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CANCER talk

› CONNECTING WITH MANITOBA'S HEALTH PROFESSIONALS

What is the Right Dose?

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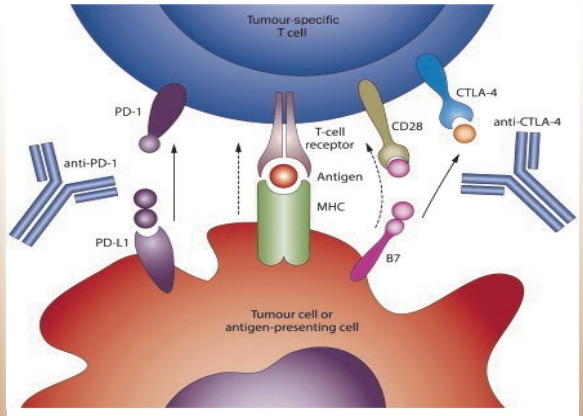

Image sourced from www.fda.gov—December 23, 2014

The use of monoclonal antibodies (MoAbs) for the treatment of cancers is rapidly increasing, with rituximab and trastuzumab amongst the most commonly prescribed antineoplastics. In the last few years, MoAbs of the immune checkpoint class, such as ipilimumab, nivolumab, and pembrolizumab, have emerged as potent treatment options for some cancers. Optimizing the dosing of these agents is very different from optimizing the dose of standard cytotoxic chemotherapies. Why is this and how do we get to the "right" dose?

Unlike standard cytotoxic chemotherapy drugs (CTX), neither the beneficial activity nor the toxicity of these MoAbs appears to be closely linked to the dose. In dose finding studies of CTX the goal is to seek the maximally tolerated dose (MTD), with the assumption being that the highest tolerated dose of a CTX drug will be the most effective. Most MoAbs do not have "dose-limiting" toxicities, and so the dose is usually established through identification of a minimum anticipated biologically effective level (MABEL) from animal toxicology data, with subsequent dose escalation in human Phase I trials based on rule-based or model-based designs that take into account drug stability, pharmacokinetic and pharmacodynamic parameters, cost, required infusion time and other considerations. In most instances weight-based dosing is explored, with the hope that flat dosing (non-weight dependent) can be achieved.

Due to the wide range of doses explored, population pharmacokinetics is often used to determine if flat dosing is feasible with a MoAb. As an example, nivolumab was initially recommended to be administered at 3 mg/kg IV every two weeks. In 2016, the Food and Drug Administration (FDA) approved a flat dose of nivolumab at 240mg every two weeks. This approval was given due to the population pharmacokinetics analyses and dose/exposure-response analyses demonstrating comparable pharmacokinetics exposure, safety and efficacy of flat dosing and weight-based dosing. The FDA determined the overall exposure of a flat dose of 240mg every two weeks is similar (less than 6% different) to 3 mg/kg every two weeks. The conclusion was that differences in exposure between flat and weight-based doses are not likely to have a clinically meaningful effect on safety and efficacy. In Manitoba, the current approach when

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nivolumab is used every two weeks is to dose at 3mg/kg (up to a maximum of 240mg) IV every two weeks. Patients who weigh less than 80 kg receive the nivolumab weight-based dosing to minimize costs without compromising efficacy. Those over 80 kg all receive the same dose, no matter how heavy they are, again without apparent loss of efficacy. Interestingly, in May 2018, an every four week dosing of 6 mg/kg IV (up to 480mg) became an option confirmed by population pharmacokinetics performed (Reference: http://www.ascopost.com) and has been clinically introduced in Manitoba.

Many of the MoAbs are now being studied using flat dosing for all patients, including some that are being given subcutaneously (saving chair time in the treatment room). Examples of MoAbs that are flat dosed are listed below:

Monoclonal antibody	Flat dose
Obinutuzumab	1000mg dose
Pertuzumab	420mg dose
Subcutaneous rituximab	1400mg dose in lymphoma 1600mg dose in chronic lymphocytic leukemia
Atezolizumab	1200mg flat dose

In conclusion, MoAbs have gained a major foothold in the treatment of solid tumors and haematological malignancies. Various dosing strategies are currently being investigated and employed such as flat dosing, increasing dose with decreased frequency of administration, decreased infusion time, and alternate routes of administration. What is increasingly clear is that “precise” dosing is not relevant in ensuring optimal efficacy and tolerance.

Lymphedema Therapy in Manitoba

Jennifer Dalke & Katherine Styrchak
Certified Lymphedema Therapists

Lymphedema (LE) is a chronic accumulation of lymphatic fluid within and beneath the skin. This causes swelling that often occurs in the arm, hand, leg and/or feet, but can also occur in the breast, chest, abdomen, head and neck, and genitals.

Lymphatic fluid is transported from the interstitium through the lymphatic vessels and nodes to rejoin the blood circulatory system in the heart. Missing or damaged lymphatic vessels can cause a backup of lymphatic fluid in the tissues.

Lymphedema can progress, fibroadipose tissue changes can occur, wounds can take longer to heal and affected areas can become a good environment for bacterial growth, increasing the risk of infection. Infections take longer to respond to treatment and often require several courses of antibiotics, or a combination of IV and oral antibiotics.

A primary care provider diagnoses LE through a differential diagnosis, excluding conditions such as DVT, infection, and metastases. Edema, when caused by congestive heart failure or renal failure is systemic, and not the result of a damaged lymphatic system.

Primary lymphedema is congenital and may be present at birth, at puberty or even develop in adulthood. There is usually a genetic component associated with primary LE, and other health conditions need to be addressed. Secondary LE is caused by surgery (cancer and non-cancer-related), radiation therapy, recurring infections, venous disease, trauma or filariasis.

In Manitoba, access to publicly-funded certified lymphedema treatment is available at two locations. In Winnipeg, services related specifically to breast cancer-related lymphedema are available at the Breast Health Centre; in Brandon, at the Regional Health Centre, all types of lymphedema are treated.

All lymphedema must be diagnosed by a primary care provider before being treated by a certified lymphedema therapist (CLT).

Private-practice CLTs are available throughout Manitoba. Most insurance plans cover a portion of this fee-for-service. Look for a CLT who has certification from an accredited program, such as Klose Training or Dr. Vodder. Therapists should follow the International Lymphedema Framework's Best Practices and include manual lymphatic drainage (MLD), compression bandaging/garments, exercise and skin care as well as patient involvement in their treatments. LANA (Lymphology Association of North America) is the highest certification a CLT can obtain.

Compression garments limit progression of lymphedema. They are not covered under Manitoba

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Formulary Changes to NIHB

Allison Wiens, RN, BN & Morgan Stirling, MSc. - Underserved Populations Program, CancerCare Manitoba

It is well recognized that the costs of cancer medications often come at great expense to patients. The introduction of the Home Cancer Drug Program has helped in reducing these costs; however, not all Manitobans benefit. Jurisdictional boundaries between the Government of Manitoba and the First Nations and Inuit Health Branch regularly leave First Nations and Inuit people without coverage for eligible oral cancer and supportive drugs.

Recent changes to the Non-Insured Health Benefits Program (NIHB) have resulted in a new formulary to facilitate access to adjunctive (non-chemotherapy) medications frequently used by patients undergoing active cancer treatment. These medications include:

- Aprepitant (e.g., Emend)
- Benzydamine Oral Rinse
- Darbepoetin alfa (e.g., Aranesp)
- Erythropoetin alfa (e.g., Eprex)
- Diphenoxylate-atropine (e.g., Lomotil)
- Minocycline
- Moistir
- Nabilone
- Pegylated filgrastim
- Pregabalin (e.g., Lyrica)
- Boost/Ensure

Patients covered through NIHB who have been approved for oral chemotherapy or other cancer treatment adjunct medications are automatically enrolled for six months and can access any medication listed on the formulary. Access can be extended if treatment lasts or is expected to last more than six months.

Please note that many other adjunct medications used during cancer treatment are available as open benefits. For more information and to view the full Drug Benefit List (DBL) visit: www.canada.ca/nihb.

CancerCare Manitoba

Strategies for Sustainability of Excellence in Cancer Services for Manitobans

Dr. Sri Navaratnam, President & CEO, CancerCare Manitoba

CancerCare Manitoba has the provincial mandate to provide cancer services to all Manitobans and strives to provide patient-centered quality cancer care to our patients. CCMB's model of care is evidence-based and aims to be fiscally sustainable. The core of the model is multidisciplinary care - comprehensive care provided by a team of specialists from all disciplines. These specialists consult with the patient and then develop an individualized plan for the best treatment for the patient.

Once a patient's treatment plan has been developed, whenever possible, we encourage patients to receive their systemic chemotherapy treatment and follow-up visits at a community site closer to their home, whether in Winnipeg or rural Manitoba. Through regional collaborations, we are able to bring quality care to patients closer to home throughout the province. This model of care is key to Sustaining Excellence in Cancer Services for Manitobans.

CancerCare Manitoba's goal is that no Manitoban's life is cut short by cancer and a life with cancer is a life well lived. This goal and the model of care can only be achieved through collaboration with healthcare partners, including those in primary care.

Earlier this year, the Department of Primary Care Oncology was established at CancerCare Manitoba with Dr. Tunji Fatoye as the Department Head. This new CCMB Department is affiliated with the University of Manitoba as the Section of Primary Care Oncology, Department of Family Medicine. We are very excited about this development and are confident it will further enhance and strengthen the important role of primary care providers to cancer patients.

Thank you for your part in continuing to provide and sustain the excellent cancer care to the people of Manitoba.

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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**
Monday to Friday: 8:30 a.m. to 4:30 p.m.
Call or text 204-226-2262

Zoledronate and Breast Cancer

Dr. Mark Kristjanson, Medical Lead, Primary Care, Community Oncology Program, CCMB

CancerCare's Transitions Initiative is drafting new guidelines for the follow up of patients with breast cancer who are to be treated adjuvantly with zoledronic acid. Zoledronic acid is a bisphosphate, similar to but more potent than pamidronate in protecting bone from osteoclast activity. Good evidence exists to demonstrate that for some patients, the adjuvant use of zoledronic acid following curative-intent treatment will reduce the risk of distant bony metastatic disease recurrence, and even improve overall survival. Deciding exactly which group of patient stands to benefit from zoledronic acid, however, is a judgement call that needs the expertise of a medical oncologist familiar with the scientific literature. In short, these are the "higher risk" patients to whom treatment is being administered with curative intent. Node positive patients, or node negative patients whose disease has certain high risk features such as lymphovascular space invasion on pathologic examination, or who have a high "Onco-Dx" score, constitute the group that enjoys the biggest absolute reduction in disease recurrence and mortality .

CancerCare Manitoba will arrange for the provision of zoledronic acid to patients who qualify, following appropriate consultation with the medical oncologist. The Transition guideline will specify that the initial bisphosphonate script will be issued by the medical oncologist, and (in most instances) supervised thereafter by an FPO (Family Physician in Oncology). A copy of the Transitions document with details of the above-noted care plan will be provided to the patient's Family Physician or Nurse Practitioner, as well as to the patient. Five years post-curative treatment, the FPO will also arrange for the patient to see her medical oncologist for discussion of the potential risks and benefits of extending hormone treatments beyond five years.

For more information: www.cancercare.mb.ca/forwardcare

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Health and patients must purchase garments every six months, as they lose their compression over time. Some private health insurance companies may cover a portion of this cost.

For additional general information on lymphedema, see the Lymphedema Association of Manitoba (LAM) website **www.lymphmanitoba.ca** and for more information on breast cancer- related lymphedema see the BHC website **www.wrha.mb.ca/BHC.**

Would your patients benefit from Cancer information?

The CancerCare Manitoba Patient and Family Resource Centre on McDermot Avenue in Winnipeg is a quiet place to relax and find information about specific cancers, treatment, side effects and support services. The lending library has books and many free relevant handouts. Materials can be requested by phone or online, for pick up or mail out.

Ph: (204) 787-4357 or Toll Free: 1-866-561-1026

www.cancercare.mb.ca/Patient-Family/support-services/resource-centre

New from CancerCare Radiation Oncology Department:

Earlier this year, CancerCare Manitoba's Radiation Oncology Dept. created a document addressing some common questions we receive from other health care providers. We are pleased to announce it is now available on the CCMB Website under the heading "**For Health Professionals/Publications**".

You can also click on this link: https://www.cancercare.mb.ca/export/sites/default/For-Health-Professionals/.galleries/files/

GO PAPERLESS!

If you would like to receive CancerTalk electronically, please email **rporter@cancercare.mb.ca**

NEWS FROM GetChecked Manitoba

CancerCare Manitoba BreastCheck | CancerCare Manitoba ColonCheck | CancerCare Manitoba CervixCheck

Colorectal Cancer Screening in Individuals with a Family History

In November 2018, the Canadian Association of Gastroenterology released a clinical practice guideline on colorectal cancer screening for individuals with a family history of colorectal cancer or advanced adenomas.

The guideline, which is based on a systematic review of the literature and consensus recommendations, advises that individuals be screened with colonoscopy if they are at increased risk of colorectal cancer due to family history. FOBT remains the screening test of choice for individuals at average risk of colorectal cancer.

Family History*	**Screening Recommendation**
Two or more 1st degree relatives diagnosed with CRC at any age	Colonoscopy every 5 years beginning at age 40 or 10 years earlier than the youngest relative's diagnosis (whichever occurs first). Screening with FOBT **is not** recommended.
One 1st degree relative diagnosed with CRC at any age	Preferred test: colonoscopy every 5 to 10 years beginning at age 40 or 10 years earlier than the youngest relative's diagnosis (whichever occurs first). Alternate test: FOBT every one to two years starting at age 40 or 10 years earlier than the youngest relative's diagnosis (whichever occurs first).
One or more 1st degree relatives with a documented advanced adenoma (≥1 cm in size, with high grade dysplasia, or villous and tubulovillous lesions) at any age	Colonoscopy every 5 to 10 years OR FOBT every 1 to 2 years beginning at age 40 or 10 years earlier than the youngest relative's diagnosis (whichever occurs first).
One or more 2nd degree relatives with CRC	Follow average-risk screening recommendation: FOBT every two years.
One or more 1st degree relative with non-advanced adenoma	Follow average-risk screening recommendation: FOBT every two years.

* 1st degree relatives include parents, brothers, sisters, and children.
2nd degree relatives include aunts, uncles, and grandparents.

Individuals are also at an increased risk of colorectal cancer if they have a personal history of:

- Colorectal cancer or adenomas requiring surveillance,
- Inflammatory bowel disease with associated colitis, or
- Confirmed/suspected hereditary colon cancer syndromes such as Lynch syndrome or Familial Adenomatous Polyposis (FAP)

These individuals should follow the endoscopic surveillance and management plan of their endoscopist.

To access the full guideline, visit https://www.cag-acg.org/images/publications/CAG_CPG_CRC_Screening_Aug2018.pdf

ColonCheck has revised its screening guidelines to reflect these new recommendations. To view the screening guidelines, visit **cancercare.mb.ca/screening**

Our website has moved: For more information for healthcare providers visit **cancercare.mb.ca/screening**

March is Colorectal Cancer Awareness Month

ColonCheck is preparing for an exciting month promoting colorectal cancer screening awareness to Manitobans with the **"Don't just sit there"** campaign. To order pamphlets, posters, and other free educational resources for your clinic, please visit **cancercare.mb.ca/screening/resources**.

HOW TO REACH US

CCMB CENTRAL REFERRAL
204-787-2176
FAX: 204-786-0621
M-F, 0830-1630, closed Stat Holidays
Emergency Referrals:
HSC PAGING: 204-787-2071
ST. BONIFACE PAGING: 204-237-2053

CANCER QUESTION? HELPLINE FOR HEALTH CARE PROVIDERS
204-226-2262 (call or text/SMS)
EMAIL: cancer.question@cancercare.mb.ca
WEB FORM: cancercare.mb.ca/cancerquestion
M-F, 0830-1630, closed Stat Holidays

CCMB SCREENING PROGRAMS
1-855-952-4325
GetCheckedManitoba.ca

CANCERCARE MANITOBA
TOLL FREE: 1-866-561-1026 (ALL DEPARTMENTS)
www.cancercare.mb.ca

Inquiry & Reception
MCDERMOT UNIT (HSC) 204-787-2197
ST. BONIFACE UNIT 204-237-2559

Pharmacy: 204-787-1902

WESTERN MANITOBA CANCER CENTRE
Brandon MB
204-578-2222 FAX: 204-578-4991

MANITOBA PROSTATE CENTRE, CCMB
204-787-4461
FAX: 204-786-0637

COMMUNITY ONCOLOGY PROGRAM (CCPN & UPCON) OFFICE, CCMB
204-784-0225

TRANSITIONS OF CARE
transitions@cancercare.mb.ca
204-784-0210

REGIONAL NAVIGATION SERVICES
Interlake Eastern: 1-855-557-2273
Prairie Mountain Health: 1-855-346-3710
Southern Health-Sante Sud: 1-855-623-1533
Northern Health: 1-855-740-9322
Winnipeg Navigation Services: 1-855-837-5400

UNDERSERVED POPULATIONS PROGRAM
TOLL FREE: 1-855-881-4395

PAIN & SYMPTOM MANAGEMENT
204-235-2033—Ask for pain & symptom physician on call (M-F: 08:30-16:30)

BREAST & GYNE CANCER CENTRE OF HOPE
204-788-8080
TOLL FREE: 1-888-660-4866

PATIENT AND FAMILY SUPPORT SERVICES, CCMB
Psychosocial Oncology, Dietitians, Speech Language Pathology, Guardian Angel Caring Room, Patient Programs, Navigator Newsletter
204-787-2109

OTHER NUMBERS:

CANCERCARE MANITOBA FOUNDATION
donations & inquiries: 204-787-4143
TOLL FREE: 1-877-407-2223

CANADIAN CANCER SOCIETY
VOLUNTEER DRIVERS: 204-787-4121
TOLL FREE: 1888-532-6982

CANADIAN VIRTUAL HOSPICE
virtualhospice.ca

WRHA BREAST HEALTH CENTRE
204-235-3906
TOLL FREE: 1-888-501-5219

WRHA PALLIATIVE CARE
204-237-2400

ANNOUNCEMENTS

Dr. Julie Kickbush has joined the Head and Neck Disease Site Group at CancerCare Manitoba.

Dr. Julie Kickbush graduated from medical school at the University of British Columbia in 2010. She went on to complete the Clinical Investigator Program and General Surgery Residency at the University of Saskatchewan and most recently was a Fellow in Head & Neck Surgical Oncology at Memorial Sloan Kettering Cancer Center.

Dr. Kickbush will be providing outpatient services in the Head and Neck Disease Site Group. Her office is located on the second floor of the CCMB MacCharles site.

Pancreatic cancer is a rare yet deadly disease, and most cases present when disease is incurable. In recent years, combination chemotherapy options (FOLFIRINOX[1*], and *nab*-paclitaxel with gemcitabine[2*]) have become available. Both of these options improve survival; however, there are still considerable gains to be made.

Practice guidelines recommend early palliative care[3*] (EPC) for all patients with advanced pancreatic cancer (APC). However, this is not yet the standard of care at most Canadian cancer centers. Patients who chose to receive palliative chemotherapy for APC are not eligible for enrollment in the WRHA palliative care program. For many, referral to palliative care occurs on an ad hoc basis, and often in the last days of life.

The CancerCare Manitoba Foundation has funded a study exploring whether EPC improves quality of life for patients with APC. Patients on this study will be assessed and followed by a team consisting of a physician and advanced practice nurse with expertise in palliative care. Assessments will address pain, symptoms, psychological distress, medication management and end of life goals of care (Figure 1). Patients are eligible **whether or not they decide to receive chemotherapy** and will continue to be followed by their medical oncologist for treatment-related decisions. Family Physicians in Oncology will continue overseeing chemotherapy administration and related symptom management.

This study opened October 18, 2018 and has been well received by patients. So far, the enrollment rate has been outstanding, at 75%. If you require more information, contact Stephanie Lelond at slelond2@cancercare.mb.ca or Dr. Christina Kim at ckim3@cancercare.mb.ca.

***1, 2, 3—References available on request**