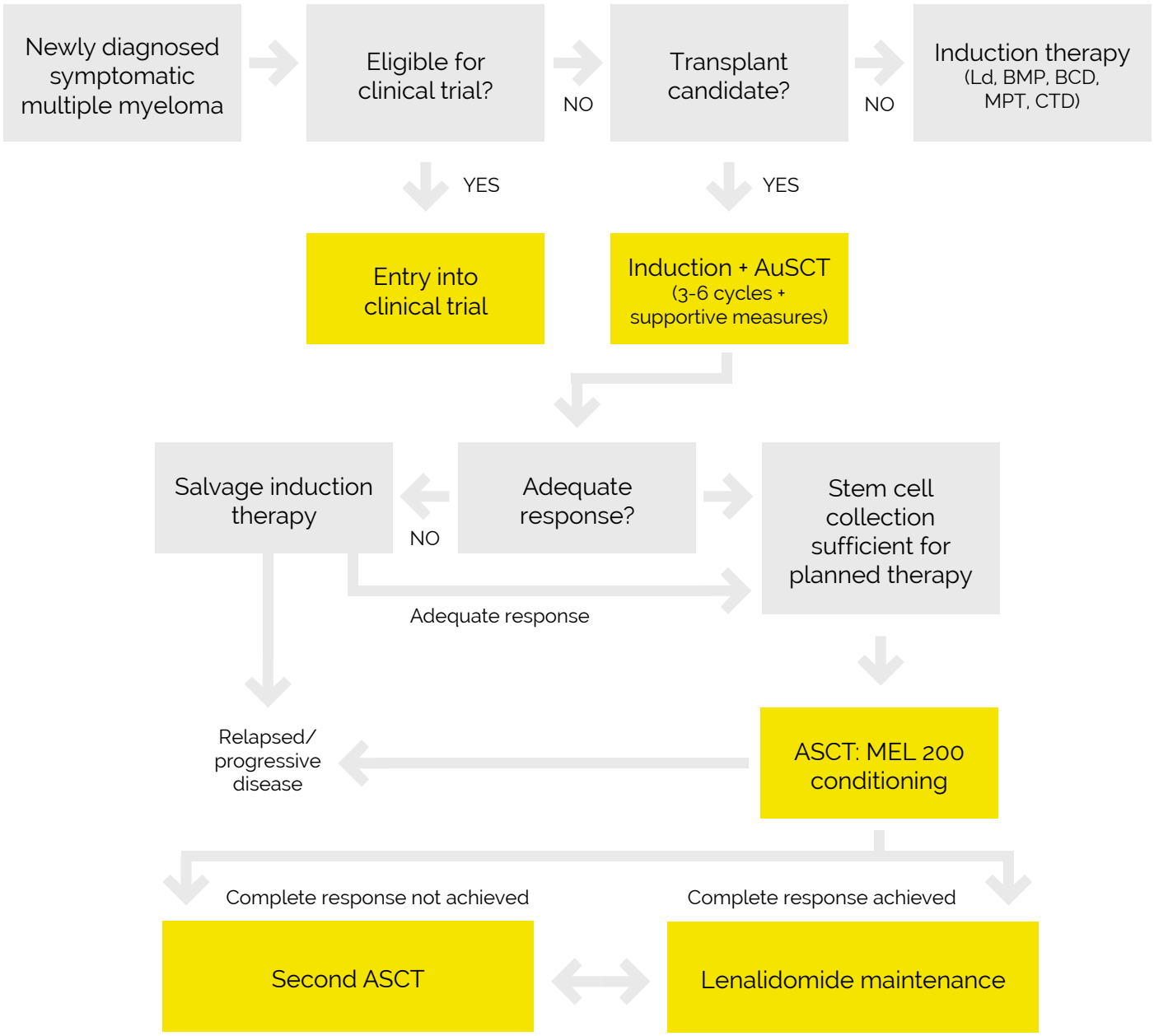


Figure 6. Treatment pathway for newly diagnosed symptomatic multiple myeloma - adapted from the Australian Clinical Practice Guideline for multiple myeloma [20].

Patient story

"I had a stem cell transplant as first line treatment, which involves high dose chemotherapy. That was brutal. I lost my hair and there were a lot of side effects… but you get through it. I was then put on a trial of two other therapies which led to peripheral neuropathy (my neuropathy is irreversible and puts me at increased risk of falls and fractures). That's been awful. I went into remission for 18 months or so, then relapsed."

Patient story

"Since my diagnosis, I've gone through horrendous treatments over eight and a half years. I've had radiation therapy where you just get fried, as well as chemotherapy and immunotherapy. I'm at the hospital for regular infusions and injections. There's nothing I can do for the fatigue, and the gastrointestinal side effects are my new normal. My hope is that, in the future, other people with multiple myeloma don't have to go through what I have."

Existing treatments are falling short

Impacts to multiple myeloma patients

Multiple myeloma patients treated in Australia experience immense challenges, with a range of unmet needs in relation to their care and their prognosis. Even with continuous use of the best available therapies, multiple myeloma patients live every day with the toll of their disease and the weight of an incurable condition.

Key unmet needs of multiple myeloma patients

Poor survival rates

Existing treatments have poor survival rates. Even with treatment, **only 51 per cent of patients live for five years** beyond their diagnosis, and only 27 per cent live beyond 10 years [13, 21].

High symptom burden

Multiple myeloma is associated with symptoms that impair physical function such as bone pain, fractures, fatigue and shortness of breath. The degree of symptom burden varies depending on each patient's tolerance of, and response to, drug therapies [19]. The severity and impact of symptoms is often underestimated by physicians [54].

"I woke up with low back and rib pain one morning, it was excruciating just to get out of bed. I went to the GP and the tests showed myeloma. I was working one day and ended up in hospital 3 days later. I became a patient." – Patient representative

High treatment burden

The standard of care for multiple myeloma involves continuous treatment to keep symptoms at bay [20]. The cytotoxic treatments used have serious side effects such as pain, fatigue, nausea and gastrointestinal problems [14]. Even when patients are in remission, the frequent medical appointments required are a constant reminder of their disease.

"There is a generation of multiple myeloma patients that do not know what it's like to be free of treatment." – Patient advocate

An estimated 75 per cent of patients undergo an autologous stem cell transplant (ASCT), a major procedure that targets a patient's stem cells to replace diseased bone marrow [55]. Recovery from an ASCT can take three to six months [35]. This has a substantial impact on both a patient and their caregiver's ability to participate in activities of daily living or continue working. "Only 51 per cent of multiple myeloma patients return to work after receiving an ASCT and only 20 per cent continue working after their first relapse [56, 57]."

"**The therapies for multiple myeloma are aggressive and there is a risk/ benefit trade-off for patients who may be frail or have comorbidities from prior treatments.**" – Clinician

Disease worsening over time

As a chronic and progressive disease, patients with multiple myeloma experience fewer and shorter remissions (symptom-free periods) as time goes on [58]. With each relapse, there is worsening disease progression. For example, Bruno et al. (2020) found that the median remission period declined from 15 months after an initial treatment to nine months after a second treatment; three months after a third treatment; and one month after a fourth treatment [58].

Loss of independence

Multiple myeloma symptoms and treatment have a physical, social and psychological toll, which can result in a loss or reduction of independence. Many patients are reliant on a partner or family member as their carer, both to navigate day-to-day activities and to manage the enormous and ongoing commitment to care.

"**My wife has become my carer 90 per cent of the time. She doesn't like to leave me in case something happens, it's like we've been in lockdown continually.**" – – Patient representative

"**The commitment to treatment is enormous. If you're on your own, you couldn't do it.**" – **PATIENT REPRESENTATIVE**

Reduced social participation

Many multiple myeloma patients are immunocompromised. This limits their freedom to socialise with family and friends or be part of their communities, particularly against the backdrop of the COVID-19 pandemic. As well as physical risk, there is a mental toll associated with the fear of acquiring an infection, as this can be life-threatening [59]. Around one third of multiple myeloma patients die of infection-related causes [59].

Incurable diagnosis

There is a unique psychological and emotional burden that comes with an incurable or terminal diagnosis. As patients come to terms with their own mortality, up to one quarter will experience depression, anxiety or PTSD and many more will suffer from psychological distress [38].

Patient story

I was diagnosed with multiple myeloma in 2014 and given 10 years to live. I was in my early forties, living a busy life with time divided between climbing the career ladder and spending time with my family. My diagnosis has changed my life significantly. I have been forced to stop working due to the debilitating effects of multiple myeloma and associated treatments on my body. Since my diagnosis I have lived in constant uncertainty about my prognosis and the fear of treatment failure, not knowing what the next line of therapy might be.

Impacts to families and communities

People living with multiple myeloma experience poorer health-related quality of life than the general population and other cancer patients. Significant difficulties in physical functioning, social participation, psychological wellbeing, mobility and overall health are common [54]. A multiple myeloma diagnosis reduces a person's capacity to be present with their families, enjoy time with loved ones, participate in community and leisure activities, remain in full-time employment and experience important events in their lives and those of their loved ones.

A recent report by Rare Cancers Australia powerfully highlighted the impact of cancers such as multiple myeloma on patients, families and societies, measured in major life milestones that are missed, relationships that are changed and opportunities for social participation that are lost [30]. For patients and their families, the importance of exploring novel treatments such as CAR T-cell therapy cannot be understated.

CAR T-cell therapy offers a unique hope for patients

Clinical trial and research findings

CAR T-cell therapy has demonstrated efficacy as a single dose treatment for multiple myeloma, with two products (Abecma® and Carvykti®) already approved by overseas regulators [22, 24]. These therapies are being used in hospitals across the United States and Europe, offering a lifeline to multiple myeloma patients who have tried and failed at least three prior lines of treatment [22]. Yet, funded access to CAR T-cell therapy for multiple myeloma remains a barrier for Australian patients today.

> My hope is that, with CAR T-cell therapy, multiple myeloma will become a chronic disease rather than a terminal one.
>
> **- MULTIPLE MYELOMA PATIENT**

CAR T-cell therapy is inducing and sustaining remissions

CAR T-cell therapy has shown an ability to induce lasting remissions in multiple myeloma patients – some without the need for maintenance therapy [4]. Clinical trial data for Carvykti® has shown that multiple myeloma patients receiving CAR T-cell therapy had response rates of up to 97 per cent By comparison, a response rate of only 30 per cent was seen with other approved treatments for relapsed and refractory disease [12]. This is extraordinary, particularly considering the difficulty of treating patients who have endured multiple rounds of treatment.

> It's not without side effects, but CAR T-cell therapy is a life-changing treatment. I feel so much better having had it. I have energy, I'm more alert and I can participate in life again. I now feel well and much more active, both physically and mentally. It's a wonderful treatment.
>
> **- MULTIPLE MYELOMA PATIENT**

The clinical benefits accrue with early use

There is growing evidence that clinical outcomes improve as CAR T-cell therapy is brought into earlier lines of treatment, leading to longer remissions and higher rates of survival [60]. While early in its evolution, this has been shown for CAR T-cell therapy in lymphoma: the original approved indication for Yescarta® was in a later line of therapy based on the evidence available at the time however the FDA approved use in April 2022 for patients whose disease was refractory to, or relapsed within 12 months of, first line chemotherapy [61]. The approval was granted on the basis of compelling evidence that CAR T-cell treated patients were 2.5 times more likely to be alive without disease progression at two years compared to those receiving standard of care [60].

Patient story

I was diagnosed with multiple myeloma in 2017. I was in my sixties and enjoying a busy working life as a General Practitioner. Multiple myeloma created a significant physical, social and emotional toll for me and my family.

I was lucky to receive CAR T-cell therapy as part of a clinical trial. Although I initially experienced some of the expected side effects, my quality of life has improved substantially. In my case I developed hypogammaglobinaemia and need monthly gamma globulin infusions. Hopefully my levels will restore with time. Even with this side effect, I am very grateful that I have had CAR-T.

CAR T-cell therapy has been a godsend for me. It has helped me feel better, have more energy, be more mentally alert and participate in life. I would have liked the opportunity to have CAR T-cell therapy earlier in my treatment journey as it might have avoided pain, hospitalisations and lasting side effects from other treatments.

Modelling of health and societal benefits

CAR T-cell therapy has demonstrated efficacy as a single dose treatment for multiple myeloma, with two products (Abecma® and Carvykti®) already approved by overseas regulators [22, 24]. These therapies are being used in hospitals across the United States and Europe, offering a lifeline to multiple myeloma patients who have tried and failed at least three prior lines of treatment [22]. Yet, funded access to CAR T-cell therapy for multiple myeloma remains a barrier for Australian patients today.

Methodology

Evohealth developed a model to enable quantitative assessment of the costs and benefits of CAR T-cell therapy for multiple myeloma compared to the current standard of care in Australia. Using an individual patient simulation model, we estimated overall survival, disease-free survival and direct and indirect costs of a cohort of patients newly diagnosed with multiple myeloma in 2022. By validating available outcomes data for CAR T-cell therapy in multiple myeloma patients with population and survival data from the Australian Institute of Health and Welfare, we were able to model the benefits of CAR T-cell therapy at different stages in the disease course. Inputs to the model and underlying assumptions have been informed by published literature. Full detail on the methodology is in Appendix A.

Longer survival and remissions

CAR T-cell therapy can have life-changing health benefits for multiple myeloma patients. Our analysis indicates that CAR T-cell treated patients could expect to be disease free for almost 6 years and live for **15 years** beyond their diagnosis, which is remarkable given that fewer than 27 percent of patients currently survive for 10 years [21]. Even when used as a fourth-line treatment after conventional medicines have failed, CAR T-cell therapy has the potential to offer up to four more years of survival and over a year of disease-free progression. This makes a dramatic difference for a cohort of patients that, having failed all other treatment options, would not typically be expected to survive beyond a matter of months. CAR T-cell therapy offers a lifeline to patients who are navigating the burden of an incurable disease where no other treatments are available, whether it is used in relapsed and refractory settings or made available as a first line treatment.

Fewer deaths from multiple myeloma

CAR T-cell therapy is safe, effective and could save thousands of Australian lives. Today, almost 99 per cent of multiple myeloma patients die from their disease. CAR T-cell therapy has the potential to change this trajectory by reducing the number of people dying from multiple myeloma by **34 per cent**, with up to **886 deaths from multiple myeloma avoided** from a cohort of patients diagnosed in 2022.

Lower burden of disease

In terms of disease-free survival, multiple myeloma patients treated with CAR T-cell therapy could enjoy vastly longer remissions than is achievable with existing treatments. CAR T-cell treated patients could experience **6 years** living free of disease when used as a first line treatment compared with just 2.4 years for current therapies. This equates to a significant reduction in the burden of disease for patients and their caregivers, alleviating them of the physical, social and psychological toll of their symptoms.

Getting patients and carers back to work

With current treatments, many multiple myeloma patients are forced into early retirement due to the debilitating effects of their disease combined with the intensive commitment to health care appointments. Often, the patient's caregiver (usually a partner or family member) also needs to reduce work hours to accommodate the commitment to treatment [56, 57].

With the gains in disease-free survival and overall survival, CAR T-cell therapy for multiple myeloma patients could produce significant returns to the economy. For a cohort of patients diagnosed in 2022 alone, the use of CAR T-cell therapy could lead to productivity and taxation gains of up to **$36 million** from patients and their carers returning to work.

Living without the burden of symptoms and side effects

CAR T-cell therapy for multiple myeloma will deliver important social benefits. With longer survival and disease-free remissions, patients will have a greater capacity to participate in paid employment, family life (including childcare), volunteering and community events. There are invaluable societal benefits of highly effective cancer treatment for parents, partners, children and young adults, family and friends, employers and Governments [30].

Preparing for CAR T-cell therapies at scale

There is an urgent need for Australian Governments to invest in funded access to CAR T-cell therapy for patients with multiple myeloma. This transformational treatment can save lives, prolong survival where no comparable or alternative treatment is available and improve quality of life for thousands of patients facing an incurable prognosis.

With the rapid pace of research and progress being seen on a global scale, we are on the cusp of a future that looks vastly different from today. For instance, with relapsed and refractory multiple myeloma patients alone, the number of patients eligible for CAR T-cell therapy in Australia could quadruple [6]. There is a window of opportunity to act now to ensure our healthcare system is **ready, willing and able** to fund and deliver CAR T-cell therapy to vulnerable Australians before a tidal wave of demand surges.

The introduction of CAR T-cell therapy for multiple myeloma could quadruple the number of patients eligible for CAR T-cell therapy in Australia [6].

Are we ready?

Readiness considers our healthcare system's recognition of the need for change to the assessment, funding and delivery of transformational therapies, as well as our preparedness to deliver CAR T-cell therapy at scale for a wider range of clinical indications. Australia has made early in-roads in its readiness for CAR T-cell therapy, with the first two therapies (Kymriah®, Yescarta®) funded for small patient populations and a third (Tecartus®) having received regulatory approval [27, 28].

However, the introduction of CAR T-cell therapy for multiple myeloma and other indications will test our healthcare system. A four-fold increase in the pool of patients eligible for CAR T-cell therapy will require upfront funding commitments from Commonwealth and State & Territory Governments with already-stretched health budgets [6], as well as the scaling up of the systems, processes and facilities that underpin clinical delivery.

Evohealth has identified key barriers that are impacting on Australia's readiness for delivery of CAR T-cell therapy at scale within the coming years: funding of new therapies, healthcare system capacity and implementation processes.

Funding of new therapies

As a highly specialised therapy that is given to the patient only once, CAR T-cell therapy has a relatively high upfront cost when compared with traditional medicines administered regularly over a longer period of time [28]. All highly specialised therapies are jointly funded by the Commonwealth Government and State & Territory Governments, currently on a 50/50 basis as per the addendum to the National Health Reform Agreement (NHRA) that applies until 2025 [34, 42]. For patients to receive timely and equitable access, Australian Governments will need to plan for investment in upcoming budget cycles.

Stakeholders have reported that to date, there has been inadequate forward planning across levels of Government to support budgeting of highly specialised therapies. For example, some State & Territory Governments indicated that they received only short notice that Kymriah® would be recommended for public funding by the Medical Services Advisory Committee (MSAC) in 2019. With no funding allocation set aside and jurisdictional budget cycles misaligned to the timing of the MSAC announcement, State & Territory Governments faced pressure to rebalance health expenditure to secure funding to cover 50 per cent of the cost of delivering CAR T-cell therapy to eligible patients [35]. This challenge will only intensify as more high-cost therapies come to market in the coming years.

An impending wave of highly specialised therapies

Rapid development of highly specialised therapies is impacting healthcare systems around the world. By 2025, the United States Food and Drug Administration (FDA) predicts that…

- **200 applications** will be received each year for new cell and gene therapies [7]
- **10 to 20** of those applications will be approved each year [7, 11]
- **50 additional clinical reviewers** will be needed to assess applications [7]

Funding coverage of all elements of care associated with CAR T-cell therapy is also a critical readiness consideration. Stakeholders have reported that there are gaps in coverage for important components of care associated with CAR T-cell therapy. For example, restrictive PBS criteria mean bridging therapy (chemotherapy administered after T-cells are harvested) is not always funded and the costs must be borne by patients, the treating site or via compassionate access schemes [35]. To avoid an accumulation of costs, public funding of all elements of care will be important for sustainable delivery of CAR T-cell therapy at scale.

Healthcare system capacity

The delivery of CAR T-cell therapy at scale will place further strain on Australia's already-stretched clinical workforce. It will predominantly impact haematologists, specialist nurses, laboratory technicians, intensivists and pharmacists, all of whom play a critical role in care for patients with multiple myeloma [35].

In addition, there will be a surge in demand for a skilled cellular manufacturing workforce to support the onshore production of CAR T-cells [62]. The consequences of CAR T-cell workforce shortages will be significant. Costs will be higher, wait times will be longer and patient will face delays in access to much-needed therapies [62].

> Nurses play a critical role in supporting patients undergoing CAR T-cell therapy, but there is a severe nursing shortage and the available workforce is very junior. It is so important to leverage the existing specialist resources we have today, such as our trained myeloma nurses, to educate and support other clinicians.
> - **PATIENT ADVOCATE**

Growing demand for CAR T-cell therapies and other HSTs is also forecast to have significant impacts on treating hospitals. Each new therapy brings increased demand for hospital beds, clinical resources such as apheresis facilities, infrastructure such as cryopreservation, and increasingly, administrative services to support programs. The development of new clinical infrastructure, processes and procedures, quality frameworks, models of care, patient support systems, referral pathways and training is critical [35, 62]. The behind-the-scenes work needed to prepare for new therapies is immense, and the wave of CAR T-cell therapies coming to Australia will test our healthcare facilities. Hospitals must be proactive in starting to prepare now for therapies in the pipeline.

> The personalised nature and toxicity profile of current CAR T-cell products places a strain on health infrastructure and staff, which will need to be significantly enhanced as more products come online for more indications. - **CLINICIAN**

Assessment and implementation processes

Establishing a new clinical service is a significant undertaking and the complexity is often not appreciated by stakeholders in the broader health landscape. From the point that a funding decision is made by MSAC, State & Territory Governments are responsible for:

- Securing budget funding to cover 50 per cent of the cost of delivering the CAR T-cell therapy (as per the addendum to the National Health Reform Agreement);
- Undertaking service planning to forecast patient volumes and service needs;
- Facilitating a process to identify treatment sites for the approved CAR T-cell therapy;
- Ensuring specialist capability and workforce capacity is available at selected sites;
- Increasing capacity of treatment sites (such as. apheresis chairs, intensive care beds);
- Establishing infrastructure (such as. cryopreservation, specialist laboratories, storage);
- In some cases, negotiating service or supply agreements with the sponsor company;
- Working with sites to secure product-specific accreditations with sponsor companies;
- Developing and implementing clinical governance arrangements to ensure the safe, consistent and compliant delivery of CAR T-cell therapy.

Evohealth acknowledges that positive steps are being taken to simplify and standardise activities, including development of the Framework for the assessment, funding and implementation of highly specialised therapies and services by Australian Governments. As this framework is rolled out, it will be critical to keep momentum in pursuing important reforms that facilitate consistent, safe and efficient care.

> It takes time to establish and ramp up a new capability. There needs to be more recognition of the behind-the-scenes work we need to do and the time needed to make it happen.
>
> - **STATE & TERRITORY GOVERNMENT REPRESENTATIVE**

Are we willing?

Willingness considers appreciation of the value of CAR T-cell therapy by stakeholders and their openness to influencing or implementing change that will equip Australia to deliver next generation blood cancer treatments. In developing this white paper, Evohealth has observed that there is a groundswell of support for improved access to CAR T-cell therapy for suitable candidates by patients, patient representatives, clinicians and researchers. In particular, there is a sense of optimism about the future of CAR T-cell therapy for multiple myeloma. Although the curative potential is not yet established, CAR T-cell therapy nonetheless offers hope as a lasting treatment option to restore quality of life where other treatments are unable to do so.

Across Australian Governments, there are differing perspectives about the reimbursement of CAR T-cell therapies on a larger scale. There are differences across jurisdictions in funding of CAR T-cell therapy, preferred implementation approaches and support to patients. As new therapies become available, the complexity of the treatment landscape will increase. It will be vital that our healthcare system strikes a balance between sufficient national consistency to uphold equitable patient access and appropriate local clinical autonomy to empower clinicians to best meet the needs of patients under their care.

> The differences in access, approach and timing of approvals by State & Territory Governments does not make sense, and it often occurs at a detriment to patients. - **CLINICIAN**

Nationally consistent referral pathways

The willingness of clinicians to refer patients for CAR T-cell therapy will be an important enabler of success for delivery at scale. A lack of nationally consistent referral pathways has been a challenge for the implementation of CAR T-cell therapies to date. There are different approaches taken in each State & Territory and variable levels of awareness among clinicians about the availability and accessibility of CAR T-cell therapy [35]. Nationally consistent referral pathways will be critical to ensure that every Australian patient can gain access to CAR T-cell therapy, irrespective of their treating haematologist or geographic location.

> We need a better approach to referrals. There are still haematologists who don't think CAR T-cell therapy is available in Australia. I'm aware of others who have been reluctant to refer patients because they're concerned about losing revenue for their hospital. **CLINICIAN**

Positive steps have been taken to improve equitable and clinically appropriate access, such as the establishment of a national meeting of clinicians to considers all referrals nationwide when CAR T-cell therapy first became available.

These processes will be tested as the volume of eligible patients increases. Standardised referral pathways and care approaches will reduce variability for patients and support consistent application of best practice care.

Nationally consistent patient support

The willingness of patients to undergo CAR T-cell therapy will be heavily influenced by their understanding of, and ability to navigate, the treatment options available to them. A blood cancer diagnosis is daunting, with a plethora of medical terminology, a commitment to healthcare appointments and choices to weigh up about treatment options (such as joining a clinical trial or having chemotherapy in tablet, injectable or infusion form) [35]. Many patients report feeling they have little input and adhere to the guidance of their haematologist [35].

> There is no playbook for multiple myeloma after you hit your first relapse, so advice will vary greatly depending on your doctor. If you're in pain and immunocompromised, you're more likely to opt for a tablet chemotherapy over an infusion that requires you to make regular long distance drives to a metro treatment site. - **PATIENT ADVOCATE**

Patient support organisations including Myeloma Australia play a critical role in supporting patients, caregivers and clinicians. They offer a suite of resources such as disease education, support groups, health professional training, advocacy and advice [4]. Specialist nurses play an important role in educating, informing and empowering patients to own their disease journey, including decisions about whether to pursue CAR T-cell therapy. Patient support organisations can equip patients with the vocabulary, skills and confidence to ask questions about their care, seek a second opinion and advocate for themselves to their teams [35].

However, patient access to, and engagement with, patient support organisations is inconsistent across the country [35]. As CAR T-cell therapy becomes more mainstream, there will be more patients in need of vital support and demand on these organisations will grow. It will be critical that patient support organisations and other trusted services are resourced to support all patients in need as they navigate life-changing decisions about their care.

Nationally consistent financial relief

In line with Australia's commitment to universal healthcare, Australian Governments must be willing to continue prioritising equitable patient access as CAR T-cell therapies are delivered at scale. Key to success will be ensuring that every patient can overcome the financial, logistical and other barriers to accessing care for treatments restricted to major capital cities.

Governments must be cognisant of the significant barriers to care that exist for patients considering CAR T-cell therapy. Many multiple myeloma patients are vulnerable as a result of their age, frailty, symptoms and immunocompromise. Navigating public transport or long drives to access care in a different town, city or state can be fraught with difficulty, as can bearing the associated travel costs [35]. To alleviate this burden, each State & Territory Government has a transport and accommodation scheme to subsidise costs for patients. However, each scheme is different and costs are not always fully covered [35]. In addition, most are reimbursement models, which means patients must have access to funds to pay for accommodation and transport upfront, potentially creating further inequity [63]. Industry has sought to bridge this gap by funding travel costs for clinical trial participants and it remains an important area of consideration in planning to deliver CAR T-cell therapy at scale.

> The limited number of treatment sites and requirement for a dedicated carer means that the patient and their carer often need to travel far distances and source accommodation. This primarily occurs via nursing/hospital social care staff and is funded ad hoc, but it is not a consistently delivered service nationally. - **CLINICAL DELIVERY EXPERT**

> Accommodation schemes help, but they only cover some of the burden of treatment. Patients must also manage a complex appointment diary, ensure blood tests are done on time, keep track of scripts, drive to appointments, complete forms and other hospital admin. It is complex and it can be exhausting. - **PATIENT ADVOCATE**

Are we able?

With at least 11 hospitals administering CAR T-cell therapy as part of clinical trials or standard of care [35], Australia's healthcare system has made good progress towards building the critical clinical infrastructure and expertise to support the next generation of cancer treatments. While this provides a strong foundation for delivering CAR T-cell therapy in the future, three barriers threaten our healthcare system's ability to deliver at scale: the pool and pipeline of subject matter expertise, our reliance on offshore manufacturing of CAR T-cells and access to real-world evidence to inform clinical decisions and health service planning.

Pool and pipeline of CAR T-cell expertise

As a highly complex and personalised therapy, the manufacturing and delivery of CAR T-cell therapy requires specialist expertise to ensure safe and consistent patient care. Australia has developed renowned capabilities in CAR T-cell therapy from experience in clinical trials and commercial delivery over recent years, and built a strong cadre of clinical, research and manufacturing experts. However, with the delivery of CAR T-cell therapy currently restricted to a small number of sites, the pool of available experts is small and concentrated in select treatment sites.
As patient demand for CAR T-cell therapy grows in the coming years, there will be a growing need for subject matter experts to fulfil roles in cellular manufacturing, clinical delivery and patient support [62]. Our healthcare system's ability to meet this demand will depend on bolstering the size and geographical distribution of CAR T-cell experts, as well as investing in the next generation of talent to build a strong pipeline of skilled resources.

Sovereign manufacturing of CAR T-cells

CAR T-cell therapy requires timely access to specialist cellular manufacturing to re-engineer T-cells to carry CARs. In recent years, Australia has benefited from onshore commercial manufacturing via a collaboration between Commonwealth Government, Peter MacCallum Cancer Centre and Novartis, however operations have now ceased for Kymriah® [35]. While the NSW Government has committed to a clinical-grade viral vector manufacturing facility in the Westmead Health District, a gap will remain in access to onshore manufacturing for commercial use [64]. This will leave treatment sites reliant on overseas manufacturing for all other commercial CAR T-cell production, which creates risks to timely access [35].

> There is always concern that manufacturing timeframes will stretch beyond 4-6 weeks, which may be too long for some patients. This issue is expected to become critical when CAR T-cell therapy is approved for large patient numbers as it is unclear if there are sufficient 'slots' available in overseas manufacturing facilities to address the anticipated demand. - **STATE & TERRITORY GOVERNMENT REPRESENTATIVE**

With more patients becoming eligible for CAR T-cell therapies in the future, global pressure on CAR T-cell manufacturing will grow. Local manufacturing of CAR T-cells will be important for Australia to enable sufficient capacity to meet patient demand within short therapeutic windows. It will also present an opportunity for the Australian economy as more countries in Asia-Pacific approve the use of CAR T-cell therapies. Investment in Australian facilities creates the opportunity for them to become manufacturing hubs for the region.

Access to real-world evidence

As a novel therapy, real-world evidence on CAR T-cell therapy is critical. Clinical outcomes data from treated patients (such as. response, overall survival, progression-free survival, adverse events, quality of life) informs decisions about its place in therapy and public funding, both for new and existing therapies. Real-world evidence also informs healthcare service planning, budgeting and implementation for new therapies to ensure timely and efficient access for patients. Analysis of CAR T-cell therapy delivery costing is also important to inform cost-effective approaches and funding models for clinical delivery at scale.

To date, stakeholders have reported challenges with data collection and sharing for CAR T-cell therapy through the Australasian Bone Marrow Transplant Recipient Registry (ABMTRR). While clinicians can access rich data for their patients, stakeholders have indicated difficulties obtaining current data at a national level. This is challenging for State & Territory Governments who have limited access to activity-based data on CAR T-cell therapy in the ABMTRR, making them reliant on manual reporting from treatment sites to inform service planning and funding decisions.

Australian Governments have an opportunity before them to redefine the way that cancer medicine is made available to patients. The future of CAR T-cell therapy represents a lifeline for thousands of vulnerable Australians living with blood cancer for whom there are no other treatments available. We must ensure we are ready, willing and able for the next era of cancer treatment.

Recommendations

The time to act is now

Australia's healthcare system is at a critical juncture. CAR T-cell therapy is set to become a mainstay of cancer treatment. With long lead-times needed to prepare for clinical delivery of novel therapies, we must prepare now to ensure we are ready, willing and able to support the next era in blood cancer treatment. Based on the research pipeline and international trends, our healthcare system must anticipate the introduction of more CAR T-cell therapies for a wider range of indications, resulting in higher patient volumes within the next five years.

Should we fail to rise to the challenge before us, Australia will fall behind our international counterparts in providing access to lifesaving treatments for patients an incurable condition. In doing so, we will rob vulnerable people of an opportunity to regain quality of life, prolong survival and have time to spend with their families, communities and societies.

Summary of recommendations

There are seven evidence-based recommendations to ensure Australia's healthcare system is ready, willing and able to implement CAR T-cell therapy at scale within the next five years. Our recommendations have been informed by a comprehensive review of academic and grey literature; interviews with policymakers, clinicians, patients and patient advocates; and the contributions of our project Advisory Committee.

1 Prioritise national reimbursement of CAR T-cell therapy

National reimbursement of safe and effective CAR T-cell therapies for suitable patients is the single greatest barrier to transforming the outlook of blood cancer in Australia. Innovative funding models have been an important pillar of success to date in bringing CAR T-cell therapies to patients. As clinical evidence to support the use of CAR T-cell therapies in earlier treatment lines grows, there will be greater pressure to ensure Australian patients have timely and equitable access to lifesaving treatments.

2 Streamline and, where appropriate, standardise the implementation and delivery of CAR T-cell therapies

Patient access to CAR T-cell therapy is being hampered by fragmented approval and implementation processes for new therapies. With the current landscape, it can take several years from the time a CAR T-cell therapy product is approved to it being available to patients in public hospitals. Even for approved therapies, barriers to equitable access and referral mean that eligible patients are missing out on CAR T-cell therapy because of their location or choice of health practitioner. Approval and implementation of CAR T-cell therapies must be streamlined, simplified and unified.

3 Invest in training and growing the next generation of CAR T-cell therapy specialists

The scaling up of CAR T-cell therapy will intensify demand on specialist healthcare staff (such as. haematologists, nurses, intensivists, pharmacists and lab technicians), clinical resources (such as. apheresis and infusion clinics, hospital and intensive care beds, laboratories) and specialist manufacturing. With an already strained healthcare workforce, urgent action must be taken to retain Australia's existing CAR T-cell experts and to invest in building a talent pipeline by training the next generation of clinical, research and technical/manufacturing leaders.

4 Develop five- and ten-year plans for delivery of CAR T-cell therapy for each State & Territory

Developments in CAR T-cell therapy are accelerating at a pace, with exponential growth occurring in parallel for other highly specialised therapies. With 40-50 CAR T-cell therapies expected to be approved globally by 2030 [29], we must anticipate significant increases in demand on existing and future treatment sites. With States & Territories responsible for the clinical delivery of CAR T-cell therapy, their development of five- and ten-year plans will be instrumental in forward planning for health expenditure, treatment site selection, service and capacity planning, workforce development and overarching clinical governance.

5 Increase funding to patient support organisations to educate and empower patients about CAR T-cell therapy

As a novel therapy, the choice to receive CAR T-cell therapy can be daunting for patients and their families. Patient support organisations play an important role in educating, informing and supporting patients to be in control of their disease journey. The demand for these services will only increase as more CAR T-cell therapies become available. A multi-pronged strategy that harnesses and builds on the expertise and resources already held by patient support organisations in the blood cancer space will go a long way to ensuring every patient is educated, empowered and equipped.

6 Build a national real-world evidence-base for CAR T-cell therapy

Real-world evidence on patient outcomes with CAR T-cell therapy is critical for informing the future treatment landscape. Clinical outcomes data will inform decisions about its place in practice and funding of new and existing therapies. Activity data is instrumental for health service planning, particularly as hospitals ramp up capacity to deliver CAR T-cell therapy at scale in the future. There is an urgent need to invest in a national real-world evidence-base that serves the needs of policy, clinical, delivery and industry stakeholders. Opportunities for industry to co-fund data collection, input and reporting should be explored.

7 Establish a collaboration to shape a national plan for onshore cellular manufacturing

There is an opportunity for Governments to benefit from investing in onshore cellular manufacturing. The ability to produce CAR T-cells onshore will simplify patient access to care, minimise exposure to disruptions in supply chains and support job creation and upskilling for Australian workers. A national approach will ensure that our brightest minds can collaborate, not compete, in advancing CAR T-cell technology here in Australia.

Abbreviations

Abbreviations	Meaning
ABMTRR	Australasian Bone Marrow Transplant Recipient Registry
ALL	Acute lymphoblastic leukaemia
ASCT	Autologous Stem Cell Transplantation
CAR	Chimeric Antigen Receptor
CR	Complete Response
DLBCL	Diffuse large B-cell lymphoma
FDA	Food and Drug Administration
HGBCL	High-grade B-cell lymphoma
HST	Highly Specialised Therapy
HTA	Health Technology Assessment
IPTAAS	Patients Travel and Accommodation Assistance Scheme
MBS	Medicare Benefits Schedule
MCL	Mantle cell lymphoma
MM	Multiple myeloma
MSAC	Medical Services Advisory Committee
NHRA	National Health Reform Agreement
OS	Overall survival
PBAC	Pharmaceutical Benefits Advisory Committee
PBS	Pharmaceutical Benefits Scheme
PFS	Progression-free survival
PMBCL	Primary mediastinal large B-cell lymphoma

Appendix A

Methodology for the economic model

An economic model was developed to enable quantitative assessment of the costs and benefits of CAR-T cell therapy for patients with multiple myeloma compared to the current standard of care in Australia. Modelling was undertaken between June and December 2022.

Approach

An individual patient simulation model was developed to estimate overall survival (OS), progression-free survival (PFS) and associated direct and indirect costs of newly diagnosed patients with multiple myeloma. Estimates of OS and PFS by line of treatment were obtained from Bruno et al., 2020. This study provides real-world observed OS in patients with multiple myeloma for up five lines of treatment by newer and older treatments (i.e., FDA approval before and during/ after 2012) as well as pooled [58]. Since no statistically significant difference in OS or PFS was observed between older and newer treatments, our analysis was informed by the pooled OS and PFS estimates for each line of therapy.

Parametric survival models were fitted to the observed OS and PFS data from Bruno et al., 2020 to enable extrapolation beyond the observed period to a lifetime (30 years) or a maximum age of 100. A hazard ratio (HR) was applied to the parametric models to ensure that modelled OS aligned with that reported by the Australian Institute of Health and Welfare (AIHW). This calibrated OS was assumed to correspond to that of patients who are currently receiving standard of care.

CAR-T cell therapy was assumed to reduce the risk of disease progression and death by 76% and 73%, respectively (i.e., PFS HR: 0.244; OS HR: 0.274). These treatment effects were estimated from the studies by Martin et al., 2021 [65] and Shah et al., 2022 [66]. Martin et al., 2021 reported on the use ciltacabtagene autoleucel in CARTITUDE1 versus physician's choice of therapy while Shah et al., 2022 presents the results of an indirect treatment comparison of idecabtagene vicleucel versus conventional care in triple-class exposed patients with multiple myeloma. Despite differences in patient demographics and disease characteristics these studies were considered to provide the best estimate of the treatment effect of CAR-T cell therapy. Given evidence that Carvykti is more efficacious than Ide-cel, the model assumes an 80% market share for Carvykti and 20% for Ide-Cel, and the weighted treatment effect HRs for PFS and OS applied in the model are based on these assumed market shares. There are no studies reporting the treatment effect of CAR-T in each line of therapy and it was therefore assumed that the reduction in risk of disease progression and death from Martin et al., 2021 and Shah et al., 2022 applied to each line of treatment.

Relevant patient demographics (i.e., age, gender, body weight) that impact outcomes and costs were derived from an Australian study by Ng et al., 2020 [55] and the report by Cancer Australia: Multiple Myeloma in Australia statistics 2021 [13]. A 5% discount rate has been applied to costs and outcomes in Year 2 onwards.

Management of multiple myeloma

Each patient entering the standard of care arm of the model was first assessed for ASCT eligibility with the probability derived from the Australian and New Zealand myeloma and related diseases registry (approx. 75%). Simulated patients were assumed to receive one ASCT with or without maintenance therapy with Ld in a lifetime. The probability of a patient receiving maintenance therapy following ASCT was assumed to be 95% (Yong et al., 2016). Patients who were simulated to experience disease progression following an ASCT were assumed to receive BLd, DBd, PBd, and Pd in the 2L, 3L, 4L, and 5L setting. ASCT ineligible patients were assumed to receive treatment BLd in 1L, DBd in 2L, PBd in 3L, Pd in 4L and Cd in 5L. The likelihood of patients receiving pharmacological treatment in each line of therapy was conditional on survival time and attrition rates.

The mean duration of treatment in each line of therapy was obtained from a European study by Yong et al., 2016 [67]. To ensure that the modelled treatment duration for each line of therapy was aligned with that reported by Yong et al., 2016, a HR was applied to the selected parametric survival model for PFS.

Each additional line of therapy is associated with lower response rates, shorter treatment duration and PFS. This paired with increased frailty, a proportion of patients with multiple myeloma do not proceed to the next line of therapy after experiencing disease progression on the previous line of therapy. Fonseca et al., 2021 analysed data from several US patient level databases and, amongst other outcomes, reports that the attrition rates across all line of therapy for ASCT ineligible patients ranged between 43 and 57% whereas this was between 21 and 37% for ASCT eligible patients [68]. The simulation explicitly incorporates these attrition rates by line of treatment and transplant eligibility status.

Due to patient and economic burden the model incorporates multiple myeloma-related hospitalisations. Bessou et al., 2022 conducted a retrospective cohort study using the French SNDS claim database and reported that there were 7,397 hospitalisations for events of interest (i.e., adverse events and comorbidity) for 6,413 newly diagnosed patients over a mean follow-up period of approximately 26 months [69]. The risk of a multiple myeloma-related hospitalisation, including differential risk in the first and subsequent years, was estimated based on these data and incorporated in the standard care arm of the model. Further, the reason for each hospitalisation was drawn from the reported distribution in Bessou et al., 2021. Since most reported multiple myeloma-related hospitalisations appeared to be due to adverse events, the risk of hospitalisation for patients who were simulated to receive CAR-T was assumed to be reduced by 90%.

Direct costs

The direct cost considered in the model are those associated with the use of interventions for the treatment of multiple myeloma (i.e., medicines, ASCT, CAR-T) including the cost of bridging therapy, conditioning therapy, and administration. Costs associated with health care practitioner (HCP) follow-up visits (such as., haematologist) and relevant laboratory tests (such as., full blood count, renal function tests, protein electrophoresis, etc.) which differ depending on the simulated patient's health status (i.e., free of disease progression or experiencing progressive disease) are also captured. It is assumed that the frequency of monitoring patients experiencing progressive disease is double that of patients free of disease progression.

The dosing regimen used for each combination of medicines was derived from the Medical Scientific Advisory Group to Myeloma Australia clinical practice guidelines for Multiple Myeloma 2019 while the cost of each individual medicine was obtained from the Schedule of Pharmaceutical Benefits.

Costs associated with HCP visits and laboratory tests were obtained from the Medicare Benefits Schedule while all other costs (such as., apheresis, ASCT) were estimated from the relevant NHCDC AR-DRG, Round 24 (2019-2020).

The cost of multiple myeloma-related hospitalisations was estimated by mapping the ICD-10 for most events of interest in Bessou et al., 2022 to the corresponding NHCDC AR-DRG, Round 24 (2019-2020). The events of interest for which a cost was estimated using this method included infections, anaemia, pneumonia, thrombotic events, skeletal related events, diarrhea, and neutropenia. The remainder were grouped in a category 'Other' for which the cost was assumed to correspond to the weighted average of all specific events where the number of separations from the relevant AR-DRG served as the weights. The cost associated with end-of-life care were sourced from Reeve et al., 2018 and inflated to 2022 values using the CPI health inflation index from the Australian Bureau of Statistics (ABS).

Indirect costs

Productivity losses: A study by Jackson et al., 2019 reported that approximately 51% of patients return to work following ASCT [56] while Robinson et al., 2017 suggests that this is only 20% for those with relapsed or refractory multiple myeloma [57]. Although most patients with multiple myeloma are diagnosed in their mid to late 60s, there are notable productivity losses for those in the workforce at the time of diagnosis. To capture these productivity losses, a simulated patient was assumed to be in the workforce if aged ≤ 65 years although this was conditional on the ABS reported employment rate (approx. 97%).

The productivity loss of patients who were simulated to enter early retirement (i.e., in the workforce but decide not to return to work) was assumed to amount to the simulated person's age and retirement age of 65 years. Simulated patients who continued employment were assumed to lose 99 productive days per year while free of disease progression. Those simulated to experienced disease progression were assumed to lose all productive days in a year. The 99 days of productivity loss was estimated from the study by Morela et al., 2018 who reported that patients lost between 87 and 110 days per year. Although the cohort in this study included predominately patients free of disease progression (i.e., some patients with progressive disease were included), estimated days of work lost is consistent with that reported in Jackson et al., 2019.

Caregiver productivity losses are also captured. All patients were assumed to require support from a caregiver who was assumed to be an immediate relative of the same age. Based on the data reported in Robinson et al., 2017, Morela et al., 2018 and Jackson et al., 2019, caregiver productivity loss was estimated to be approximately 50% of that lost by the patient. The cost of productivity losses was estimated by considering the total number of productivity days lost and the mean annual income from employment as reported by the ABS. Additionally, the loss of tax receipts was approximated using the same method but applied the relevant tax rate to the income from employment.

Other indirect consequences: There are very limited published Australian studies reporting on the financial burden of patients with multiple myeloma, and especially out of pocket expenses. However, Parker et al., 2022 describe and quantify the financial burden of adult patients with haematological malignancies in Melbourne, Victoria [70]. The out-of-pocket expenditure data by category (such as., prescription medications, doctor fees, allied health, home aid devices, travel cost) from this study were captured in the model with the relevant cost category applied if the patients was simulated to incur that expense category. Out of pocket costs for prescription medicines were capped at PBS safety net values, assuming that 55% of the multiple myeloma population are concession card holders [71]. Travel/accommodation costs were based on Gordon et al, 2009 inflated to 2022 $AUD via the transport component of CPI, and assume that metropolitan patients (accounting for 70% of the multiple myeloma population) incur ~19% of the travel/accommodation costs of their rural/remote counterparts (Gordon et al, 2009). The risk of the patient incurring an expense category in the standard care arm was based on the reported proportion of patients that incurred the expense in Parker et al., 2022, but these out-of-pocket expenses were assumed to cease six months after successfully completing CAR-T cell therapy up until such time that the disease recurred.

References

1. Dickinson, M., Expert Series interview: Associate Professor Michael Dickinson discusses CAR T-cell therapy, Leukaemia Foundation, Editor. 2021.
2. Peter MacCallum Cancer Centre. CAR-T Cell Therapy. 2022; Available from: https://www.petermac.org/car-t.
3. Peter MacCallum Cancer Centre. CAR T-Cell Therapy: A guide for patients, carers and families. 2021; Available from: https://www.petermac.org/services/cancer-information-resources/car-t-cell-therapy-guide-patients-carers-and-families.
4. Myeloma Australia. CAR-T cell therapy. 2022; Available from: https://myeloma.org.au/wp-content/uploads/2022/05/CAR-T_may22.pdf.
5. Myeloma Australia. What is myeloma? 2022; Available from: https://myeloma.org.au/what-is-myeloma/.
6. MedNews. Clinicians ready for myeloma 'cure'. 2022; Available from: https://mednews.com.au/clinicians-ready-for-myeloma-cure/.
7. US Food & Drug Administration. Statement from FDA Commissioner Scott Gottlieb, M.D. and Peter Marks, M.D., Ph.D., Director of the Center for Biologics Evaluation and Research on new policies to advance development of safe and effective cell and gene therapies. Available from: https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-and-peter-marks-md-phd-director-center-biologics.
8. Berdeja et al., Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study. Lancet, 2921. 398(10297): p. 314-324.
9. Bergin, K et al The Myeloma Landscape in Australia and New Zealand: The First 8 Years of the Myeloma and Related Diseases Registry (MRDR). Clin Lymphoma Myeloma Leuk, 2021. 21(6).
10. Leukaemia Foundation. Myeloma Awareness Month 2022. 2022; Available from: https://www.leukaemia.org.au/blood-cancer-information/myeloma-awareness/.
11. US National Library of Medicine. ClinicalTrials.gov - CAR-T. 2022; Available from: https://clinicaltrials.gov/ct2/results?cond=&term=CAR-T&cntry=&state=&city=&dist=.
12. National Cancer Institute. Carvykti Approval Marks Second CAR T-Cell Therapy for Multiple Myeloma. 2022; Available from: https://www.cancer.gov/news-events/cancer-currents-blog/2022/fda-carvykti-multiple-myeloma.
13. Cancer Australia. Multiple myeloma in Australia statistics. 2022; Available from: https://www.canceraustralia.gov.au/cancer-types/myeloma/statistics.
14. The Leukaemia Foundation. National Strategic Action Plan for Blood Cancer. 2020; Available from: https://myeloma.org.au/wp-content/uploads/2020/10/National-Strategic-Action-Plan-for-Blood-Cancer_June-2020.pdf.
15. Evohealth, Cell and Gene Therapies: Rising to the Challenge. 2021. Available from: http://evohealth.com.au/media/reports/Evohealth_Cell_and_gene_therapies_rising_to_the_challenge_FA.pdf
16. Australian Institute of Health and Welfare. Cancer data in Australia. 2022; Available from: https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia/contents/cancer-survival-data-visualisation.
17. Insight Economics. State of the Nation: Blood cancer in Australia. 2019; Available from: https://www.leukaemia.org.au/wp-content/uploads/2020/06/State-of-the-Nation-Blood-Cancer-in-Australia_Leukaemia-Foundation.pdf.
18. Leukaemia Foundation. Blood cancer facts and figures. 2022; Available from: https://www.leukaemia.org.au/blood-cancer-information/types-of-blood-cancer/understanding-your-blood/blood-cancer-facts-and-figures/.

19. Cancer Council Australia. Myeloma. 2022; Available from: https://www.cancer.org.au/cancer-information/types-of-cancer/myeloma.
20. Quach, G. and M. Prince, Clinical Practice Guideline: Multiple Myeloma. 2019. Add: Available from: https://myeloma.org.au/wp-content/uploads/2019/10/myeloma_clinical_practice_guideline_oct19.pdf
21. Zamasa Foundation. Multiple Myeloma. 2021; Available from: https://zamasafoundation.org.au/multiple-myeloma/.
22. National Cancer Institute. CAR T Cells: Engineering Patients' Immune Cells to Treat Their Cancers. 2022; Available from: https://www.cancer.gov/about-cancer/treatment/research/car-t-cells.
23. Tichich, E. The Future of CAR T-Cell Therapy: Will Off-the-Shelf Options Soon Enter the Playing Field? 2022; Available from: https://www.oncnursingnews.com/view/the-future-of-car-t-cell-therapy-will-off-the-shelf-options-soon-enter-the-playing-field-.
24. Moretti, A., et al., The Past, Present, and Future of Non-Viral CAR T Cells. Frontiers in Immunology, 2022. 13.
25. Shadman, M. The Future of CAR T-Cell Therapy. 2019; Available from: https://www.cancernetwork.com/view/future-car-t-cell-therapy.
26. United States Food and Drug Administration. ABECMA (idecabtagene vicleucel). 2021; Available from: https://www.fda.gov/vaccines-blood-biologics/abecma-idecabtagene-vicleucel.
27. Lymphoma Australia. New CAR T Cell Therapy option now available in Australia for some patients with Lymphoma. 2021; Available from: https://www.lymphoma.org.au/media/new-cart-available-therapy/.
28. Mallik, S., C.G. Bailey, and J.E.J. Rasko, Approved gene therapies in Australia: coming to a store near you. Internal Medicine Journal, 2022. 52(2022): p. 1313-1321.
29. Gye, A., S. Goodall, and R. De Abreau Lourenco, A Systematic Review of Health Technology Assessments of Chimeric Antigen Receptor T-Cell Therapies in Young Compared With Older Patients. VALUE HEALTH, 2022. 25(1): p. 47-58.
30. Rare Cancers Australia and Canteen. Counting the cost: The true value of investing in cancer treatment. 2022; Available from: https://rcararecancers.blob.core.windows.net/assets/contentpage_htmlcontent/RCA4279%20Counting%20the%20Cost%20Report-final.pdf.
31. Williamson, S. Implementing CAR T cell therapy in the NHS. Available from: https://www.theattcnetwork.co.uk/wp-content/uploads/2019/06/Steve-Williamson-Commissioning-for-Advanced-Therapy-Medicinal-Products-NHS-England-Perspective.pdf.
32. Zozaya, N., et al., A strategic reflection for the management and implementation of CAR-T therapy in Spain: an expert consensus paper. Clinical and Translational Oncology, 2022. 24: p. 968–980.
33. Stolz, S.e.a., Introducing innovative cellular therapies into the clinic: a 2-year retrospective experience of a chimeric antigen receptor T-cell programme at a single centre in Switzerland. Swiss Medical Weekly, 2022.
34. Independent Hospital Pricing Authority. National Efficient Cost Determination 2022-23. 2022; Available from: https://www.ihacpa.gov.au/resources/national-efficient-price-determination-2022-23.
35. Evohealth, Expert and stakeholder discussions - CAR T-Cell Therapy Preparedness Project. 2022.
36. BioInformant. Global CAR-T Cell Therapy Market – Market Size, Forecasts, Trials & Trends, 2022. 2022; Available from: https://bioinformant.com/product/car-t-report/.
37. PRMA Consulting. CAR-T Therapy: The future begins to take shape. 2019; Available from: https://www.prmaconsulting.com/webinars/car-t-therapy-the-future-begins-to-take-shape/.
38. Benyon, B. Prognostic Awareness in Patients with Multiple Myeloma Negatively Affects Quality of Life. 2021; Available from: https://www.targetedonc.com/view/prognostic-awareness-in-patients-with-multiple-myeloma-negatively-affects-quality-of-life.
39. Clarivate. CAR T-cell Therapy Pipeline and Forecast Snapshot. 2020; Available from: https://clarivate.com/lp/car-t-cell-therapy-pipeline-and-forecast-snapshot/.
40. Dana-Farber Cancer Institute. CAR T-Cell Therapy for Multiple Myeloma. 2022; Available from: https://www.dana-farber.org/cellular-therapies-program/car-t-cell-therapy/.

41. O'Sullivan, G., J.G. Philips, and J.E.J. Rasko, Clinical gene technology in Australia: building on solid foundations. MJA Perspectives, 2022. 217(2): p. 65-70.
42. Australian Government. Addendum to the National Health Reform Agreement 2020-2025. 2020; Available from: https://federalfinancialrelations.gov.au/sites/federalfinancialrelations.gov.au/files/2021-07/NHRA_2020-25_Addendum_consolidated.pdf.
43. Medicines Australia. Federal Government takes first major step in adopting new wave of personalised medicine for Australian patients. 2019; Available from: https://www.medicinesaustralia.com.au/media-release/federal-government-takes-first-major-step-in-adopting-new-wave-of-personalised-medicine-for-australian-patients/.
44. Teoh, P.J. and W.J. Chng, CAR T-cell therapy in multiple myeloma: more room for improvement. Blood Cancer Journal, 2021. 11(84).
45. Charrot, S. and S. Hallam, CAR-T Cells: Future Perspectives. HemaSphere, 2019. 3(2).
46. AusBiotech, Australia's Regenerative Medicine Clinical Trials Database. 2021: Australia.
47. Novartis. The pioneers of CAR-T Cell and Gene Therapy. 2022; Available from: https://www.novartis.com/research-development/technology-platforms/cell-therapy/car-t-cell-therapy-and-beyond/car-t-healthcare-professionals/pioneers-car-t-cell-and-gene-therapy.
48. Consult QD - Cleveland Clinic. The Future of CAR T-Cell Therapy: Improving safety, efficacy and access of emerging therapies. 2022; Available from: https://consultqd.clevelandclinic.org/the-future-of-car-t-cell-therapy/.
49. University of Pennsylvania. Researchers shorten manufacturing time for CAR T cell therapy. 2022; Available from: https://www.sciencedaily.com/releases/2022/03/220329114723.htm.
50. Cheng, J., et al., Understanding the Mechanisms of Resistance to CAR T-Cell Therapy in Malignancies. Frontiers in Oncology, 2019. 9.
51. Mackensen, A.e.a., Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus. Nature, 2022. 2022.
52. Wang, M., et al., Automation Platform for CAR-T Manufacturing: The Benefits and the Clinical Outcomes. Blood, 2019. 134(Supplement_1): p. 1960-1960.
53. Abou-el-Enein, M., et al., Scalable Manufacturing of CAR T Cells for Cancer Immunotherapy. Blood Cancer Discovery, 2021. 2(5): p. 408-422.
54. Ludwig, H., et al., Quality of life in patients with relapsed/refractory multiple myeloma during ixazomib-thalidomide-dexamethasone induction and ixazomib maintenance therapy and comparison to the general population. Leukemia & Lymphoma, 2019. 61(2).
55. Ng, T.F., et al., Patients with multiple myeloma over a large catchment of 2.5 million square kilometres: a Western Australia retrospective survival review. Internal Medicine Journal, 2020. 50(7): p. 869-872.
56. Jackson, G., et al., Productivity losses in patients with newly diagnosed multiple myeloma following stem cell transplantation and the impact of maintenance therapy. European Journal of Haematology, 2019. 103(4): p. 393-401.
57. Robinson et al., Supporting Information. 2017.
58. Bruno, A.S., et al., Recent real-world treatment patterns and outcomes in US patients with relapsed/refractory multiple myeloma. Expert Review of Hematology, 2020. 13(9): p. 1017-1025.
59. Mohty, M., M. Cavo, and K. ... Yong, Understanding mortality in multiple myeloma: Findings of a European retrospective chart review. European Journal of Haematology, 2019. 103(2): p. 107-115.
60. Gilead, Yescarta® Receives U.S. FDA Approval as First CAR T-cell Therapy for Initial Treatment of Relapsed or Refractory Large B-cell Lymphoma (LBCL). 2022.
61. United States Food and Drug Administration, FDA approves axicabtagene ciloleucel for second-line treatment of large B-cell lymphoma. 2022.
62. Ho, L.D., H.L. Robbins, and A.D. Levine, Assessing workforce needs for the emerging CAR-T cell therapy industry. Nature Biotechnology, 2022. 40: p. 275-278.

63. NSW Government. IPTAAS: Isolated Patients Travel and Accommodation Assistance Scheme. 2022; Available from: https://www.iptaas.health.nsw.gov.au/.
64. NSW Government. Viral Vector Manufacturing Facility Stage 2. 2022; Available from: https://www.hinfra.health.nsw.gov.au/projects/project-search/viral-vector-manufacturing-facility-stage-2.
65. Martin, T., et al., Comparative effectiveness of ciltacabtagene autoleucel in CARTITUDE-1 versus physician's choice of therapy in the Flatiron Health multiple myeloma cohort registry for the treatment of patients with relapsed or refractory multiple myeloma. eJHaem, 2021. 3(1): p. 97-108.
66. Shah, N., et al., Indirect treatment comparison of idecabtagene vicleucel versus conventional care in triple-class exposed multiple myeloma. Journal of Comparative Effectiveness Research, 2022. 11(10).
67. Yong, K., et al., Multiple myeloma: patient outcomes in real-world practice. British Journal of Haematology, 2016. 175(2): p. 252-264.
68. Fonseca, R., et al., Frontline treatment patterns and attrition rates by subsequent lines of therapy in patients with newly diagnosed multiple myeloma. BMC Cancer, 2020. 20(1): p. 1087.
69. Bessou, A., et al., Assessing the treatment pattern, health care resource utilisation, and economic burden of multiple myeloma in France using the Système National des Données de Santé (SNDS) database: a retrospective cohort study. Eur J Health Econ, 2022.
70. Parker, C., et al., Do patients with haematological malignancies suffer financial burden? A cross-sectional study of patients seeking care through a publicly funded healthcare system. Leukemia Research, 2022. 112: p. 106748.
71. Clinton-McHarg, T., et al., Anxiety and depression among haematological cancer patients attending treatment centres: prevalence and predictors. Journal of affective disorders, 2014. 165: p. 176-181.

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