

CANCER *talk*

CONNECTING WITH MANITOBA'S PRIMARY CARE PROVIDERS

ASK the Expert

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CAR-T IMMUNOTHERAPY



Immunotherapy in cancer has seen tremendous progress in the past decade. Harnessing the body's immune system to target cancer cells has led to improved outcomes and better (but different) toxicity profiles than traditional cytotoxic chemotherapies in many cancers.

One of the most exciting immunotherapies is chimeric antigen receptor T-cell therapy (CAR-T) in hematologic B-cell malignancies.

What is CAR-T?

It has long been known that T-cells play a role in normal immune surveillance of cancer cells in the body. CAR-T cells enhance this role by altering patient T-cells *ex vivo* to specifically target cancer cells. In the late 1980s, Gross and colleagues were able to genetically engineer human T-cells to express antibody-like receptors using a viral vector¹. Further development of this technology has led to CAR-T products that target specific cancer cell antigens and elicit a cytotoxic effect against the cancer cells. CD19 on B-cells is the antigen most often targeted with currently approved CAR-T cell products.

How does CAR-T work?

A visual representation of the process of CAR-T is seen in **Figure 1**². The immunosuppressive chemotherapy typically used is fludarabine and cyclophosphamide and is used to "make room" for the CAR-T cells when re-infused.

In what diseases is CAR-T used?

Currently, in Canada, CAR-T is approved and funded for relapsed/refractory diffuse large B-cell lymphoma (DLBCL) after autologous stem cell transplant and relapsed/refractory B-cell acute lymphoblastic leukemia (B-ALL) in patients between the ages of 3-25^{3,4,5}. Emerging data, currently only available in abstract form, indicates that CAR-T is superior to a consolidative autologous stem cell transplant in relapsed/refractory DLBCL. Health Canada has also approved products in Mantle cell lymphoma and multiple myeloma; however, no funding agreements have been reached for these products^{6,7}.

What are the unique toxicities of CAR-T?

In the first 28 days after CAR-T re-infusion, the unique toxicities include cytokine release syndrome (CRS) and immune effector cell-mediated neurotoxicity syndrome (ICANS). CRS is characterized by fever, hypotension and hypoxia and is treated with tocilizumab^{8,9}. ICANS is characterized by aphasia, altered level of consciousness, impaired cognition, motor weakness with seizures and cerebral edema in severe cases and is primarily treated with steroids^{8,9}. Both CRS and ICANS should be managed in a centre with a cellular therapy specialist, intensive care unit and neurology service. Long term toxicities of CAR-T include cytopenias, B-cell aplasia, hypogammaglobulinemia as well as the requirement to revaccinate patients.

Continued on page 2

What is the status of CAR-T in Manitoba and Canada?

Although approved by Health Canada, CAR-T is not currently funded or delivered in Manitoba. CAR-T has significant “financial toxicity” making the funding of products difficult. Patients who require CAR-T in Manitoba are currently referred to other centres. The CAR-T procedure is performed at these centres, and care is transferred back to CancerCare Manitoba after one month. Delivery of CAR-T in Manitoba is planned for the future.

What is the future of CAR-T?

CAR-T use is likely to increase in the coming years as it is approved for more indications with CD19 B-cell malignancies. In addition, investigation into the potential use of different antigen targets is underway, broadening the use of different antigen targets and the use of CAR-T in hematologic malignancies and solid tumours.

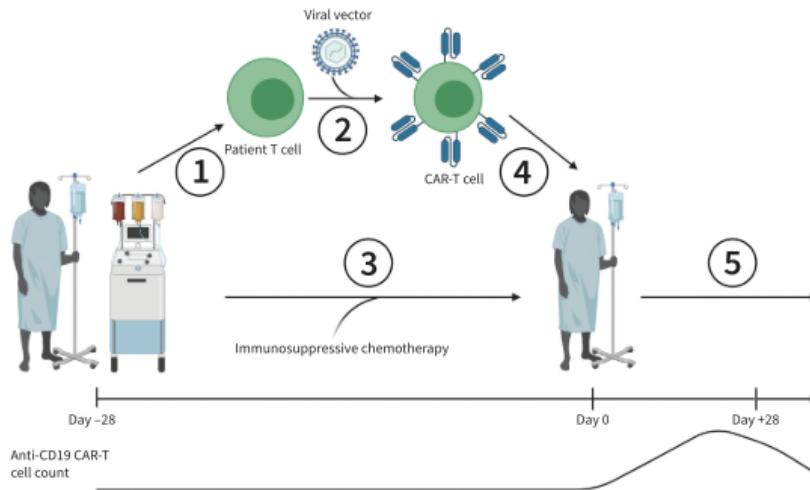


Figure 1: Process of manufacturing and administration of chimeric antigen receptor T-cell therapy (CAR-T). 1. The patient's T cells are collected via apheresis and transported to a manufacturing facility. 2. The patient's T cells are transduced with a viral vector and allowed to proliferate in vitro. 3. The patient is treated with immunosuppressive chemotherapy while the CAR-T cells are manufactured. 4. The CAR-T cells are transported back to the patient's centre and infused. 5. The patient is monitored for cytokine release syndrome (CRS) and immune effector cell-associated neurologic syndrome for up to 28 days and monitored long term for B-cell hypoplasia, hypogammaglobulinemia, cytopenias and opportunistic infections. Manufacturing timeline (not to scale) and patient CAR-T cell count are also shown.

References

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2. Brown K, Seftel MD, Hay KA. Innovations in cancer immunotherapy: Chimeric antigen receptor T-cell therapy (CAR-T). CMAJ [Internet]. 2021 Aug 23;193(33):E1300–2. Available from: <http://www.cmaj.ca/lookup/doi/10.1503/cmaj.202907>.
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8. Lee DW, Santomasso BD, Locke FL, Ghobadi A, Turtle CJ, Brudno JN, et al. ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells. Biol Blood Marrow Transplant [Internet]. 2019;25(4):625–38. Available from: <https://doi.org/10.1016/j.bbmt.2018.12.758>.
9. Neelapu SS. Managing the toxicities of CAR T-cell therapy. Hematol Oncol. 2019;37(S1):48–52.

If you have questions regarding the work-up of suspected cancer or any other cancer-related questions, please contact The CancerQuestion Helpline for Healthcare Professionals

(204) 226-2262 or cancer.question@cancercare.mb.ca

Monday to Friday 8:30 a.m. to 4:30 p.m.



Sri Navaratnam, MBBS, PhD, FRCPC
President & CEO,
CancerCare Manitoba

MESSAGE FROM CCMB PRESIDENT AND CEO, DR. SRI NAVARATNAM

With the new year upon us, I trust you had moments of rest and renewal over the holiday season to maintain resilience as we continue to live in unprecedented times. Throughout the pandemic, at CCMB, we committed to maintaining high-quality cancer services in a COVID-adapted environment while keeping both staff and patients safe. We applaud and admire our patients and their families for bravely continuing their journey and supporting us in the operational changes made to accommodate pandemic restrictions.

We are very grateful to our staff who quickly adapted their usual practices to be available to patients during adversity. And we are grateful to you, the primary care community, for your support and care of cancer patients through the pandemic. You too have committed to being available to your patients. Together with our partners such as you, we faced the challenges and provided the best care to cancer patients.

As we move into the new year, 2022, we will continue the implementation of the *Roadmap to Cancer Control for Manitoba 2020*. We have had very good engagement with primary care providers to date; this has been very

encouraging and beneficial for all. Increasing engagement with you is an Objective of Priority 2 of the *Roadmap*. Your key role in the care of cancer patients including cancer prevention, early diagnosis and timely referral is vital to the patient experience and outcome. We look forward to continued interaction with you as we create action plans that correspond with the priorities and objectives of the *Roadmap*.

Key areas of focus we are excited about for the new year, which are foundational to cancer control, are research and innovation, patient- and community-centred care, and equitable care. Primary care plays a big part in these areas. Thank you for your part in working towards cancer control in Manitoba!

UPCOMING VIRTUAL EDUCATION EVENTS

Wednesday, January 19, 2022, 12:00 p.m. - 1:00 p.m.

Community Oncology Rounds: Updates in Breast Cancer Treatment & Strategies for Addressing Barriers to Care - Dr. Marshall Pitz. [Register here.](#)

Friday, February 25, 2022, 12:00 p.m. - 1:00 p.m.

Cases in Cancer: Pediatric Leukemia - Dr. Cielle Wachnian. [Register here.](#)

Wednesday, March 2, 2022, 12:00 p.m. - 1:00 p.m.

ColonCheck Webinar: Increased Risk Management for Colorectal Cancer - Dr. Ross Stimpson, and Dr. Kadriah Lupitasari. [Click here for details.](#)

Wednesday, March 16, 2022, 12:00 p.m. - 1:00 p.m.

Community Oncology Rounds: CLL - Dr. Lin Yang. [Register here.](#)

Friday, April 8, 2022, 1:00 p.m. - 4:00 p.m.

Cases in Cancer: Lung Cancer Diagnostic Work-up - Dr. Biniyam Kidane and Dr. James Bras. [Register here.](#)



COVID-19 VACCINATION - THE THIRD DOSE

SARS-CoV-2-infected cancer patients are at high risk for poor outcomes. Cancer patients demonstrate a range of deficits in their innate and adaptive immune defenses. T-cell and memory B-cell memory immune responses may be enhanced by viral spike (S) protein vaccines.

Anti-S antibody titres correspond roughly to the titre of protective neutralizing antibody following SARS-CoV-2 infection or vaccination¹. In healthy individuals, anti-S titres peak at approximately 1-2 weeks following the second dose of an mRNA vaccine and then decline by as much as 79% and 94% after 3 and 6 months, respectively². SARS-CoV-2 breakthrough infections (BTI) reflecting, in part, this waning immunity have been observed to occur at a median of 4-5 months following the second dose³.

There are two objectives for third COVID-19 vaccine dosing. “Booster” dosing at 6 months following the second dose for the general population can mitigate waning humoral immunity over time by re-awakening (or boosting) the memory immune response. Third dosing administered to persons 60-years-of-age or older at least 5 months after the second dose may confer as much as an 11-fold reduction in SARS-CoV-2 BTI and a 19-fold reduction in severe COVID-19⁴. Post-two dose

seroconversion among solid tumour patients is initially high (85% to 90%; somewhat lower among chemotherapy recipients)⁵; however, 3rd dosing 6-8 months after the second dose significantly increases the waning anti-S titres⁶.

In contrast, “adjuvant” 3rd dosing at ≥ 1 month after the second dose is a strategy for select subgroups of immune suppressed patients for whom the primary two-dose vaccine schedule fails to elicit an adequate humoral and cellular response⁷. Approximately half of haematological malignancy patients and even fewer (<10%) after anti-B cell immunotherapy seroconvert after two doses⁵. Adjuvant third dosing given 6-8 weeks after the second for immune suppressed two-dose non-responders may stimulate seroconversion in approximately half of cases⁸. The CDC is also considering a role for a 4th “booster” dose for these patients.

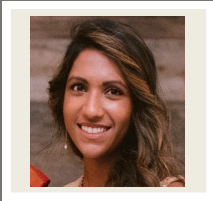
Based upon these observations, Manitoba Health Seniors & Active Living and CancerCare Manitoba Infection Control Services have recommended that a 3rd dose be given ≥ 1 month (28 days) after the second vaccine in immune suppressed patients with cancer.

References

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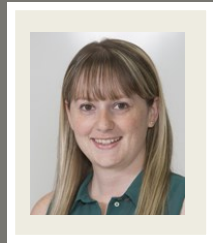


WELCOME TO CANCERCARE MANITOBA



Dr. Sangita Sequeira

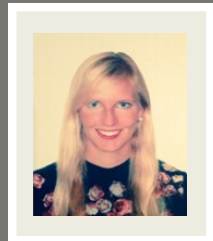
Sangita Sequeira is a breast surgeon who is new to CancerCare Manitoba. She will join us in the New Year. Dr. Sequeira's clinical interests include oncoplastic breast surgery to improve cosmetic outcomes for breast cancer patients. Her research interests include surgical outcomes and patient reported outcomes of breast cancer patients. Welcome Dr. Sequeira!



Dr. Stacy Chapman

On July 12, 2021, Dr. Stacy Chapman joined the Pediatric Oncology & Hematology Department at CancerCare Manitoba as a Pediatric Oncologist-Hematologist. Dr. Chapman is an Assistant Professor, Department of Pediatrics & Child Health at the University of Manitoba.

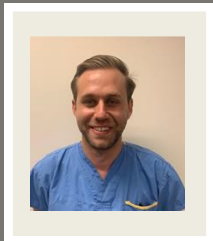
Dr. Chapman's clinical interests are in AYA with sarcomas and other malignancies, palliative care, survivorship and supportive care for children with cancer. You can welcome Dr. Chapman in person if you join us for CancerDay for Primary Care on Friday, May 27, when Dr. Chapman will discuss the workup of abdominal masses in the pediatric population.



Dr. Cielle Wachnian

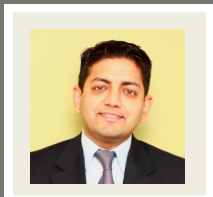
As of September 7, 2021, Dr. Cielle Wachnian has joined the Pediatric Oncology & Hematology Department at CancerCare Manitoba as a Pediatric Oncologist-Hematologist and Assistant Professor in the Department of Pediatrics and Child Health at the University of Manitoba.

Dr. Wachnian's areas of special interest are Precision Medicine and Developmental Therapeutics, Global Health, and Quality Improvement. She recently published as the first author of a manuscript in Pediatric Blood and Cancer regarding the use of point of care genomics for Pediatric ALL. We are delighted to have Dr. Wachnian join our team here at CCMB.



Dr. Kevin Brown

As of August 16, 2021, Dr. Kevin Brown has joined the Section of Hematology/Oncology, Department of Internal Medicine, and the Department of Medical Oncology and Haematology at CancerCare Manitoba. Dr. Brown has expertise in CAR-T therapy and outpatient stem cell transplantation. Dr. Brown will primarily be working in the Leukemia Bone Marrow Transplant Program at CCMB and the GD6 inpatient unit at Health Sciences Centre. He will also participate in clinics within the Hematology Disease Site Group at CCMB. Please join us in warmly welcoming Dr. Brown to our team.



Dr. Rahul Bansal

Dr. Rahul Bansal joins the Manitoba Prostate Center as a consulting urologist as of December 15, 2021. Welcome Dr. Bansal!



STAFF HIGHLIGHTS

CAMRT HONORARY AWARDS



The CAMRT Honorary Awards are a collection of awards presented to members at the pinnacle of the profession. The winners of these awards earn the highest recognition from their association by their dedication, commitment and exceptional contributions to our profession. Due to the restrictions of the COVID-19 pandemic, this year the award recipients are being recognized virtually and their awards will be presented to them in person at CAMRT 2021 in Ottawa, Ontario.

Dr. Marshall Mallett *Lamp of Knowledge Award*

This award was established in 1957 to honour a member of the CAMRT who has made a significant contribution to the profession and/or association, at a national level, in the field of education. The CAMRT is pleased to present this award to **Christina Zeller**, RTT, ACT, from Manitoba.

Chris has always been an active and passionate advocate for not only Radiation Therapy, but all MRT disciplines. She has sat on numerous CAMRT and MAMRT committees (past and present) as well as received numerous awards from the MAMRT. She played a key role in converting the Radiation Therapy program from a diploma to a degree at the University of Winnipeg. She has also been published in JMIRS. Chris is a lifelong learner and has a passion for continuing education, volunteering and the importance of being engaged in the MRT profession and its associations.

THE CANADIAN SOCIETY OF HEMATOLOGY



The Canadian Society of Hematology has selected Dr. Zarychanski's paper entitled "Therapeutic Anticoagulation with Heparin in Non-Critically ill Patients with Covid-19" as the paper of the year for the society. This paper, and a companion paper evaluating heparin anticoagulation in critically ill patients with Covid-19, was published in the *New England Journal of Medicine* in August 2021 and included Dr. Brett Houston from CCMB as a co-author. The results of the paper forwarded a new global standard of care for the treatment of hospitalized moderately ill patients with Covid-19 and introduced new clinical trial methods and processes of global collaboration developed specifically to meet the challenging needs of a pandemic.



Professional Development Calendar We're Staying Virtual!

Cancer Education For Health Care Professionals

2021 –2022			
Date	Event	Topic	Location & Time
September 24 2021	Cases in Cancer	Immunotherapy Guest Expert: Dr. Jeffrey Graham Facilitator: Dr. Mark Kristjanson	12:00—13:00 Zoom Register here
October 20, 2021	Community Oncology Rounds	Multiple Myeloma Presenter: Dr. Emily Rimmer	12:00-13:00 Zoom Register here
October 22, 2021	Prevention and Screening Webinar	HPV Triage: Enhancing cervical cancer screening in Manitoba	12:00-13:00 Zoom Click here for details
November 4 & 5	Provincial Cancer Care Conference	See CancerCare Manitoba website for details	
November 24, 2021	Community Oncology Rounds	Ovarian Cancer & PARP inhibitors Presenter: Alon Altman	8:00-9:00 Zoom Register here
December 3, 2021	Cases in Cancer	Toxicities from Radiation Guest Expert: Dr. Andrew Cooke Facilitator: Dr. Mark Kristjanson	12:00—13:00 Zoom Register here
January 19, 2022	Community Oncology Rounds	Updates in Breast Cancer Treatment & Strategies for Addressing Barriers to Care Presenter: Dr. Maclean Thiessen	12:00-13:00 Zoom Register here
March 2, 2022	ColonCheck Webinar	Increased Risk Management for Colorectal Cancer Presenters: Dr. Ross Stimpson, Dr. Kadriah Lupitasari	12:00 – 13:00 Zoom Click here for details
February 25, 2022	Cases in Cancer	Pediatric Leukemia Presenter: Dr. Cielle Wachnian	12:00-13:00 Zoom Register here
March 16, 2022	Community Oncology Rounds	CLL Presenter: Dr. Lin Yang	12:00-13:00 Zoom Register here
April 8, 2022	Cases in Cancer	Lung Cancer Dr. Biniam Kidane and Dr. James Bras	13:00-16:00 Western Manitoba Cancer Centre or Microsoft Teams/Telehealth Register here
April 22, 2022	Cases in Cancer	Management of Comorbidities Guest Expert: Dr. Davinder Jassal Facilitator: Dr. Mark Kristjanson	12:00—13:00 Zoom Register here
May 27, 2022	Cancer Day for Primary Care	See registration website for details	All Day
On Request 1-1.5 hours	Education in your office	Cancer Diagnosis Workshops, Follow up Care Guidelines, Introduction to Cancer Services in Manitoba To request an event, email CCMBPrimaryCareEducation@cancercare.mb.ca	

Schedule subject to change. For more information and updates visit: www.cancercare.mb.ca/For-Health-Professionals/conferences/index.html

CancerCare Manitoba’s Community Oncology Program offers many excellent oncology and hematology education sessions and conferences throughout the academic year.



CCMB PREVENTION & SCREENING UPDATE

HPV Triage: Enhancing Cervical Cancer Screening in Manitoba

In early 2022, cervical cytology labs in Manitoba will automatically perform high-risk human papillomavirus (hrHPV) testing on the Pap test specimens of patients:

- 30 years of age and older with ASCUS Pap test results, and
- 50 years of age and older with LSIL Pap test results.

HPV triage:

- identifies which patients would most benefit from colposcopy,
- decreases time to colposcopy by eliminating extra Pap tests,
- avoids over-treatment for patients who do not need a colposcopy, and
- reduces anxiety for those who do not need follow-up.

The lab report will contain the cytology interpretation, high-risk HPV test result, follow-up recommendation, and educational note.

Other resources will be available at <https://www.cancercare.mb.ca/screening/hcp>, including a recorded webinar by Dr. S. Kean, CervixCheck Medical Lead, and panelists.

Save the Date!

March 2, 2022

12:00-1:00 p.m. (Central Standard Time)

Increased risk management for colorectal cancer

Join us for an informative webinar about screening management for individuals at increased risk for colorectal cancer. This Group Learning program has been certified by the College of Family Physicians of Canada for up to 1 Mainpro+ credits.

Sign up for email notification at <https://www.cancercare.mb.ca/screening/enews> to be notified of webinar registration and HPV triage implementation.



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