ANZCHOG
Australian & New Zealand Childrens Haematology/Oncology Group

Neuroblastoma AUSTRALIA

Paediatric Solid Tumour Immunotherapy Funding Proposal 2025

Background

There has been significant improvement in survival rates for common adult cancers and for childhood blood cancers (eg leukemia and lymphoma). However, for other childhood cancers, survival rates remain unacceptably low. Cancers such as high-risk neuroblastoma and sarcomas have survival rates of 50% or less. Despite maximal use of intensive conventional cancer therapies, children continue to relapse and there is little hope of long-term survival for these patients. There are very few options available within Australia in such circumstances and families often have to resort to fundraising to access clinical trials overseas, often needing to raise many hundreds of thousands of dollars and take a vulnerable child abroad.

One key area of promising research is understanding how the immune system can be harnessed to treat cancer. Two areas are being explored: immuno-oncology (how cancer manages to evade the immune system) and immunotherapy (treatments which use the immune system to attack cancer cells) including cellular therapies (CAR T cells, CAR NK cells), anti-cancer antibodies and vaccines. The most substantial treatment gains in immunotherapy have been for adults with cancer and children with blood cancers, in line with current and prior research investment. The few promising options for children and teenagers developed for solid tumour cancers are mainly overseas and can only be accessed by Australian families if they fundraise hundreds of thousands of dollars. One example is the current clinical trial of CAR T cells for Neuroblastoma open in Rome which has shown positive results for children who have relapsed from high-risk neuroblastoma. The current cost of accessing this trial for children in Australia is $700 000.

The small number of immunotherapy treatments approved for use in Australian children and teenagers with cancer are nearly all focused on blood cancers. It's also important to recognise that pharmaceutical companies won't invest in developing new treatments for children in this space unless they primarily benefit adults with cancer, due to the commercial imperative for a return on investment. While Australia is seen internationally as an excellent place to perform cancer clinical trials, the small paediatric population in Australia makes it particularly unprofitable for pharmaceutical companies. Therefore many families must consider travelling overseas to find immunotherapy treatments if their child's cancer fails to respond to conventional treatment or relapses.

It is important to note that although CAR T therapies and other immunotherapies are being developed as options for resistant or recurrent disease, they may also have the potential to be part of front-line treatments and help improve response to treatment and possibly lead to more targeted and less toxic treatment over time reducing late effects such as hearing loss, infertility, lung/liver damage and secondary cancers.

The Opportunity

Australia has the capacity and capability to make cell therapy products (CAR T cells and CAR NK cells), antibodies and cancer vaccines. Currently the approach to developing these therapies is uncoordinated and dependent on limited academic and philanthropic research funding.

A national coordinated approach coupled with investment is required to coordinate and enable these promising immunotherapy initiatives to be more broadly available to Australian children with high risk and relapsed solid tumours (solid tumour cancers including those of the central nervous system account for around 60% of all childhood cancers). This will lead to a far more equitable situation as well as accelerating the speed of research in solid tumours, sarcomas and other rare cancers. Existing resources (hospitals, staff and research centres) can be leveraged to minimise the cost.

Currently CAR T cells are being made and tested in following locations:

- University of South Australia – currently running some CAR T clinical trials for adults with blood cancers. UniSA also have a collaboration with Sydney Childrens Hospital and a CAR T clinical trial for DIPG (funded by Levi's Catch philanthropic initiative)
- Queensland Institute of Medical Research Berghofer and the Ian Frazer Centre of Children's Immunotherapy Research, University of Queensland – making a variety of CAR T cell treatments for blood cancers at a cost of $50,000 per patient. They would switch focus to childhood solid cancers with appropriate investment such as through this proposal, and have a collaboration with Queensland Children's Hospital
- Childrens Cancer Research Unit, Westmead Children's Hospital – plan to open a CAR T clinical trial for sarcomas
- Peter MacCallum Cancer Centre, University of Melbourne – have funding for CAR T therapy in adult cancers but specifically excludes the development of cellular therapies for children

The above locations are mostly focused on blood cancers and adults. With investment into paediatric solid tumour immunotherapy research and clinical trial development, the potential of immunotherapy, and CAR T therapy in particular, can be developed and tested in childhood solid cancers. In this way the survival of children with high-risk cancers can be improved and aim to meet survival rates achieved for blood cancers in children.

Existing resources and infrastructure could be leveraged to accelerate development of CAR cell therapies and other immuno-oncology treatments. This avoids the cost of creating new facilities. Australian clinicians, researchers and consumers held an Australian & New Zealand Children's Haematology/Oncology Group (ANZCHOG) sponsored workshop in December 2023 to discuss the incorporation of immunotherapy to the treatment of children with solid tumours. It was agreed that this would be best

achieved by working together and developing a national collaborative network focused on immunotherapy for children.

Additional benefits:
Australian national collaboration would facilitate collaboration with similar international academic cellular therapy programs and networks to bring relevant international clinical trials to Australian children and families in a timely fashion.

With more treatment options in Australia, this would reduce the need for Australian families to travel overseas to access CAR T and other immunotherapy treatments for their children, and likely increase overall survival rates.

Proposal

The Three Point Plan – increasing Australia's immunotherapy capacity to include paediatric solid tumours with funding of $10 million provided over 4 years.

1. **Development of a National Paediatric Immunotherapy Network (including CAR-T cell therapy and other cellular therapies)**
   Estimated cost $1 million
   The creation of an Australian Paediatric Immunotherapy Network is essential in creating a co-ordinated and strategic approach to the development of Australia's immunotherapy capability. A national CAR T and NK cell therapies and immunotherapy strategy would be developed, focused on solid tumours, involving all paediatric hospitals and research centres in Australia which are working on CAR T cell therapy and other immunotherapy options for solid tumours. This network would have consumer representation.

   The funding includes one part-time project manager, organisation and communication of research and trials and meetings for four years.

2. **Research - $4 million**
   Funding provided for collaborative research in Australia to support the development of CAR T and CAR NK cell therapy and other immune-oncology therapies (antibodies and vaccines), and to enable children with solid tumours to catch up with the current advances in immunotherapy being achieved in other areas of cancer care. This investment will support the development of immunotherapy targets, immune competent animal models vital to preclinically test novel therapies, ways to overcome the immunosuppressive tumour microenvironment, identification of immune-modulatory agents, vaccination strategies and novel delivery systems. This research, led by Australian oncologists and researchers from the academic world would lead to significant new knowledge and treatments which would be tested in clinical trials and most importantly translate into improved outcomes for our patients and families.
   Proposed funding mechanism would be via NHRMC but other options could be considered. Although the funding would be provided within 4 years, the grant term

would be for a longer period due to the time it takes to conduct and evaluate research.

3. International and national Clinical trial development - $5 million

3.1 International Clinical Trial Collaboration: to bring international phase 2 cellular therapy trials to Australia to provide better options for relapsed children

This would cover the cost of sponsoring and administering a CAR T clinical trial in centres in Australia and associated clinical costs of performing a phase I/II CAR T cell immunotherapy trial.

3.2 National Clinical Trial Development: to create a pathway for Australian-led research to hospitals

This would cover the cost of developing and setting up a locally developed cellular therapy clinical trial across Australian cancer centres. Research undertaken in the fields of CAR T cell therapy and alternative immunotherapies will enable the Australian Paediatric Immunotherapy Network to develop clinical trials from the research conducted by Australian oncologists and research scientists for paediatric cancers. These would be locally led clinical trials managed by the hospital and research institutes rather than be led by a pharmaceutical company. Outcomes expected include the development of new therapies which can potentially be exported to other countries for children with cancer along with potential benefits for other diseases.

The cost of $5 million would be based on the following:

- $1 million for the purchase of viral vectors required to transduce immune cells into CAR T and CAR NK cell therapies
- $2 million MRFF grant focused on CAR-T cell therapies for solid tumours
- $2 million MRFF grant focused on alternative Immunotherapies for solid tumours

The proposal is to use MRFF grants to provide the funding as this represents a straightforward option but other funding mechanisms could be considered. Although funding would be provided within 4 years, the grants would extend for a longer period based on the time to set up trials and assess results.

Total cost: $10 million

Additional Notes

- Neuroblastoma Australia and ANZCHOG would be supportive of all potential government funding sources, such as the Medical Research Future Fund, direct Commonwealth funding or funding in partnership with state governments.
- The proposal could commence from 1 July 2025.
- While the above proposal is put forward by Neuroblastoma Australia and ANZCHOG, should the funding be committed, the proposal is anticipated to have

widespread support from paediatric solid tumour charities and consumer groups, and hospitals.

- Solid tumour cancers include cancers such as neuroblastoma, rhabdomyosarcoma, retinoblastoma, Wilms tumor, osteosarcoma, Ewing sarcoma, as well as Central Nervous System (CNS) tumours.