Systemic Therapy Update

BC Cancer Agency
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For Health Professionals Who Care For Cancer Patients

Inside This Issue:

EDITOR'S CHOICE

HIGHLIGHTS OF CHANGES IN PROTOCOLS, PPOS AND PATIENT HANDOUTS

Reclassification of Anthracycline and Cyclophosphamide-Containing Protocols as Highly Emetogenic:

All BCCA chemotherapy protocols containing the combination of an anthracycline (doxorubicin, epirubicin) and cyclophosphamide have been reclassified as highly emetogenic. This reclassification is based on the latest American Society of Clinical Oncology (ASCO) antiemetics guidelines, the US National Comprehensive Cancer Network (NCCN), the Multinational Association of Supportive Care in Cancer (MASCC), and the European Society of Medical Oncology (ESMO).[1,2,3]

Highly-emetogenic chemotherapy is defined as those causing emesis in greater than 90% of patients if not premedicated with antiemetics. Data from placebo-controlled studies indicate that the combination of an anthracycline and cyclophosphamide results in vomiting in nearly 90% of patients not receiving antiemetic prophylaxis.[1] Some patients may still experience nausea and/or vomiting despite premedication with ondansetron and dexamethasone. The addition of aprepitant to ondansetron and dexamethasone has been shown to further reduce the rate of chemotherapy-induced nausea and/or vomiting. [Warr et al. JCO 2005;23:2822-2830]

Aprepitant is on the PharmaCare benefit list from the first cycle of anthracycline-cyclophosphamide

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containing chemotherapy regimens. For all affected BCCA protocols, pleases see the table of reclassified chemotherapy protocols below.

References:
1. Basch E, Prestrud AA, Hesketh PJ, et al. Antiemetics: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol 2011;29(31):4189-98.
2. National Comprehensive Cancer Network. Antiemesis: National Comprehensive Cancer Network guidelines, Version 1.2012. 20 July 2011.
3. Roila F, Herrstedt J, Aapro M, et al. Guideline update for MASCC and ESMO in the prevention of chemotherapy- and radiotherapy-induced nausea and vomiting: results of the Perugia consensus conference. Ann Oncol 2010; 21(Suppl 5): v232–v243.

PROVINCIAL SYSTEMIC THERAPY PROGRAM

NEW PROGRAM TO SUPPORT CHEMOTHERAPY PATIENT EDUCATION SESSIONS

A multidisciplinary working group at the BCCA has developed and implemented an online Tool Kit to be used to facilitate and evaluate chemotherapy patient education sessions. The name of the program is "Introduction to Chemotherapy: A Presentation for Patients and Families". These introductory chemotherapy education group sessions are recommended for all new patients receiving oral or parenteral chemotherapy. They provide an overview of chemotherapy, the management of potential side effects, and self-care strategies.

The Tool Kit is intended to standardize the material and resources used when teaching new patients about chemotherapy to promote consistency in information sharing throughout the BCCA, and to utilize teaching strategies that optimize patient health literacy. The Tool Kit is available on the BCCA website and consists of the following items:

- Facilitator Criteria and Assessment
- PowerPoint Presentation and Outline
- Patient Information Package
- Evaluation Tool

DRUG UPDATE

DRUG SHORTAGE OF IM VITAMIN B12 – USING ORAL VITAMIN B12 AS ALTERNATIVE PROPHYLACTIC THERAPY FOR PEMETREXED TOXICITY

Canada is facing intermittent shortages of the parenteral formulation of vitamin B12 injectable for intramuscular (IM) administration. This affects treatment regimens that use pemetrexed, an antifolate chemotherapy agent indicated for non-small cell lung cancer (ULUAVPP, LUAVPEM, ULUAVPMTN) and malignant mesothelioma (LUMMPP). Pemetrexed is associated with significant grades 3 and 4 febrile neutropenia if given without prophylactic supplementation using IM vitamin B12 and oral folic acid (9% vs. 1%).[1] Standard supplementation consists of vitamin B12 1000 mcg IM every 9 weeks and folic acid 400 to 1000 mcg orally daily, both starting 1 week before pemetrexed therapy and continued until 3 weeks after the last dose of pemetrexed.

During the intermittent shortages of IM vitamin B12, the BCCA Lung Tumour Group suggests the following

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for patients who are recommended to receive pemetrexed treatment:

- Oral vitamin B12 250 mcg daily and folic acid 400-1000 mcg orally daily for patients who are starting pemetrexed – start 1 week before and continue until 3 weeks after completion of pemetrexed therapy.
- Patients already on pemetrexed who started with IM vitamin B12 may substitute with oral vitamin B12 as above.
- In both cases, patients should be monitored more closely for myelosuppression with weekly CBC and differential.
- Oral vitamin B12 should be switched to IM injection as soon as the latter becomes available.

The effectiveness of oral vitamin B12 in minimizing pemetrexed-associated hematologic toxicities is uncertain. The pemetrexed product monograph also states that oral vitamin B12 should not be substituted for IM vitamin B12. Therefore, the BCCA Lung Tumour Group emphasizes that supplementation with oral vitamin B12 should ONLY be used when IM vitamin B12 is not available AND when pemetrexed is the therapy of choice.

MEDICATION SAFETY CORNER

CABAZITAXEL DILUTION ERRORS

Health Canada has issued a Medication Alert regarding a potential medication error in the preparation of cabazitaxel. Reconstitution errors that occurred in the dilution phase of the cabazitaxel reconstitution process have been reported in Europe where only the nominal volume (4.5 mL) of the supplied diluent vial content, rather than the entire diluent content (5.67 mL), was transferred to the concentrate drug vial. This resulted in overdoses of 15% to 20% higher than the prescribed dose. Pharmacies are reminded to ensure that the entire content of the diluent vial is used during the preparation of cabazitaxel. This information has been updated on the Chemotherapy Preparation and Stability Chart.

IMPACT OF A STRONG PATIENT SAFETY CULTURE ON MEDICATION INCIDENT LEARNING

Approximately 7.5% of patients in Canadian acute care hospitals experience an adverse event, with 37% of these being preventable and may be due to medical errors. [1] Many medical errors cannot be attributed to a single cause or individuals, but are often rooted in issues within a complex health care system. Therefore, it is imperative to review the system and develop broad spectrum improvement strategies to prevent future occurrences.[2]

A key strategy to creating sustainable solutions for medical errors is to create a strong patient safety culture. This would allow open and honest sharing of information, as well as encourage a collaborative approach to creating systems-based solutions for future error prevention.[2] Such a strategy would also enable sharing of learning within and between organizations to create far reaching and sustainable impact on the health care system.

One of the Provincial Health Services Authority's (PHSA) goals is to create a culture of patient safety, where heath care staff feels safe to report events and participate in improvement initiatives. Within this environment, health care staff should be confident that incidents will be managed fairly while upholding professional standards and codes of conduct. The following case illustrates a medication error that

occurred at a BCCA centre that resulted in positive changes and learning that reached health care institutions across Canada.

Case Review:

- Staff at a BCCA centre discovered phenylephrine vials in a bin intended for diphenhydrAMINE in a patient care area. Mix-up between phenylephrine (a vasopressor) and diphenhydrAMINE (an antihistamine) could have resulted in serious patient harm.

Immediate Actions:

- Phenylephrine vials were immediately removed.
- Patient care records were reviewed, and direct follow-up with patients was completed as appropriate.
- Leaders from the patient care area interviewed the affected frontline staff members for their perspectives and feedback.
- An interdisciplinary team consisting of nurses, pharmacists, physicians, clerical supervisor, senior leadership and quality team members met to review the case.

Outcomes:

Contributing Factors

The primary contributing factor to the medication error was identified as the look-alike packaging of phenylephrine and diphenhydrAMINE. Therefore, the two drugs were immediately isolated in the affected patient care areas. In addition, products with distinct labelling were sourced and purchased from an alternate supplier.

Secondary systems improvement opportunities were also identified, including:

- Creating standardized work and communication procedures in receiving and ward stock replacement processes,
- Reorganizing and relabeling medication storage carts in the patient care area, and
- Establishing methods to reduce interruptions in the unit's medication preparation area.

Communication of Findings

A safety alert regarding the look-alike products was communicated to the BCCA and CON centres through the June 2013 issue of the Systemic Therapy Update, throughout the PHSA via a Patient Safety Alert, and to the rest of the province through the BC Patient Safety and Quality Safety Council Alert system. A product complaint was also filed with the manufacturer, and communicated to Health Canada and the Institute for Safe Medication Practices (ISMP) Canada. As a result, the manufacturer will implement a new product label design in early 2014. Also, ISMP Canada has issued an alert to inform institutions across Canada about the packaging concern and provided recommendations to manage the situation.[3]

Learning:

This case highlights how a strong patient safety culture supported the BCCA teams to use a systems-based, no-blame approach to identify contributing factors and develop sustainable solutions to prevent future medication errors. It also showcases the far reaching impact of shared learning that is possible even when initiated from a single health care centre.

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MEDICATION SAFETY CORNER

Director, Risk Management, BCCA

References:

1. Baker GR, Norton PG, Flintoft V, Blais R, Brown A, Cox J, et al., The Canadian adverse events study: The incidence of adverse events among hospital patients in Canada, CMAJ. 2004 May 25; 170(11):1678-86.
2. Incident Analysis Collaborating Parties. Canadian Incident Analysis Framework. Edmonton: Canadian Patient Safety Institute; 2012. 133p.
3. Alert: Look-alike labelling and packaging for diphenhydramine and phenylephrine. ISMP Can Saf Bull [Internet]. 2013 Dec 5 [cited 2013 Dec 9]; 13(12): 1-2. Available from: http://www.ismp-canada.org/download/safetyBulletins/2013/ISMPCSB2013-12_LabellingPackaging_DiphenhydraminePhenylephrine.pdf

CANCER DRUG MANUAL

REVISED MONOGRAPHS AND PATIENT HANDOUTS

Highlights of key changes and/or updates to the Monographs, Patient Handouts and Chemotherapy Preparation and Stability Chart (CPSC) are listed below:

Bortezomib CPSC:

- *Special Precautions/Notes* – added auxiliary label warning *"For SUBCUTANEOUS or INTRAVENOUS use only. FATAL if given by other routes"* in response to a Health Canada safety alert (please see the February 2013 issue of the Systemic Therapy Update for further details)

Cabazitaxel CPSC:

- *Reconstitution* – revised the reconstitution directions in response to a recent Health Canada safety alert as discussed in the Medication Safety Corner section above

Everolimus Monograph:

- *Uses* – added breast cancer and pancreatic neuroendocrine tumour as Health Canada approved indications
- *Dosing* – added new hepatic dosing recommendations from the manufacturer

Lenalidomide Monograph:

- *Side Effects* – added hepatotoxicity in response to a recent Health Canada safety alert

Oxaliplatin Handout

- *Side Effects* – added supportive care handout "*Coping with/preventing Oxaliplatin Cold Dysesthesias*" to the Management section of *tingling or loss of feeling*

Tretinoin:

- **Monograph:**
  - *Special Precautions* – added pregnancy and nursing mothers to Contraindications, and new cautions for driving, and increased drug toxicity in children; revised Pregnancy section to include new recommendations for contraception

CANCER DRUG MANUAL

- *Side Effects* – added thrombosis and hypervitaminosis A
- *Interactions* – revised information regarding vitamin A interaction

- **Handout:**
  - *"See Your Doctor" section* – added signs of hypervitaminosis A

BENEFIT DRUG LIST

DELETED PROGRAMS

The following programs have been removed from the Benefit Drug List effective 01 February 2014:

Protocol Title	Protocol Code
Summary for Palliative Therapy For Lymphoma Using Radioimmunotherapy: Tositumomab-Priming for I^{131} Tositumomab	LYRITB
Palliative Therapy For Lymphoma Using Radioimmunotherapy: riTUXimab-Priming for Ibritumomab ^{90}Y	LYRITZ

Please see the January 2014 issue of the Systemic Therapy Update under "Drug Update" for further information regarding the removal of the above BCCA protocols from the Benefit Drug List.

LIST OF NEW AND REVISED PROTOCOLS, PRE-PRINTED ORDERS AND PATIENT HANDOUTS

BC Cancer Agency Protocol Summaries, Provincial Pre-Printed Orders (PPPOs) and Patient Handouts are revised periodically. New, revised or deleted protocols, PPPOs and patient handouts for this month are listed below. Protocol codes for treatments requiring "Compassionate Access Program" (previously Undesignated Indications Request) approval are prefixed with the letter "U".

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED):

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
BRAJACTT	☑	☑	☐	*Brand name for trastuzumab added*	Adjuvant Therapy for Breast Cancer using DOXOrubicin and Cyclophosphamide followed by PACLitaxel and Trastuzumab (HERCEPTIN)
BRAJACTTG	☑	☑	☐	*Brand name for trastuzumab added*	Adjuvant Therapy for Breast Cancer using Dose Dense Therapy: DOXOrubicin and Cyclophosphamide followed by PACLitaxel and Trastuzumab (HERCEPTIN)

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED):					
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Changes**	**Protocol Title**
BRAJACTW	☑	☑	☐	*Brand name for trastuzumab added*	Adjuvant Therapy for Early Breast Cancer using DOXOrubicin and Cyclophosphamide followed by Weekly PACLitaxel
BRAJDTFEC	☑	☑	☐	*Brand name for trastuzumab added*	Adjuvant Therapy for Breast Cancer Using DOCEtaxel and Trastuzumab (HERCEPTIN), and Fluorouracil, Epirubicin and Cyclophosphamide
BRAJFECDT	☑	☑	☐	*Brand name for trastuzumab added*	Adjuvant Therapy for Breast Cancer using Fluorouracil, Epirubicin and Cyclophosphamide followed by DOCEtaxel and Trastuzumab (HERCEPTIN)
BRAJTAM	☑	☐	☐	*Eligibility clarified*	Adjuvant Therapy for Breast Cancer Using Tamoxifen
BRLAACDT	☑	☑	☐	*Brand name for trastuzumab added*	Treatment of Locally Advanced Breast Cancer using DOXOrubicin and Cyclophosphamide followed by DOCEtaxel and Trastuzumab (HERCEPTIN)
GIFFIRB	☐	☑	☐	*Updated 24 hr urine for total protein checkbox under Return Appointment Orders*	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer using Irinotecan, Fluorouracil, Folinic Acid (Leucovorin) and Bevacizumab
UGIFIRINOX	☑	☐	☐	*Eligibility expanded; Title revised*	Palliative Combination Chemotherapy for Advanced Pancreatic Adenocarcinoma Using Irinotecan, Oxaliplatin, Fluorouracil and Folinic Acid (Leucovorin)
GOCXCAT	☐	☑	☐	*Dosing options and lab tests clarified*	Primary Treatment of Advanced/ Recurrent Non-Small Cell Cancer of the Cervix with CARBOplatin and PACLitaxel in Ambulatory Care Settings
GOOVCARB	☑	☐	☐	*Baseline tumour markers revised*	First or Second Line Therapy for Invasive Epithelial Ovarian Cancer using Single-Agent CARBOplatin
GUNAJPG	☐	☑	☐	*Cisplatin dosing clarified*	Neo-Adjuvant Therapy for Urothelial Carcinoma Using CISplatin and Gemcitabine
GUPDOC	☐	☑	☐	*Lab tests clarified*	Palliative Therapy for Metastatic Hormone Refractory Prostate Cancer using DOCEtaxel

DELETED Protocols, PPPOs and Patient Handouts (AFFECTED DOCUMENTS ARE CHECKED):				
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Protocol Title**
LYRITB	☑	☑	☐	Summary for Palliative Therapy For Lymphoma Using Radioimmunotherapy: Tositumomab-Priming for I^{131} Tositumomab
LYRITZ	☑	☑	☐	Palliative Therapy For Lymphoma Using Radioimmunotherapy: riTUXimab-Priming for Ibritumomab ^{90}Y

The following Anthracycline and Cyclophosphamide-Containing Protocols have been reclassified as "Highly Emetogenic":

CODE	Protocol Title
BRAJAC	Adjuvant Therapy for Breast Cancer using DOXOrubicin and Cyclophosphamide
BRAJACT	Adjuvant Therapy for Breast Cancer Using DOXOrubicin and Cyclophosphamide followed by PACLitaxel
BRAJACTG	Adjuvant Therapy for Breast Cancer using Dose Dense Therapy: DOXOrubicin and Cyclophosphamide followed by PACLitaxel
BRAJACTT	Adjuvant Therapy for Breast Cancer using DOXOrubicin and Cyclophosphamide followed by PACLitaxel and Trastuzumab (HERCEPTIN)
BRAJACTTG	Adjuvant Therapy for Breast Cancer using Dose Dense Therapy: DOXOrubicin and Cyclophosphamide followed by PACLitaxel and Trastuzumab (HERCEPTIN)
BRAJACTW	Adjuvant Therapy for Early Breast Cancer using DOXOrubicin and Cyclophosphamide followed by Weekly PACLitaxel
BRAJCAFG	Adjuvant Therapy for Breast Cancer using Cyclophosphamide, DOXOrubicin , Fluorouracil and Filgrastim (G-CSF)
BRAJCAFPO	Adjuvant Therapy for Breast Cancer using Oral Cyclophosphamide, DOXOrubicin and Fluorouracil
BRAJCEFG	Adjuvant Therapy for Breast Cancer Using Cyclophosphamide, Epirubicin, Fluorouracil and Filgrastim (G-CSF)
UBRAJDAC	Adjuvant Therapy for Breast Cancer using Cyclophosphamide, DOXOrubicin and DOCEtaxel
BRAJDTFEC	Adjuvant Therapy for Breast Cancer Using DOCEtaxel and Trastuzumab (HERCEPTIN), and Fluorouracil, Epirubicin and Cyclophosphamide
BRAJFEC	Adjuvant Therapy for Breast Cancer Using Fluorouracil, Epirubicin and Cyclophosphamide
BRAJFECD	Adjuvant Therapy for Breast Cancer Using Fluorouracil, Epirubicin and Cyclophosphamide and DOCEtaxel
BRAJFECDT	Adjuvant Therapy for Breast Cancer using Fluorouracil, Epirubicin and Cyclophosphamide followed by DOCEtaxel and Trastuzumab (HERCEPTIN)
BRAVAC	Palliative Therapy for Metastatic Breast Cancer using DOXOrubicin and Cyclophosphamide
BRAVCAF	Palliative Therapy for Metastatic Breast Cancer using Cyclophosphamide, DOXOrubicin and Fluorouracil
BRINFCAF	Therapy for Inflammatory Breast Cancer using Cyclophosphamide, DOXOrubicin and Fluorouracil

CODE	Protocol Title
BRINFCEF	Therapy for Inflammatory Breast Cancer using Cyclophosphamide, Epirubicin and Fluorouracil
BRINFCEFG	Therapy for Inflammatory Breast Cancer Using Cyclophosphamide, Epirubicin, Fluorouracil and Filgrastim (G-CSF)
UBRLA2	Therapy for Locally advanced breast cancer using Cyclophosphamide, DOXOrubicin and Fluorouracil
BRLAACD	Treatment of Locally Advanced Breast Cancer using DOXOrubicin and Cyclophosphamide followed by DOCEtaxel
BRLAACDT	Treatment of Locally Advanced Breast Cancer using DOXOrubicin and Cyclophosphamide followed by DOCEtaxel and Trastuzumab (HERCEPTIN)
BRLAACTW	Treatment of Locally Advanced Breast Cancer using DOXOrubicin and Cyclophosphamide followed by Weekly PACLitaxel
UBRLACEF	Therapy for Locally Advanced Breast Cancer using Cyclophosphamide, Epirubicin and Fluorouracil
BRLACEFG	Therapy for Locally Advanced Breast Cancer Using Cyclophosphamide, Epirubicin, Fluorouracil and Filgrastim (G-CSF)
HNSAVFAC	Palliative Therapy for Advanced Salivary Gland Cancers using Cyclophosphamide, DOXOrubicin and Fluorouracil
LUOTCAV	Treatment of Thymoma/Thymic Carcinoma with Cyclophosphamide, DOXOrubicin and vinCRIstine (CAV)
LUSCCAV	Treatment of Extensive Small Cell Lung Cancer (SCLC) with Cyclophosphamide, DOXOrubicin and vinCRIstine (CAV)
LYCHOP	Treatment of Lymphoma with DOXOrubicin, Cyclophosphamide, vinCRIStine and predniSONE
LYCHOPR	Treatment of Lymphoma with DOXOrubicin, Cyclophosphamide, vinCRIStine, predniSONE and riTUXimab
LYCODOXMR	Treatment of Burkitt's Lymphoma and Leukemia (ALL-L3) with Cyclophosphamide, vinCRIStine, DOXOrubicin, Methotrexate, Leucovorin (CODOX-M) and riTUXimab
SAVAC	Adjuvant Therapy for Newly Diagnosed Ewing's Sarcoma/Peripheral Neuroectodermal Tumor (PNET) or Rhabdomyosarcoma using vinCRIstine, DOXOrubicin and Cyclophosphamide
SAVACM	Therapy for Newly Diagnosed Ewing's Sarcoma/Peripheral Neuroectodermal Tumor (PNET) and Rhabdomyosarcoma with Pelvic primaries or chemotherapy induced hematuria using vinCRIstine, DOXOrubicin and Cyclophosphamide

Website Resources and Contact Information

Website Resources	www.bccancer.bc.ca
Systemic Therapy Update	www.bccancer.bc.ca/HPI/ChemotherapyProtocols/stupdate
Reimbursement & Forms: Benefit Drug List, Class II, Compassionate Access Program	www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Forms
Cancer Drug Manual	www.bccancer.bc.ca/cdm
Cancer Management Guidelines	www.bccancer.bc.ca/CaMgmtGuidelines
Cancer Chemotherapy Protocols, Pre-printed Orders, Protocol Patient Handouts	www.bccancer.bc.ca/ChemoProtocols
Systemic Therapy Program Policies	www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Policies
CON Pharmacy Educators	http://www.bccancer.bc.ca/HPI/Pharmacy/ContactUs.htm

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