AUSTRALIA CELL AND GENE THERAPY RESEARCH AND COMMERCIALIZATION: LESSONS LEARNED

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DIRECTOR OF CLINICAL APHAERESIS

Peter Mac

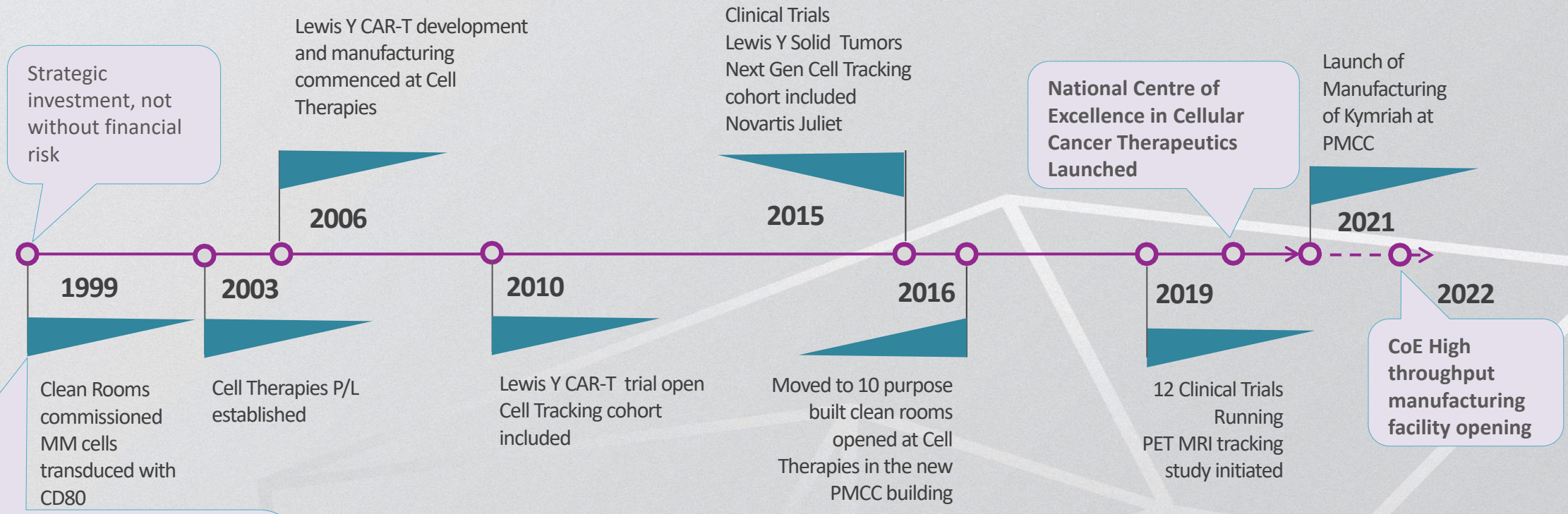
Peter MacCallum Cancer Centre
Victoria Australia

Disclosures

- *AbbVie:* Consultancy, Advisory Board, investigator on studies
- *Amgen:* Consultancy, Honoraria, Advisory Board, Research Funding, investigator on studies
- *Celgene:* Consultancy, Honoraria, Advisory Board, Research Funding, investigator on studies
- *GSK:* Consultancy, Research Funding, Advisory Board
- *Janssen Cilag:* Consultancy, Honoraria, Advisory Board, Research Funding, investigator on studies
- *Novartis:* Consultancy, Honoraria, Advisory Board, Research Funding, investigator on studies
- *Roche/ Genetec:* Consultancy, Honoraria, Advisory Board, investigator on studies
- *Takeda:* Consultancy, Honoraria, Advisory Board

CAR T Trials and Manufacturing at Peter Mac

Philanthropy and Government investment was essential to establish manufacturing capability, the process of manufacturing CAR T-cells is extremely complex and expensive.



Commencement of CAR-T manufacturing was made possible through philanthropic donations

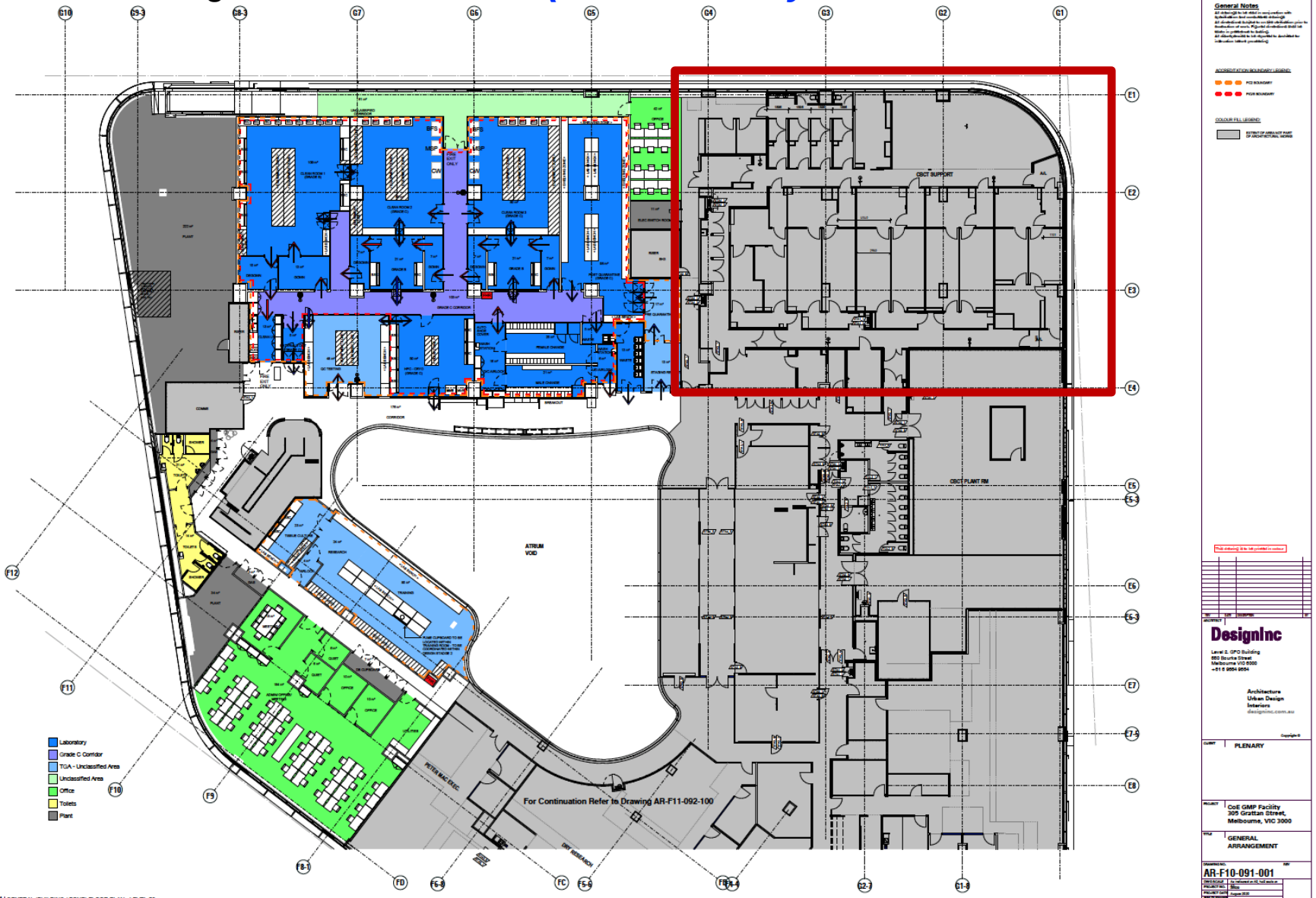
Onsite manufacturing is essential for:

- Translational research
- Commercial contracts
- Timely patient treatment.

Facility #1 1998

New manufacturing facility & laboratory/training space

practical Completion of Stage I Works Achieved ***(late 2021/early 2022)***



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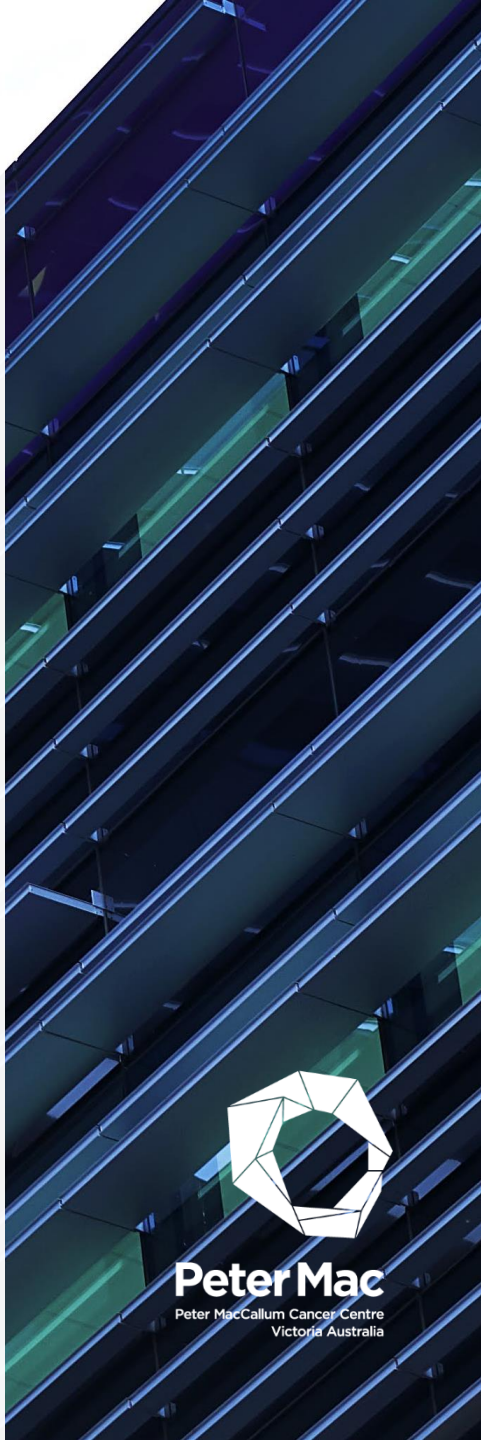
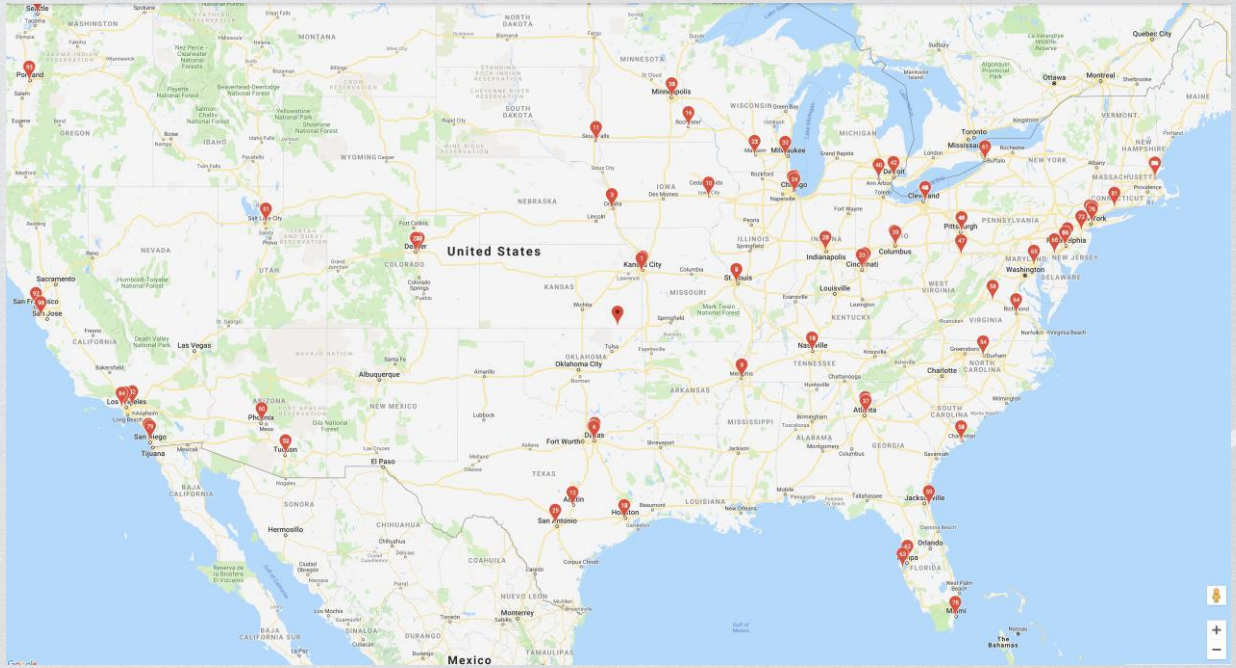
Funding Approval in a Universal Health Care System

- ALL and DLBCL indication approved by MSAC April 2019 and January 2020; patients treated at Peter Mac / RCH Melbourne
- Throughout 2020/21, other sites approved: RPA Sydney, Westmead, Royal Brisbane Women's Hospital, Fiona Stanley Hospital
- Funding: National Health Reform Agreement 50% state; 50% fed (for product).
- Kite/Gilead has MSAC approval, funding decision imminent
- Looking forward to the first myeloma submissions mid 2021



Jurisdictional differences



Site Qualification

no direct FDA governance

lightly controlled deployment

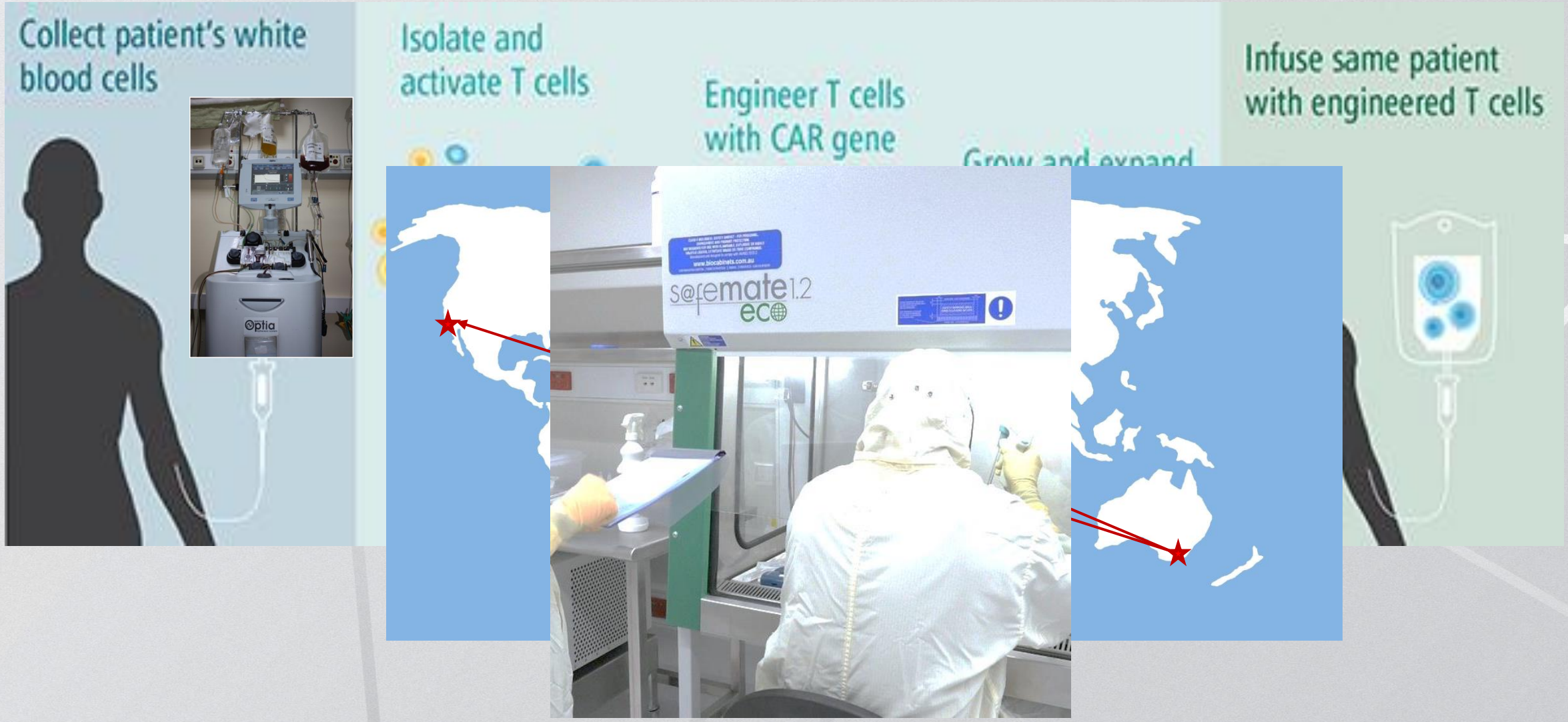
Site Qualification, named site approval by agency

Restricted central funding model

Extra work for apheresis and quality team

Defined IEC sites

CAR-T cell therapy is logistically and technically complex. Especially from the other side of the world!



INSTITUTIONAL STRATEGIC PRIORITIES FOR 2019

1. **Establish a Centre of Excellence in Cellular Immunotherapy**
2. Electronic Medical Record
3. Strategic review of research
4. Commercialisation

Centre of Excellence in Cellular Immunotherapy

Established 2019

Purpose: To bring CAR-T/cellular immunotherapy projects into the CoE CIT pipeline for development, manufacturing and into proof of concept clinical trials

Funding: $104.5 million co-investment from the Australian government, Peter Mac, the Peter Mac Cancer Foundation & Cell Therapies Pty Ltd

Translational Research
Develop novel immunotherapy concepts

Manufacturing
Specifically for clinical delivery in trials

Clinical Research
Pilot, early phase, first in human clinical trials

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CoE CIT Translation Laboratory

CoE CIT Translation Laboratory

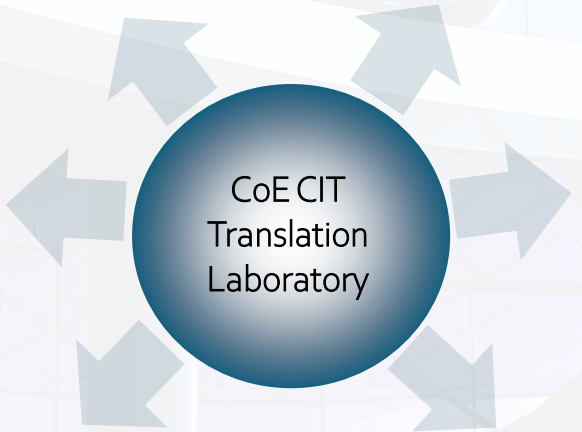
- Develop internal and external cell therapy projects
- Foster industry partnerships
- Develop CoE CIT translational research pipeline
- Establish CAR-T mouse models
- CAR-T patient sample biobanking

Cell Therapies Pty Ltd

- Manufacturing scale-up
- Training and Education
- Clinical delivery CAR-T/cell therapies

Core Facilities Peter Mac

- TRL: mouse models & expertise
- Flow cytometry
- Genomics
- VCFG: High-throughput screening
- CAHM: Imaging



Clinical Teams & PPCTU

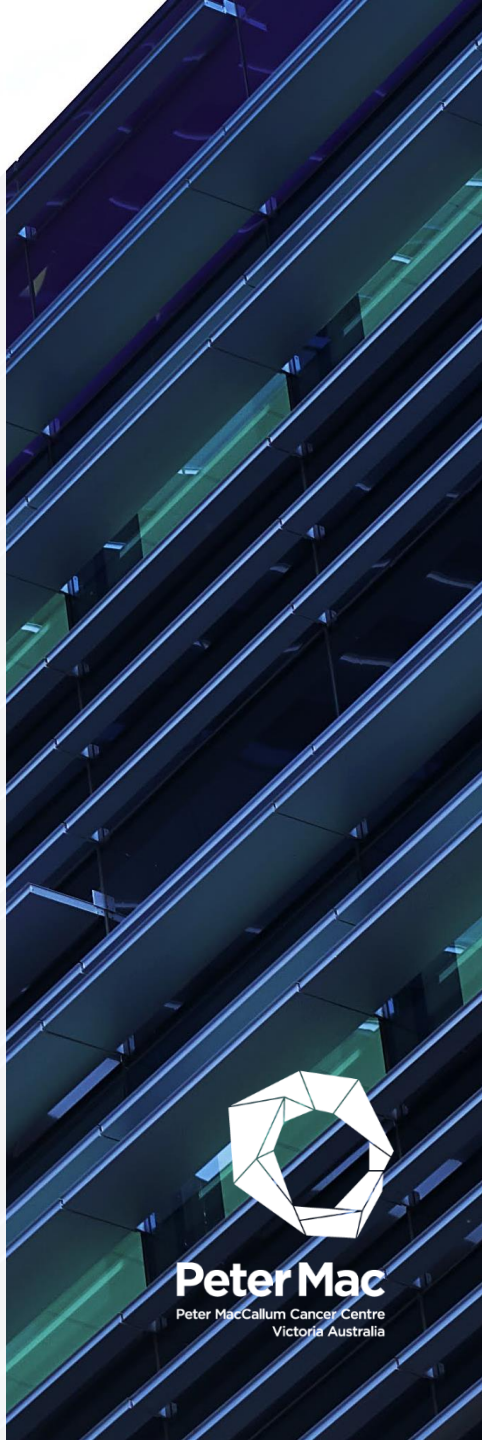
- Pilot Clinical Trials
- Standard of Care CAR-T delivery

Research Support Services

- Commercial Office
- Industry Alliance and Partners
- Grants team

Precinct Partners

- Precinct hospitals and clinical teams
- Research institutes
  (WEHI, UoM, Murdoch)



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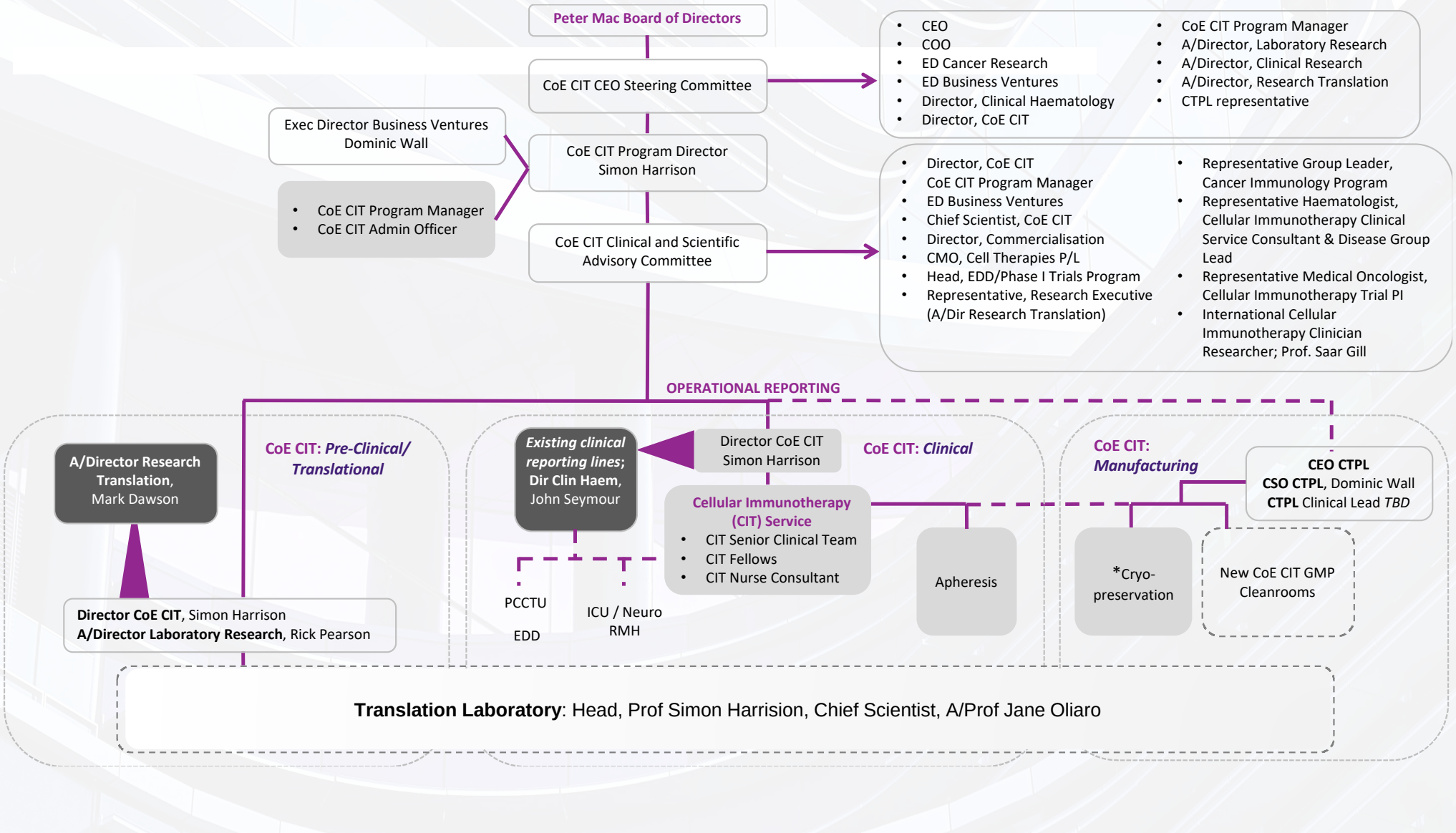
CoE CIT Organisational Chart



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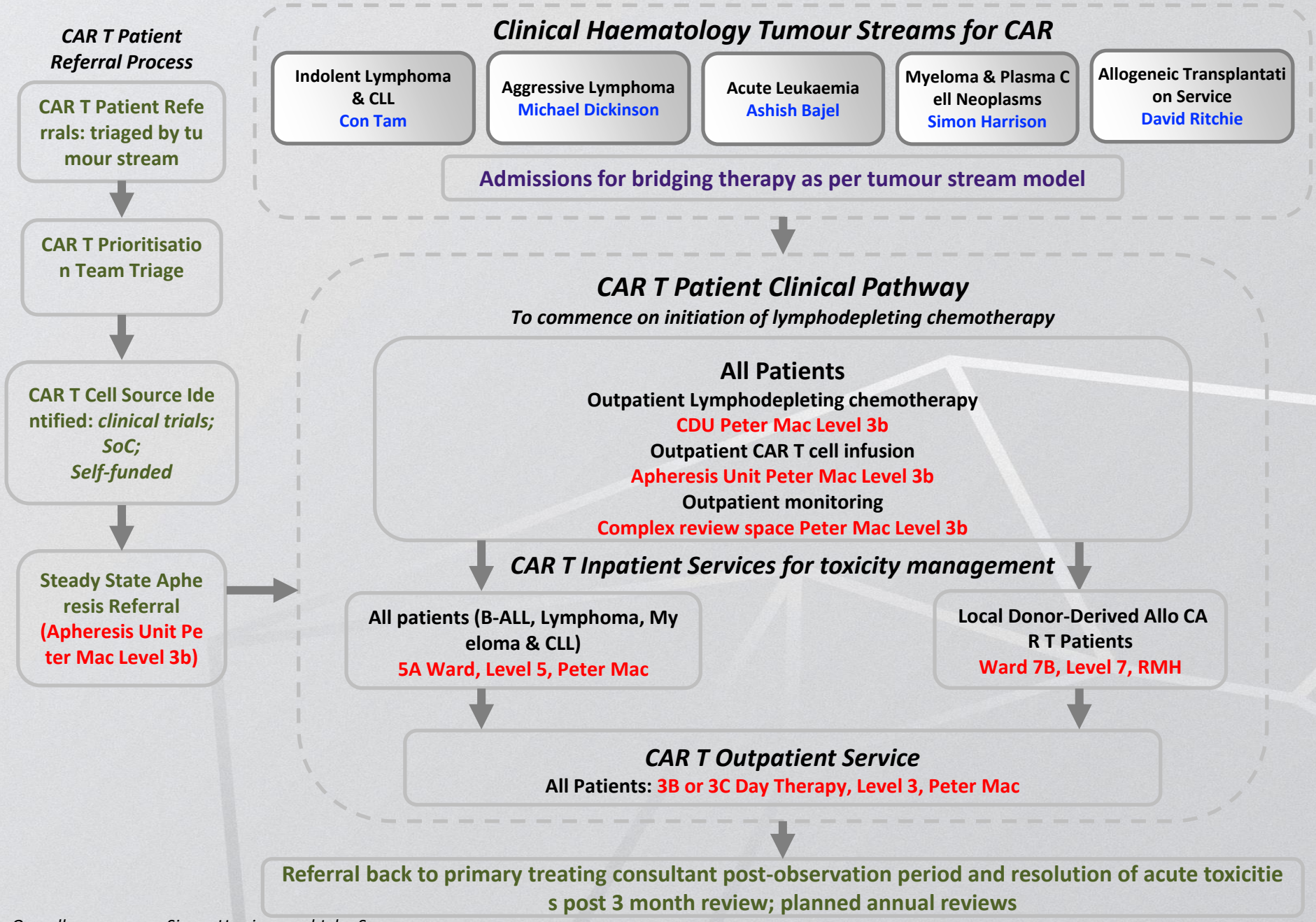
CoE IN CELLULAR IMMUNOTHERAPY: CAR T PATIENT CARE MODEL



Overall governance: Simon Harrison and John Seymour

PMCC CAR-T PATIENT JOURNEY

1. Referral
Triage by Disease Stream Lead
Acute Leuk (AB)
Agg Lymphoma (MD)

2. Enrolled in CAR-T program
(work up completed- medical , psychosocial, education etc..)

3. Apheresis collection
PMC Day Apheresis Unit
Cells sent for manufacture

4. Lymphodepleting chemotherapy
PMC Day Therapy Unit

5. Infusion day
PMC Day Therapy Unit
Post infusion review
CAR-T fellow/ and nurse consultant
Discharge to OP setting

6. Alert Strategy to Key Areas
Access Managers, ED, ICU, pmac@h
CAR-T medical and nursing group
inpatient units

7. Patient Monitoring

M-F : PMC Day Therapy Unit
CAR-T fellow and nurse consultant

S-S : OP via pmac@h and Telehealth IP team
(established outpatient transplant model)
*Readmit as per deteriorating patient CAR-T triage pathway *

8. Transition Care to Referring Centre
D 28 Restaging and clinic review
Continue to monitor or transfer of care back to referring centre

Referral and Eligibility

1. Referral

Patient eligibility for CAR-T discussed at Standard Tumour Stream MDM's (internal or external)

2. Patient Consultation

- Consent to MDT discussion for CAR-T
- New case consultation as outpatient or via Telehealth
- Consider patient social context; assistance for interstate patient organised
- Review patient's prior medical history
- Consider ordering specialist pathology tests: flow cytometry of CD3+ cells

3. CAR-T Patient Weekly Prioritisation Meeting

- Patient triage based on urgency and eligibility
- **Attendees:** CAR-T SMS (including Tumour Stream Leads); CAR-T Fellow; CAR-T Haem Nurse Consultant; representative PCCTU Haem Group Leads/Research Nurses; external Haem SMS; Cellular Therapies Logistics Project Manager; CoE CIT Program Manager
- CoE CIT PM reports active patient activity for commercial Kymriah product to PMCC finance, State DHHS
- Tele/video conference

CAR-T Program: Cell Collection

Patient Eligibility for CAR-T (consent required)

4A. Patient in remission (not yet eligible)

- Expected to relapse imminently
- Patient requires regular consultations

4B. Patient relapsed (eligible)

Disease Restaging*

5A. Patient booked for pre-emptive cell collection: official entry into the CAR-T Program

5B. Patient booked for cell collection: official entry into the CAR-T Program

Disease Restaging*

6. Organ fitness tests:

- Cardiac assessment
- Respiratory function tests
- Renal function tests

Disease Restaging:

- Bone marrow biopsy (radiology)
- Lumbar puncture (radiology); +/- intrathecal chemotherapy
- ALL patients may require **general anesthesia (GA)** for above
- Peripheral blood tests
- Consider pet scan
- May conclude progressive disease, thus alter treatment plan

Patient requires chemotherapy

- Requires IP admission; additional CAR-T-associated costs
- Patient may never receive CAR-T due to medical complications

7. Apheresis suitability assessment:

- Viral screen
- Standard Pathology tests
- Specialist pathology tests: flow cytometry of CD3+ cells
- Relevant anti-infective therapies
- Determine vein access

8. Radiology: central line insertion (if required)

- GA for ALL

9. Leukapheresis:

- Occurs over 1-2 days
- 1:1 nursing
- DTU admission

10A. Pre-emptive cell collection patient product processing:

- Cryopreservation
- Storage (until order placed)
- Cell Therapy logistics required

10B. Cell collection patient product processing:

- Cryopreservation
- PO placement process (multiple depts)
- Order placed in Cell Chain (Novartis); 2 SMS required to log order
- Coordination of shipment for CAR T-cell manufacturing (complex 8 hr process of 2-person checks)
- manufacturing in US takes up to 6 weeks

CAR-T Program: Bridging

11. Patient receives bridging therapy

- SoC chemotherapy
- ALL patients (IP or DTU admission)
- Multiples cycles possible
- Potential complications due to medical event will extend bridging period

- **Pathology: OP Q3D or inpatient BID***
- **Central line care: PICC line dressing; weekly pathology***

Disease Restaging*

Medical Review* (clinical appt.)

Potential complications due to manufacturing event; requires re-consent

12. Lymphodepleting chemotherapy
Low dose, 4 days (IP or DTU admission)

CAR-T Program: Reinfusion

- **Pathology: OP Q3D or inpatient BID***
- **Central line care: PICC line dressing; weekly pathology***

Disease Restaging*

Medical Review* (clinical appt.)

13. CAR-T product reinfusion

- Day 0: DTU admission; 6hr
- Requires 1:1 nursing
- Product handling/thawing & infusion checklist (2-person check process)

14. Day 1-7 Patient Monitoring

- Plan minimum IP, 7 days
- Day 1-7, patients at highest risk of toxicities (see below)
- Patients seen BID by a CAR-T consultant (also CAR-T Fellow or Nurse Consultant) in addition to usual consultant care model
- CAR-T consultant also reviews (via call in) patient daily on weekend

CAR-T Toxicity: CRS

- ≥Grade 3 (Penn) 49% r/r ALL; median time to first event at Day 3
- HDU, requires 1:1 nursing; ICU may be required for observation or direct intervention
- Treated with tocilizumab (and potentially steroids); two doses of tocilizumab required on-site prior to Kymriah infusion
- Can prolong IP stay

CAR-T Toxicity: Neurological

- ≥Grade 3 (Penn) 21% r/r ALL; median time to first event at Day 6
- HDU, requires 1:1 nursing; ICU may be required for observation or direct intervention
- Requires observation/involvement of Neurology/Neurosurgery Depts.
- Can prolong IP stay

CAR-T Program: Patient Follow-up

15. OP monitoring up to week 5

- Patient seen daily or Q3D by a CAR-T Fellow or Nurse Consultant
- At day 30, if immunoglobulin levels at 50% patient may require IVIG or SCIG

- **Pathology: OP Q3D or inpatient BID***
- **Central line care: PICC line dressing; weekly pathology***

Disease Restaging* (30 day)

Medical Review* (clinical appt ≤5/week)

16. Transition to referring centre (if applicable)

- Central line removed (DTU admission)
- Telehealth consultation
- Administrative transfer
- Discharge summary
- Ongoing interstate logistics

Disease Restaging (60 day)

Disease Restaging (11-13 months)

Leukaemia Registry

As a requirement of MSAC (Federal), DHHS (Victoria) and Novartis, patients are added to and maintained on the national leukaemia registry (ABMTRR) and international registry (CIBMTR). This requires 1.5-2 hrs per patient.

KEY: IP, inpatient; OP, outpatient; DTU, day therapy unit; *indicates multiple occurrences; BID, twice daily; Q3D, three times/week

NATIONAL REFERRAL MANAGEMENT PROCESS

- Within State & Nationally
- Equity starts with equity of knowledge
- Accommodation / coordination of patient care must be resourced

Patient presented for discussed in Haematology MDT. Note: a peer haematologist from referring centre will be involved for bridging therapy management locally

Statewide Clinical prioritisation committee with external physicians

Parkville members
Simon Harrison
John Seymour
Michael Dickinson
Ashish Bajel
Con Tam
David Ritchie
Apheresis nurse manager
CAR T program nurse
RCH

Non-Parkville members
Monash Health
Cabrini Group
Austin Health

Enrol in CAR-T program

Reports weekly to DHHS

National CAR-T eligibility committee of currently approved CAR-T treatment sites

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RMH
RCH
Sydney Children's
RPA (Sydney)
Westmead (Sydney)
RAH (Adelaide)
FSA (Perth)
RBH (Brisbane)

Allows redirection of patients to sites with capacity

Referral process follows established tumour disease practice

Triage responsibility by disease stream lead

Key Appointment Resources

Funded by CoE

- Program Manager – Gretchen Poortinga
- Admin Officer

Funded by PeterMac

- Haematologist 1EFT Clinical Car T Team Established
  - Harrison, Dickinson, Tam, Bajel, Anderson, Chee + Seymour and Ritchie
- Clinical Nurse Consultant - Nicole O'Leary

Funded by PCCTU

- 2x research nurses in Haem B
- Clinical Fellow - Adrian Selim

Funded by Cell Therapies

- Logistic manager - Shae Disney
- Apheresis nurse – Paige Marino
- Cryopreservation time – 0.4 EFT

Education and Training

- Precinct-wide Car T readiness training >500 people trained Haem, ED, ICU, Neurology, Ward 5a and 7b, Day care, Access Managers
- Preceptorships
  - MSAC, State Government, TGA
  - Industry
    - Novartis
    - Kite/ Gilead
    - Janssen
- HSANZ CAR T Nursing Education

CAR-T TOXICITY TREATMENT ALGORITHMS

- DETERIORATING PATIENT - CAR-T TRIAGE PATHWAY
- Access- Transition for OP to IP
- **Standard Escalation Pathway**
  - **MET CALL AS APPROPRIATE**
    - PMCC: High Acuity Team
    - RMH: ICU CNC
- Cytokine Release Syndrome
- Neurotoxicity
- Infection
- Hypersensitivity
- Tumour Lysis Syndrome
- Delayed Marrow Recovery

COE CIT PATIENT INCLUSION CRITERIA

CRITERIA FOR PROCEEDING TO CAR-T THERAPY

- **PERFORMANCE STATUS ANTICIPATED TO BE ADEQUATE AT THE TIME OF CAR-T REINFUSION**

  In paediatric/AYA ALL: ECOG score of 2 or less/ Karnofsky of at least 50,

  In DLBCL: ECOG score <2

- **ANTICIPATED ABILITY TO EFFECTIVELY MANAGE (BRIDGE) DISEASE DURING LYMPHOCYTE COLLECTION AND MANUFACTURING, TO ALLOW FOR ABSENCE OF RAPIDLY PROGRESSIVE DISEASE AT THE TIME OF LYMPHOCYTE INFUSION.**

- **ADEQUATE END ORGAN FUNCTION**

  Sufficient renal function to allow safe delivery of lymphodepleting chemotherapy Creatinine clearance > 40mL/min

  Serum ALT/AST < 5 x ULN

  Total bilirubin < 2 x ULN except in patients with Gilbert's syndrome (or if attributed involvement of the liver by disease)

  Adequate cardiac function to tolerate apheresis, and sustained cytokine release syndrome, as indicated by absence of symptomatic heart failure (ie NYHA grade <2) and cardiac left ventricular ejection fraction >/= 40% *or* supplementary functional tests and cardiology assessment demonstrating adequate cardiopulmonary reserve , no evidence of clinically significant pericardial effusion as determined by echocardiogram, or history of life-threatening arrhythmias without definitive management.

  Baseline oxygen saturation >91% on room air (except if attributed to disease involvement)

- **ANTICIPATED ADEQUATE HAEMATOLOGICAL FUNCTION AT THE PLANNED TIME OF CAR-T RE-INFUSION**

  Platelet count > 50 x 10^9/L (unsupported for lymphoma indications)

- **FEMALES OF CHILDBEARING POTENTIAL MUST HAVE NEGATIVE SERUM OR URINE PREGNANCY TEST**
- **ABLE TO REMAIN WITHIN 30 MINUTES OF TREATMENT SITE WITH FULL TIME SUPERVISING CARER FOR THE FIRST 28 DAYS POST CAR-T INFUSION**
- **SUFFICIENT PSYCHOSOCIAL SUPPORT**

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EXCLUSION CRITERIA

- **Uncontrolled / rapidly progressive disease** for the foreseen duration of manufacturing
- **Active Infection** that requires intravenous medications for management at the time of CART re-infusion, or blood culture positivity around the time of apheresis
- **Uncontrolled HIV infection** or active hepatitis B or C infection
- **Active, uncontrolled graft-versus-host disease** grade 2 or above, or with ongoing need for GVHD therapy
- **Uncontrolled CNS disease** or disease anticipated to be symptomatic at the time of CART reinfusion.
- Presence of active CNS disorder such as **poorly controlled seizure disorder**, dementia,, or autoimmune disease with CNS involvement requiring ongoing immunosuppression.
- Live vaccination < 6 weeks prior to planned start of conditioning regimen
- Prior chimeric antigen receptor therapy or other genetically modified T-cell therapy using the same target antigen
- **History of malignancy** other than non-melanoma skin cancer or carcinoma in situ (eg. cervical, bladder, breast) unless disease free for at least 3 years or considered to be at low risk of progression in the subsequent 5 years.
- Any medical conditions with an expected prognosis of less than 5 years
- A history of repeated and sustained non-compliance to mandatory clinic visits and reviews

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CAR-T delivery at Peter Mac (SOC & clinical trials)

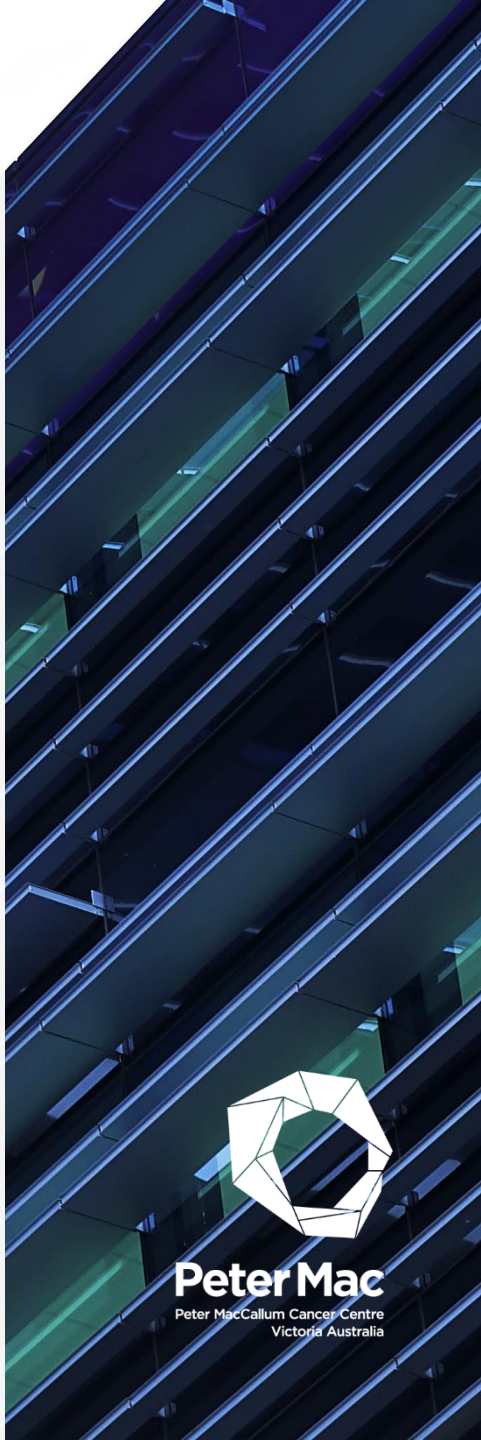
Standard of Care (SOC) CAR-T : AYA B-ALL and DLBCL indications

- Peter Mac has accepted **66 patient referrals** for both SOC indications for commercial CAR-T (tisagenlecleucel):
  - 9 for B-ALL
  - 57 for DLBCL

- **40 patients have proceeded to product reinfusion**, with a typical week including 1-2 commercial CAR-T infusions (maximum of 5 CAR-T infusions performed in one week).
- The overall median number of days from cell pick up to delivery for SOC is ~35 (and ~6-8 from cell collection to reinfusion).

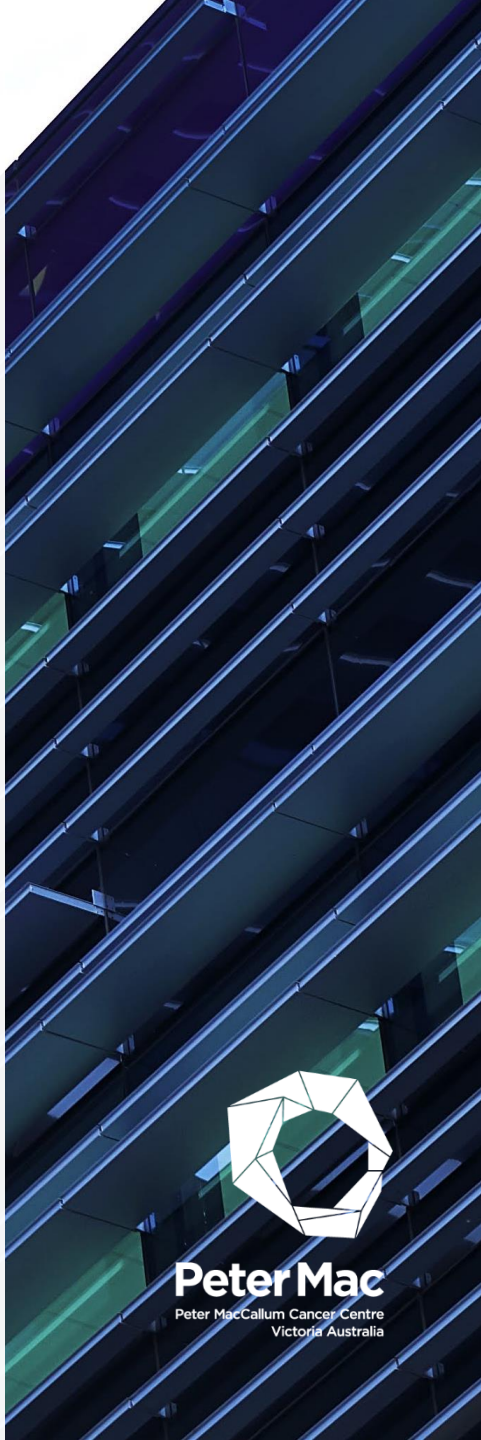
- From 44 additional patient referrals for CAR-T only available overseas, Peter Mac has supported **20 patients for Medical Treatment Overseas Program** (MTOP) funded SOC CAR-T treatment.
- In addition to SOC CAR-T, Peter Mac has supported up to **13 CAR-T clinical trials** with 6 active trials in our current CAR-T trial portfolio.

- Through CAR-T clinical trials, we have identified treatments for **57 haematology patients** and for **21 patients with solid malignancies**.



AUSTRALIAN KYMRIAH TOXICITY

NR = not reported		pALL (n=29)	DLBCL (n=28)
Characteristics	Median Age	13	65
	Male / Female (%)	52/45 (3% NR)	75/25
	Prior HSCT (%)	39%	50%
	Bridging	76% (17% NR)	79% (3.6% NR)
		pALL (n=18)	DLBCL (n=24)
Toxicity	CRS	61% (17% Gr 3)	88% (0% Gr 3/4)
	Neurotoxicity	11% (1 pt Gr3)	4%
	TLS	4%	Nil
	Hospitalisation	61% (NR in 39%)	79% (NR in 17%)
	ICU	17%	4%
	Toci Use	22%	33%



LEARNINGS TO INFORM PATIENT SELECTION FOR COMMERCIAL CAR-T

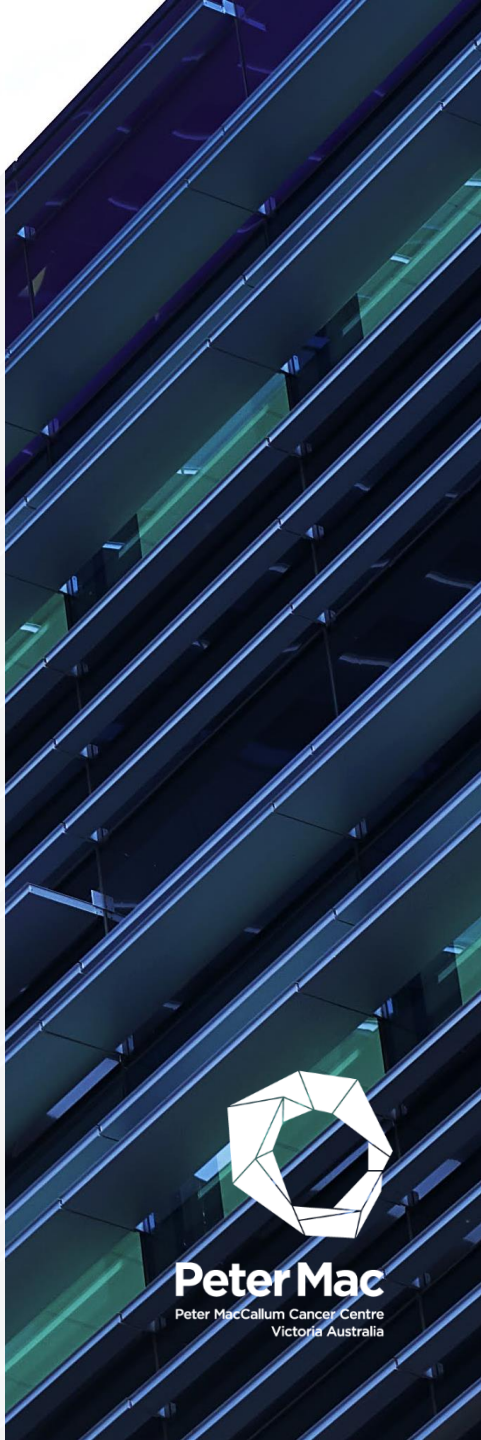
- The CoE CIT Clinical Service conducted 2-year clinical review to assess patient selection
- No overt concern regarding ALL at this time
- Driver to reduce the 'failure to infuse' rate for DLBCL –
- Initial unpredictable delivery time 4-16 weeks at the start. NOW 4 weeks
- Ongoing Questions:

What is the trigger for ordering CAR-T in high risk patients?

Move away from order then bridge to DISEASE CONTROL then order

Prior MDM assessment for CAR-T critical

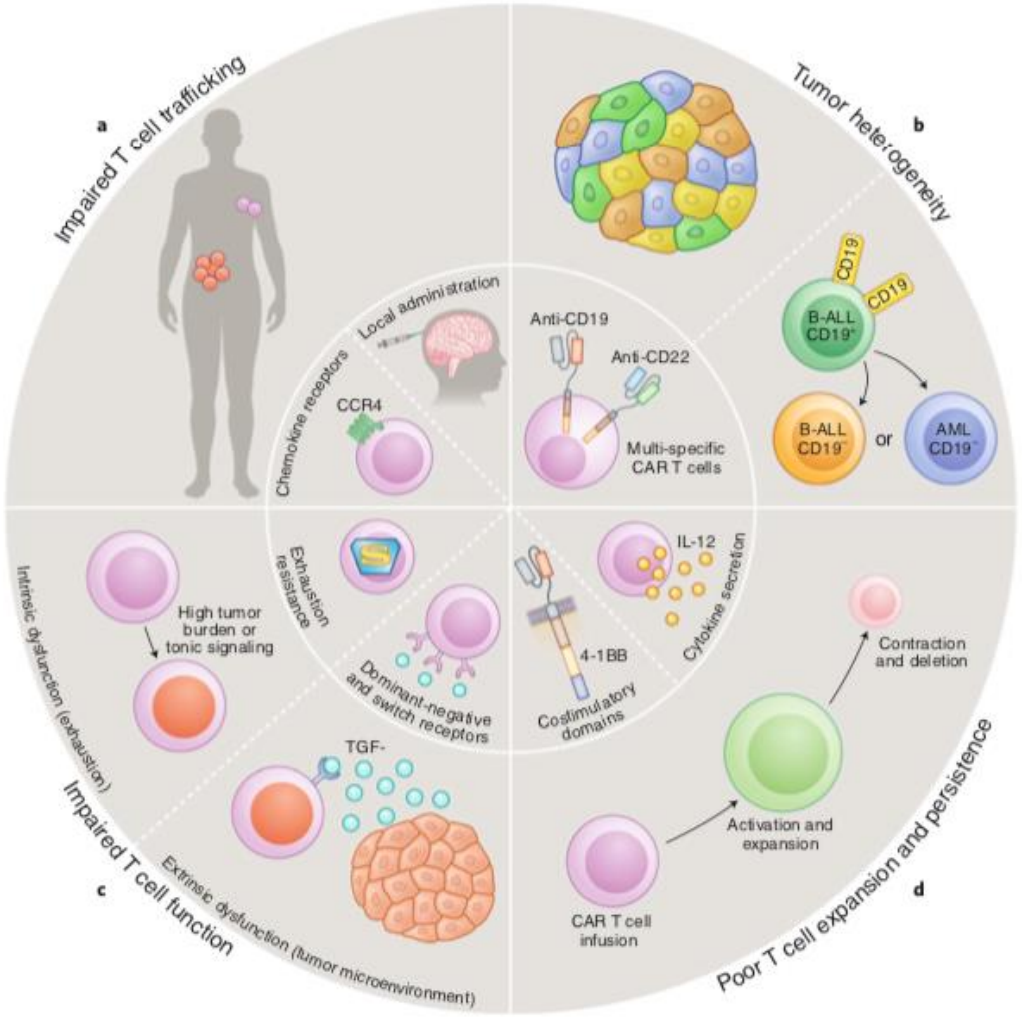
Lower threshold to decline patients - National meeting very important for consistency!



Mechanisms of failure

trafficking

impaired T cell function



tumor heterogeneity

poor T cell Expansion/ persistence

Mazjner & Mackall, Nat Med 2019

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Poor Car-T trafficking is a cause of treatment failure?

- Mode of Delivery
  - IV vs local injection
    - Mesothelin studies infusing into pleural Space
    - Infusion into CNS for brain tumors

- Do the cells arrive at the tumor site?
- Do the cell penetrate the tumor bed?

- Developing new tools to access distribution post infusion
  - Blood assess only measure one compartment
  - Biopsy unreliable

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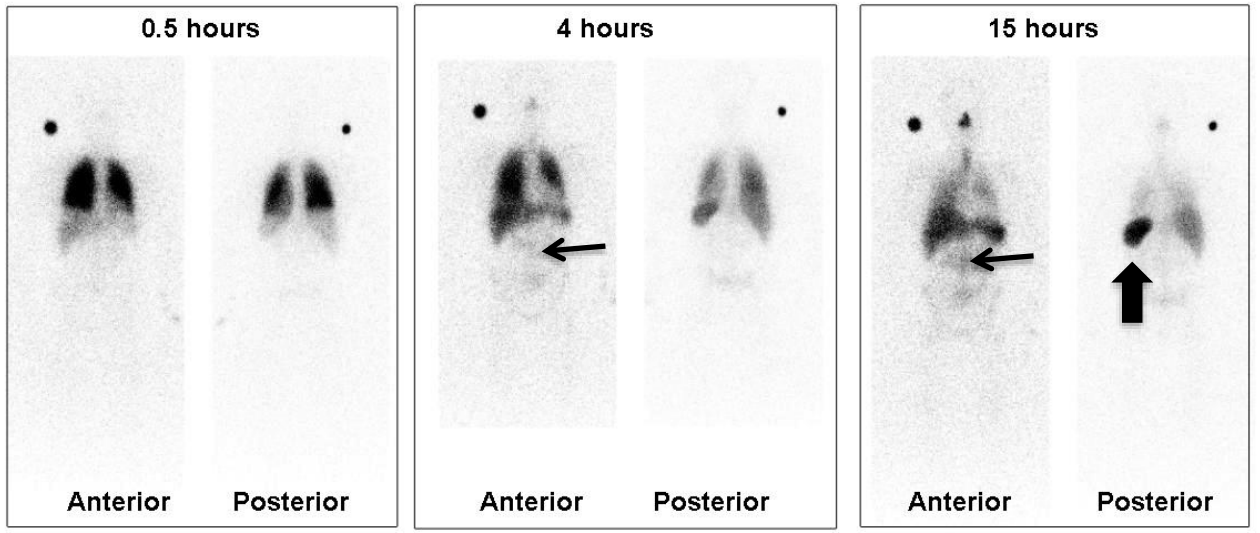
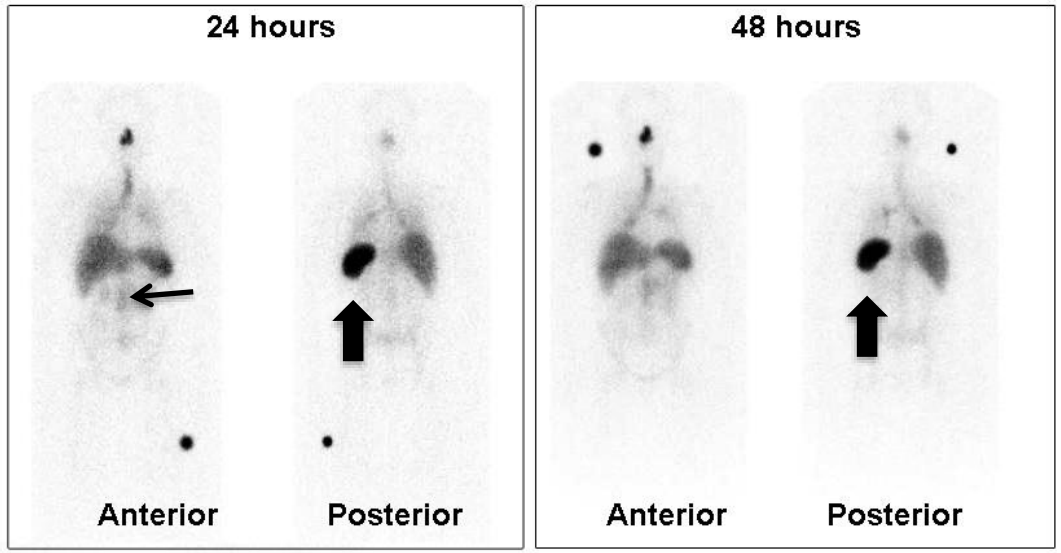
Autologous Peripheral Blood T lymphocytes Transduced with an Anti LewisY Chimeric Receptor Gene can be Infused Safely and Persist in Patients with LewisY Positive Acute Myeloid Leukaemia

Amit Khot [1], Paul Neeson[1], Stefan Peinert[1],Tsin Tai, Karen Chen, Dominic Wall[1], Dirk Honemann[1], Mandy Shin[1], Javier Haurat[1],Michael Kershaw[1], Jennifer Westwood[1], Joseph Trapani[1], Mark Smyth[1], Phillip Darcy[1], Andrew Scott[2], Lucy Kravets[1], Peter Gambell[1] , David Westerman[1] ,Rodney Hicks[1], Michael Dickinson[1], David Ritchie[1,], H Miles Prince[1]

[1]Peter MacCallum Cancer Centre, Melbourne, Victoria
[2]Ludwig Institute for Cancer Research, Melbourne, Victoria, Australia.

^{111}In-labelled T cells traffic to bone marrow





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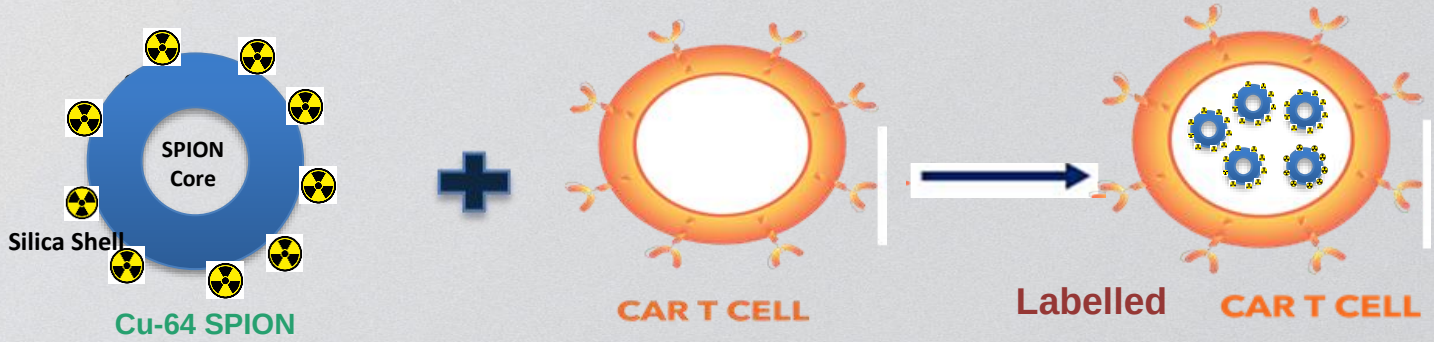
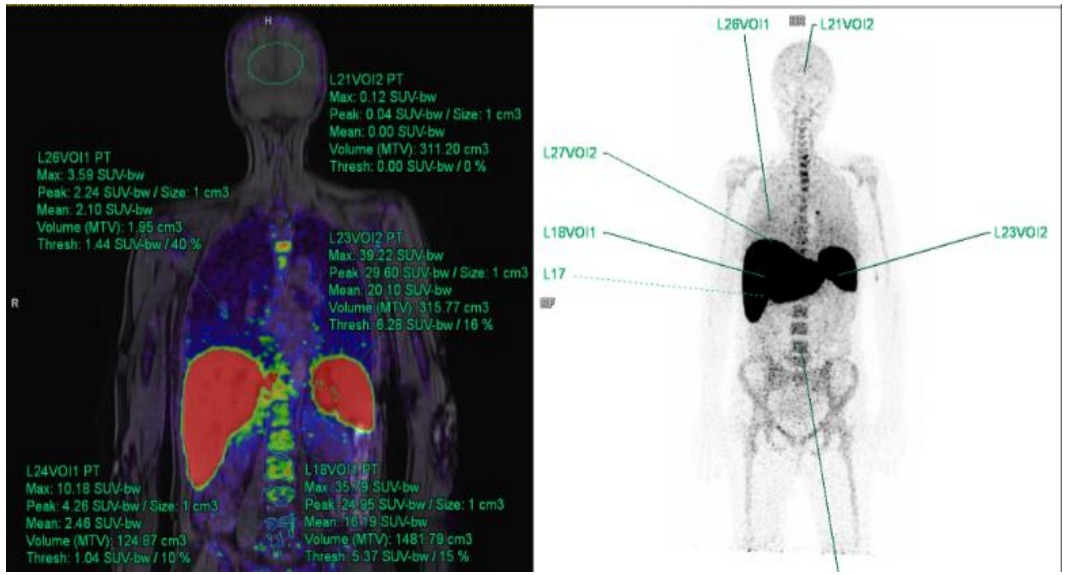
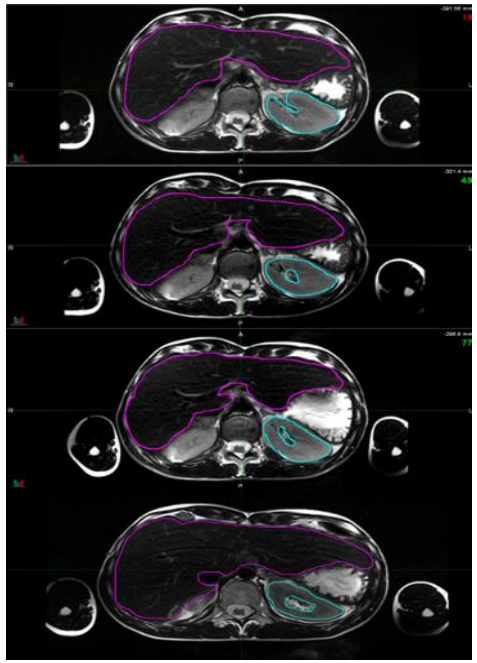
Human Real Time In-Vivo PET/ MRI CAR-T Cell Tracking





Patient #19: Day +1 PET Scan (injected activity 186 MBq)

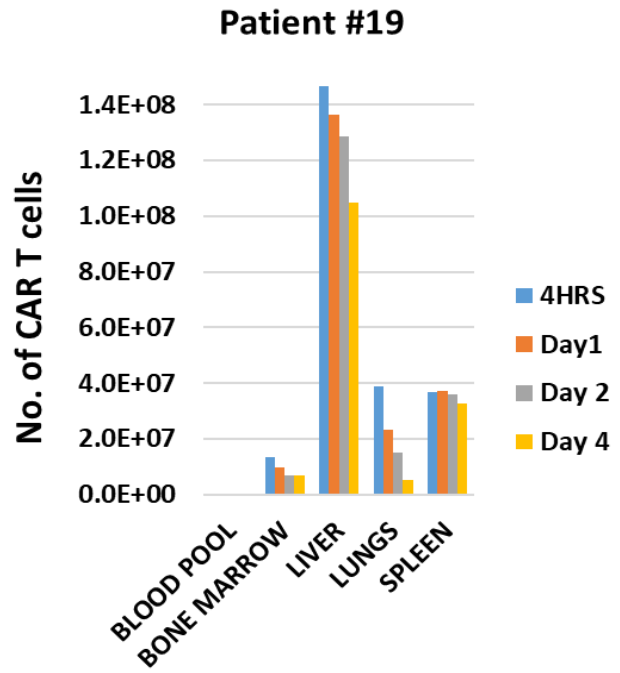


Baseline

Day +1

Day +3

Day +21



Quantification of labelled CAR-T cells

- Adapted from Singla et al, ASCO 2020 Poster presentation 3557.

MRI Findings: Change in T2w signal in liver Day +1 (-41.3%), Day +3 (-43.1%), Day +21 (-39.9%) indicates that tracking is possible up to a month

Westmead Hospital Pathogen and Malignancy Specific T-cell Therapies

IIT of T-cell therapies since 2003 donor-derived and banked 3rd party T-cells targeting

- CMV
- EBV
- Adenovirus
- BK virus
- Influenza
- VZV
- Yeasts and moulds
- WT1
- PRAME
- CD19 CAR T-cell

Over 200 patients treated on trials and compassionate access programs

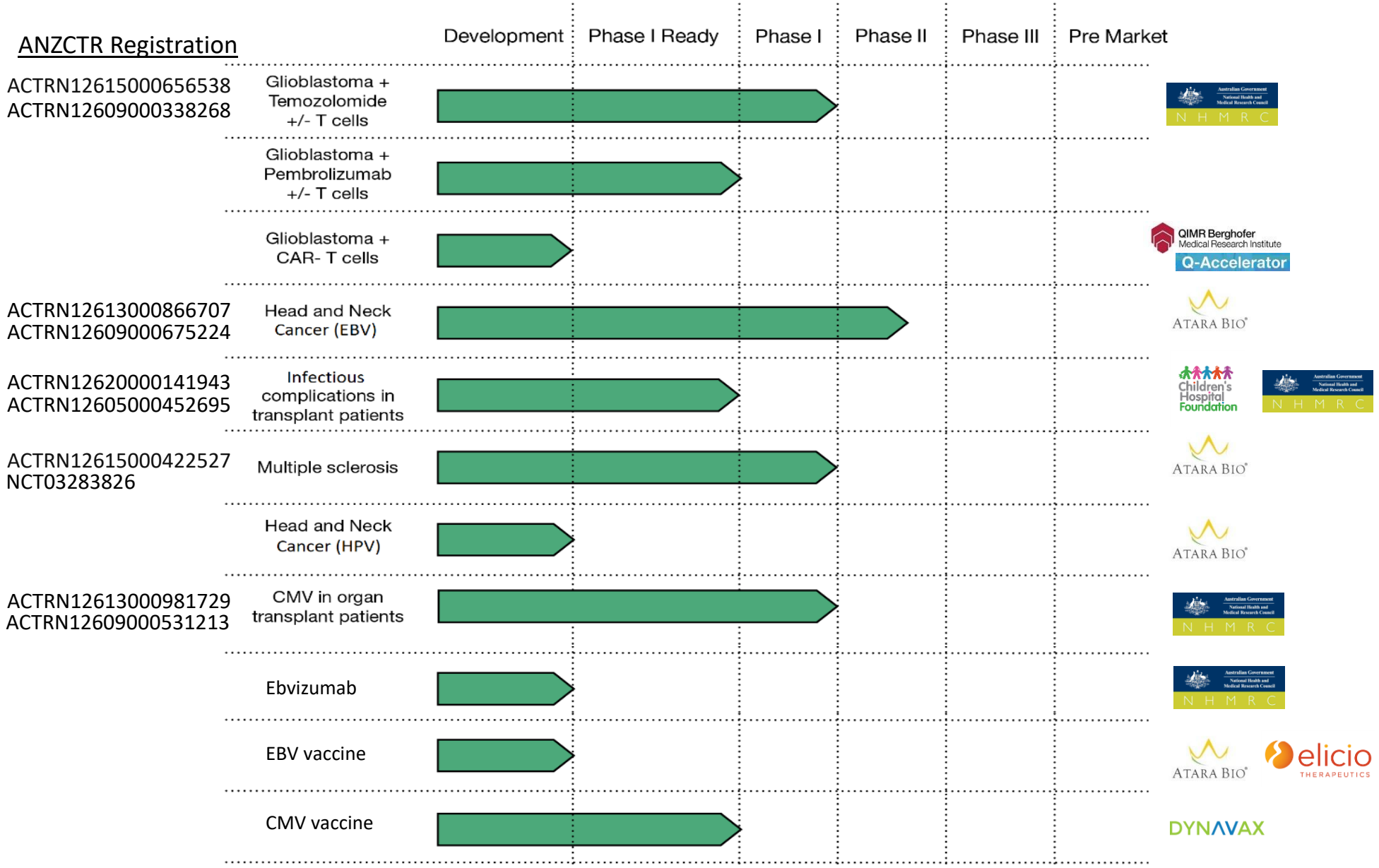
Current open trials

- 3rd party donor CMV- and EBV-specific T-cells for first viral reactivation after allogeneic stem cell transplant (phase 3)
- 3rd party donor fungus-specific T-cells for proven or probable invasive fungal disease after allogeneic stem cell transplant (phase 1)
- Donor-derived CMV-, EBV- and Aspergillus-specific T-cells in association with WT1 and PRAME-specific T-cells after allogeneic stem cell transplant for MDS and AML (phase 1)
- Donor-derived CMV-, EBV- and Aspergillus-specific T-cells in association with CD19 CAR T-cells or WT1 and PRAME-specific T-cells after CD34-selected allogeneic stem cell transplant for acute leukemia (phase 1)

Selected publications

- Gottlieb et al CTI 2021: Prophylactic administration of T-cell product targeting 7 viral and fungal antigens after allogeneic transplant
- Castellano-Gonzalez et al Blood Adv 2020: Rapidly expanded partially HLA DRB1 matched fungus-specific T-cells
- Withers et al BBMT 2018: Establishment of a virus-specific T-cell bank within a stem cell transplant program
- Withers et al Blood Adv 2017: Long term control of refractory viral infection using 3rd party virus-specific T-cells after allogeneic stem cell transplant
- Ma et al BBMT 2017: Addition of DC vaccination to T-cell therapy for CMV
- Ma et al Cytoptherapy 2015: VZV, CMV, EBV and Adeno T-cell therapy
- Blyth et al Blood 2013: CMV T-cells reduce need for pharmacotherapy after transplant

QIMR Pipeline: Delivering breakthrough immunotherapies for patients



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Centre of Excellence for Cellular Immunotherapy

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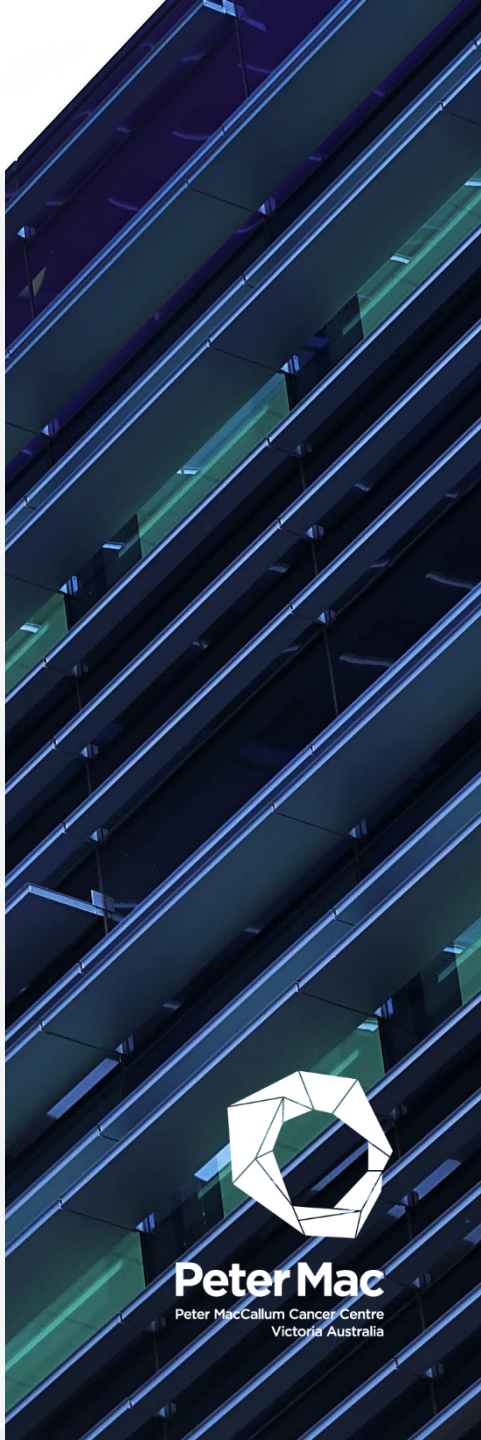
Australian Government
Department of Health

VICTORIA State Government | Health and Human Services



cell therapies

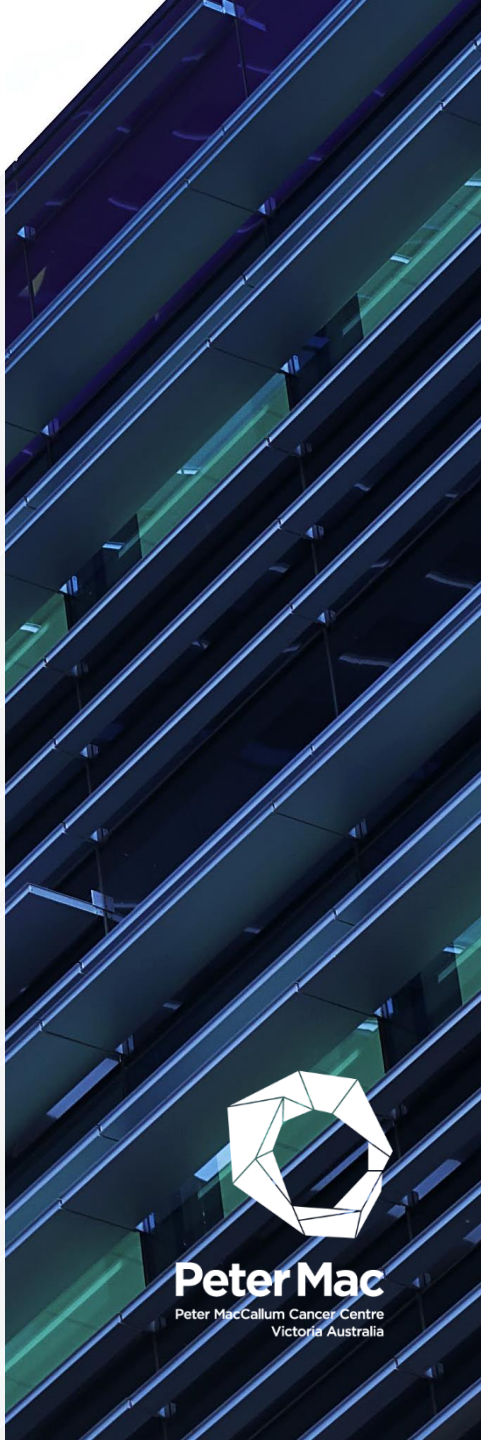
The Royal Melbourne Hospital

Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

Thank You
Questions?

Centre of Excellence in Cellular Immunotherapy

	Translational Research	Manufacturing	Clinical Research
Commonwealth Department of Health Funding Objectives	**Translation Research Laboratory** Develop novel immunotherapy concepts Cultivate new translational and research talent	**New Manufacturing Capacity** Commercial GMP Facility Translation Research & GMP Training Space **Support for CTPL Manufacturing for Pilot Clinical Trials** Production of cellular immunotherapy doses	**Increased Clinical Capabilities** New 14 bed/chair clinical care unit **CoE CIT Sponsored Pilot Clinical Trials** Pilot, early phase, first in human clinical trials
Capital works	**Laboratory space** Translational Research, GMP Training & Education	**GMP Facility** $$ GOVT	**Clinical Unit** $$ GOVT
Capabilities / Activity	**Research FTE & DRC** $$PMCC Foundation	**Trial Doses** $$ GOVT	**Trials** $$ GOVT $$ PMCC Foundation
PMCC	**Across Program:** $$ (CAR-T clinical service FTEs, commercialisation capabilities, CAR-T Registry development & translational research)		
Cell Therapies	**Across Program:** $$ (rent/returns from CTPL and tech transfer from manufacturing doses)		



COMMERCIAL CAR-T LAUNCH 2019

Tisagenlecleucel (Kymriah) ALL and DLBCL

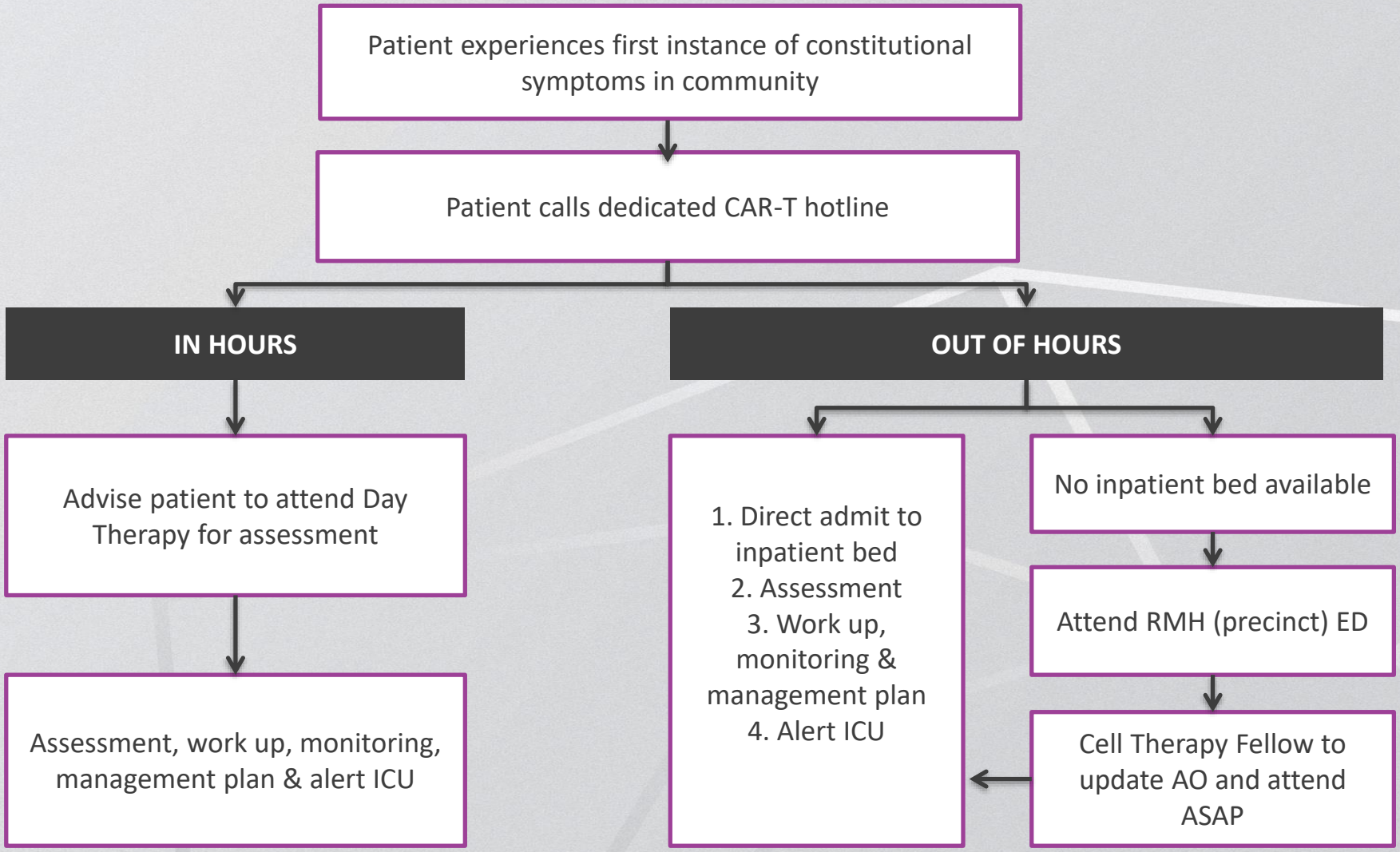
4-1BB and lentiviral vector, frozen in and out

Local Manufacturing Jan 2021

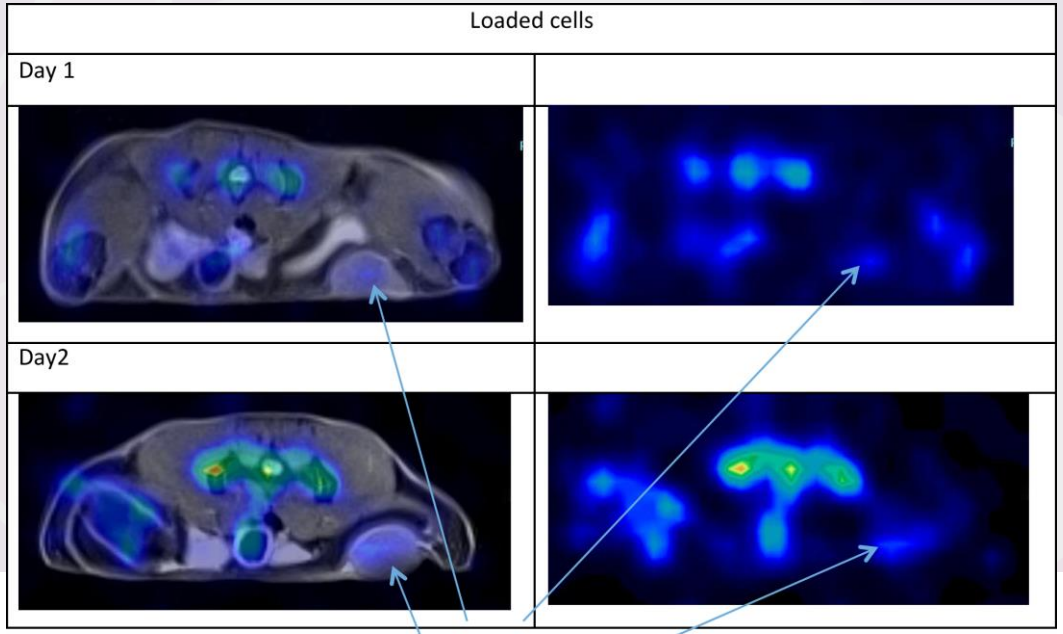
Axicabtagene ciloleucel (Yescarta) DLBCL

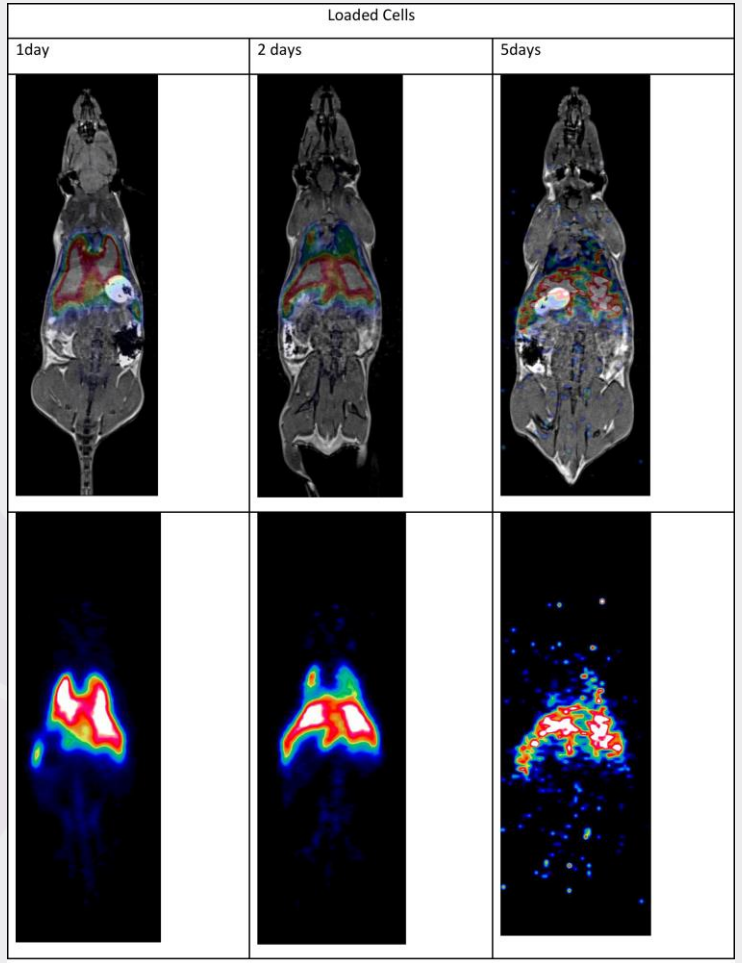
CD28 and γ retroviral vector, fresh in, frozen out

DETERIORATING PATIENT - CAR-T TRIAGE PATHWAY



PET MRI tracking of CAR-T cell In-Vivo





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cell therapies

Peter Mac
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CAR-T MEDICAL ALERT CARD

UNLESS LIFE THREATENING, STEROID USE SHOULD BE AVOIDED

PLEASE CALL CAR-T TEAM - 0436 847 642

NAME:

UR:

DATE OF INFUSION:

Clinical Haematology

Peter Mac Peter MacCallum Cancer Centre Victoria Australia

The Royal Melbourne Hospital

CAR-T MEDICAL ALERT

Treat Grade 2 > CRS with TOCILUZUMAB

UNLESS LIFE THREATENING, STEROID USE SHOULD BE AVOIDED

PLEASE CALL CAR-T TEAM IMMEDIATELY TO COMMUNICATE MANAGEMENT PH : 0436 847 642

This patient has received autologous CAR-T cell therapy

Patients are at a high risk of Cytokine Release Syndrome (CRS) and Neurotoxicity (ICANS)

Clinical Haematology

Peter Mac Peter MacCallum Cancer Centre Victoria Australia

The Royal Melbourne Hospital