



New horizons: New Zealand's first CAR T-cell clinical trial begins

New Zealand's first clinical trial of CAR T-cell therapy, a revolutionary new approach to fighting cancer, is underway after receiving final regulatory approval.

The phase I safety trial, called ENABLE, is the culmination of over three years of dedicated work by the Institute's clinical trials team in partnership with Wellington Zhaotai Therapies Limited.

Clinical Director Dr Robert Weinkove says the production of CAR T-cells is a major step in the development of the Institute's cell therapy capabilities.

"Chimeric antigen receptor T-cell therapies are being offered to treat certain types of B-cell lymphoma

(lymph node cancer) in countries such as Australia and the UK. For this early phase safety trial of a new type of CAR T-cell therapy, we'll be manufacturing the cells in the dedicated cell therapy suite at the Malaghan Institute in Wellington.

"Because the safety and effectiveness are not yet known, this will be a small trial for a limited number of participants. Nonetheless, this is a very exciting milestone, and we hope the experience and knowledge we gain from the ENABLE trial will help more New Zealanders benefit from CAR T-cell therapies in the future."

Dr Weinkove says the trial will not be the right option for everyone, and it is important that patients speak

Above: The Malaghan Institute's cancer immunotherapy research team

with their specialist about their treatment options. "Referrals for the trial can only be accepted from haematologists or oncologists, who will be advised of the criteria and how to refer."

Dr Weinkove says the trial is taking place at a single centre, to allow close monitoring of participants, but referrals from other hospitals will be considered. "With support from Leukaemia and Blood Cancer New Zealand, we hope to be able to provide travel and accommodation support for participants from outside our region."

Phase I trials assess the safety of a new treatment, and determine the

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From the Director



After nearly three years of dedicated and tireless work by our clinical trials team, it's fantastic to have finally begun New Zealand's first CAR T-cell clinical trial.

I want to acknowledge the amazing effort of our Clinical Director, Dr Rob Weinkove, in assembling a world-class team to deliver this technology in New Zealand. The amount of work involved in establishing the manufacturing capability, including the quality and safety controls for this kind of programme, is staggering.

I would also like to thank the many people, organisations and foundations that supported our journey to this point. There are too many to name in this small space, but know that your efforts and belief in us is truly appreciated.

However, this phase I trial is by no means the end of the road. Rather, it is the first step in bringing these types of ground-breaking cancer treatments to New Zealand and improving and extending them by using the power of the body's own immune system.

I look forward to sharing that future with you.

Prof Graham Le Gros
CNZM FRSNZ FRCPA (Hon)
Director

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optimal dose. Participants will be recruited gradually, to allow safety monitoring between each participant. Dr Weinkove says it is unclear exactly when the first participant will receive treatment, as this will depend on the results of pre-treatment tests, successful CAR T-cell manufacture and on ensuring that all necessary checks are satisfied before the cells are given.

"We anticipate that it will take 18 months to complete recruitment to this trial. While we will get preliminary response data over the course of the trial, full analysis of the primary outcome data could take up to a further year."

CAR T-cell therapy is an emerging form of cancer treatment which has recently been licensed in Australia, the United States and Europe to treat patients with certain types of lymphoma and leukaemia. The Malaghan Institute's CAR T-cell product is a new 'third generation' CAR T-cell technology, based on new and unique intellectual property.

"While we hope our CAR T-cells' unique properties translate to clinical benefits, they may not. The differences mean we cannot rely on results of trials undertaken with other CAR T-cell products overseas, and must establish the optimal dose and safety of our cells before we can progress to larger trials to establish its effectiveness."

Dr Weinkove says the aim of the Institute's Freemasons CAR T-cell Research Programme and its clinical programme is to accelerate availability of the treatment locally.

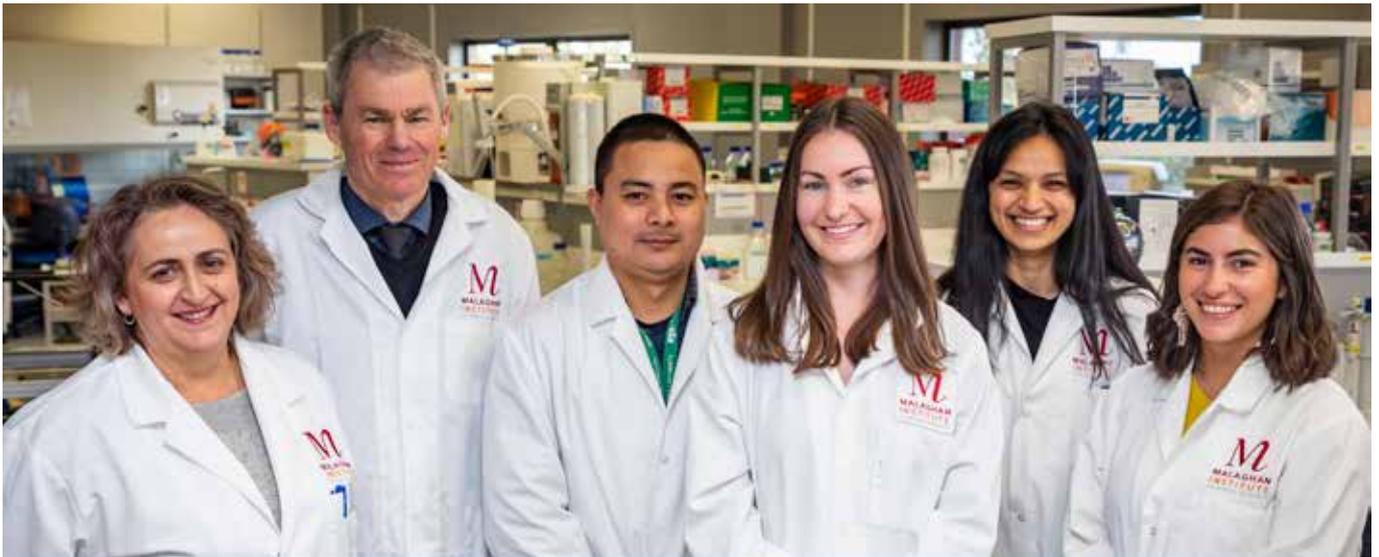
"By establishing the production of CAR T-cells for research and early phase clinical trials, we hope to develop and support the regulatory and clinical environment for safe CAR T-cell delivery in New Zealand.

"We are also undertaking parallel laboratory research focusing on improving CAR T-cell therapies and potentially extending them to other cancers in future," says Dr Weinkove.



Above: Inspecting CAR T-cells under a microscope

"This is an exciting time for cancer research, only made possible thanks to the support of a whole cast of donors and funders including Freemasons New Zealand, David Downs' Down with Cancer campaign, the Thompson Family Foundation, the Florence Petersen Leukaemia Trust, the Hugh Green Foundation, the K.I.A. Taylor Charitable Trust, the Tonks Family Foundation, the Lion Foundation, the Infinity Foundation, the Health Research Council and the Ministry for Business, Innovation and Employment."



Clinical study to investigate potential benefits of human hookworm

Exploring the potential therapeutic benefits of human hookworms, the Malaghan Institute has initiated a benchmark clinical study to investigate how these 'friends with benefits' may positively impact our health.

Funded by the Health Research Council, and in collaboration with the University of Otago Wellington, the trial's ultimate aim is to find better treatment options for a range of inflammatory and autoimmune diseases, including coeliac, asthma, allergy, MS and inflammatory bowel disease.

"Hookworms are masters at dampening down the human immune system to evade detection and expulsion," says Professor Graham Le Gros, whose team is leading the investigation. "This offers huge therapeutic potential. Inflammatory and autoimmune diseases are characterised by an overactive immune system, so subduing this response is an obvious line of treatment. We want to better understand how these hookworms modulate the immune system and how we might manipulate this effect in a positive way to treat a range of diseases."

Dr Stephen Inns, a gastroenterologist and senior lecturer at the University of Otago Wellington's Department of Medicine says the increasing rates of inflammatory disease in the Western world raises the question – what's changed?

"When we look at improvements in standards of living, hygiene and access to medicine, it seems likely that the loss of gut parasites, such as hookworms, from humans may be partially to blame. There could be a mutually beneficial relationship we're missing out on."

Dr Inns says there is a lack of depth of treatment options for inflammatory disease and all have significant adverse effects.

"A safer, natural therapeutic alternative is very appealing, and that's what we're exploring in this clinical trial."

The Malaghan Institute has recruited 15 volunteers who will be infected with a low, safe dose of *Necator americanus* larvae. These participants will be closely monitored and studied over the course of a year, to determine exactly how these worms modulate their hosts, to establish a baseline control for future trials.

Malaghan Institute Head of Laboratories Mali Camberis says hookworm is a uniquely human adapted species that can be tolerated by their human host with very little side effects.

"They can't multiply inside their host, or be transmitted through physical contact or exchange of bodily fluids. With standard hygiene practices, there is absolutely no risk of participants infecting others."

One of the goals of this trial – which has met strict regulatory and safety requirements – is to develop a good manufacturing practice (GMP) grade worm that can be used safely for ongoing trials and ultimately in some form as an approved therapeutic product.

"There is a significant unregulated industry for helminth therapy, involving people self-medicating for serious allergic and autoimmune conditions. We want to do the groundwork to ensure the safety and effectiveness of this type of treatment," says Ms Camberis.

"We see a future where hookworms, or a hookworm-derived product, are an established therapy for autoimmune-inflammatory or immune-mediated diseases, to treat patients and improve their overall quality of life."

Above: The hookworm clinical study team

A health research system worth investing in



Above: Professor Kath McPherson

As the agency responsible for managing the Government's investment in health research, the Health Research Council of New Zealand (HRC) plays a vital role in enabling research and discovery at the Malaghan Institute..

Through long-term capability funding via the Independent Research Fund, and contestable funding for specific research projects and researchers, the HRC's investment has been transformative.

Leading the helm at the HRC for the past five years has been Professor Kath McPherson, who stepped down from the role in August. A champion for the need for better, more robust and better-funded health research, Prof McPherson shared some of her insights from her time in the role before her departure.

What's the HRC's role in New Zealand health research?

In a nutshell, we're the Government's main agent for investing in and driving health research in New Zealand. We've got this important role, that's mandated in legislation, which is to support the very best health research in New Zealand.

Our main focus is on science that has the potential to improve human health. Part of this is ensuring this science is performing at the global level. If you're not globally connected, globally relevant, globally at the highest standard, then the work's not going to benefit your own country.

Why is homegrown research so vital?

For me, it's that connection to being globally relevant, attracting the very best people to our country and generating knowledge which is such an important part of our economy. It's a no-brainer really. Which is to

say, health research is about global connectiveness. If we're locally relevant but not globally considered excellent then it's a disaster for our country in all sorts of ways, not in the least which would be the quality of research.

What impresses you about health research in New Zealand?

I think Kiwi researchers are known for being incredibly enthusiastic, hugely collaborative and very positive, despite the difficulties there are in getting funding. I think that's a pretty exciting thing.

What's the future of health research and funding for health research in New Zealand?

Our job is to prove to the Government that the health research system is worth investment. Thanks to the refresh of the HRC we have forward momentum. Now we just have to keep it going by demonstrating to the Government that its investment is a good investment.

To do this, we need to tell the stories of how health research and our investment has made a difference.

At times in the past we've been disconnected from that story. Just like how the Malaghan Institute knows the importance of the highest levels of communication with your philanthropic funders, the same thing is true for government funding. If we're disconnected from outcomes, why would the Government invest more through it? This communication and connectedness will be so important moving forward, and I think the future is very positive because of it.

Why study worms?

As long as there have been humans, there have been human parasites – opportunistic hitchhikers that seek resource and refuge inside our bodies. So what makes them of such interest to the scientists who study them?

- They're the most successful organisms to infect humans – dating back as far as archaic humans.
- They're skilled at establishing themselves in the body without harming their host. You can live for years with a friendly worm and show no negative symptoms.
- Parasitic worms have developed mechanisms to modulate the immune system of their host to promote their own survival and avoid detection and expulsion from the body.

Ian Paterson: a tireless champion for the Malaghan Institute



Above: Prof Le Gros with Ian Paterson

It is with great sadness that we farewelled Trustee and generous supporter of the Malaghan Institute, Ian Paterson, in August this year.

Ian's decade-long relationship with the Malaghan Institute began following the sudden death of his wife Sally from glioblastoma multiforme, a form of brain cancer, during a family holiday in Thailand in August 2009.

The following year, Ian, with his daughters, donated \$56,000 towards the Institute's cancer research – a combination of agent fees, staff and community contributions from Just Paterson Real Estate, the company he and Sally co-founded in 1989.

The donation wasn't a one off. Over the ensuing years, Just Paterson Real Estate has donated more than \$300,000 to the Institute, and championed the Institute's cancer research across the Wellington region, and the importance of joining together in the fight against the disease.

In 2016, Ian was appointed to the Malaghan Institute's Trust Board. The same year he was awarded a Queen's Service Medal for services to philanthropy.

We miss him greatly and will work tirelessly to ensure his legacy will be a better future for all those affected by cancer.

Remembering Malaghan Friend Jill Kinloch

We are also greatly saddened to lose Jill Kinloch, our long-term Wellington Friend and outstanding advocate, to cancer.

Jill joined the Wellington Friends of the Malaghan Institute in 1998 where her PR skills and passion for golf were first put to use in organising the highly successful and now annual Friends' charity golf tournament. This year she celebrated 21 years as a Friend.

Jill made an outstanding contribution to the Institute, giving her time and expertise generously and contagiously, and championing the Institute at every opportunity.

As Prof Graham Le Gros said, "Jill was such a force for good in the world. We will all miss her and carry a bit of her spirit in each of us."



Thank you to our partners



The Malaghan Institute acknowledges the support of Freemasons New Zealand for the Freemasons CAR T-cell research programme.



Upcoming events 2019 & 2020

Wellington Friends of the
Malaghan Institute Cocktail Party
Kumutoto
7 November

Wilderness Foods Malaghan Institute
Bay of Plenty Charity Golf Tournament
Summerhill Golf Course
6 March

Auckland Research Update
Microsoft House
19 November

Lexus of Wellington and Jarden
Malaghan Institute Charity Golf
Tournament
Royal Wellington Club
24 March

For more information about these events please contact Gay Keast, Development Operations Manager:
gkeast@malaghan.org.nz | 04 499 6914

BEQUESTS: ANOTHER WAY TO GIVE

Leaving a gift in your will to the Malaghan Institute is a personal and enduring investment in the future of biomedical research and discovery.

All gifts in wills, whatever the size, mean a great deal to us and the longevity of our research. You can help us shape advances in medical science and develop treatments that will benefit generations to come.

If you would like more information on how to make a bequest to the Malaghan Institute, or would like us to advise your lawyer, please contact Jenny Sim, Head of Development on jsim@malaghan.org.nz or 04 499 6914 x 811.

Please also get in touch if you have already made a bequest in your will, to let us thank you personally, involve you more in the Malaghan Institute today, and plan for the future.

Recent grants May - July 2019

The Chingford Trust
The Dr Marjorie Barclay
Charitable Trust

Freemasons New Zealand
The Herbert Teagle Masonic
Perpetual Trust

System Consulting Services
Sdn Bhd
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Florence Petersen Leukaemia Trust
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Please call to inform us of your donation so we can send your tax receipt. Donations over \$5 are eligible for a tax refund of up to 33%.

Or call **0800 MALAGHAN (0800 625 244)** to make a donation over the phone.



Research is our journey. Cure is our destination.