BC Cancer Agency

Systemic Therapy Update

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Website access at http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/stupdate.htm

INSIDE THIS ISSUE

EDITOR'S CHOICE

MAXIMUM NUMBER OF CYCLES OF ADJUVANT TRASTUZUMAB (HERCEPTIN®) FOR CURATIVE TREATMENT OF NEWLY DIAGNOSED BREAST CANCER

Evidence supporting the use of adjuvant trastuzumab in Her-2 over-expressed breast cancer comes from four randomized controlled trials comparing chemotherapy vs. chemotherapy plus trastuzumab. In three of these studies, trastuzumab was given weekly for 52 weeks. In the fourth study, trastuzumab was given every 3 weeks for 17 (51 weeks) or 18 (54 weeks) treatments.

On this basis, 17 treatments are considered appropriate evidence-based standard of care. Therefore, the BC Cancer Agency Provincial Systemic Therapy Program only funds a maximum of **SEVENTEEN (17) CYCLES** of trastuzumab (HERCEPTIN®) after chemotherapy for women with Her-2 over-expressing cancer receiving adjuvant therapy. Protocols and pre-printed orders have been revised to reflect this (BRAJACTT, BRAJACTTG, BRAJTR).

BC Cancer Agency pharmacists will monitor and remind oncologists if they have reached the maximum number of treatments. All oncologists in the 4 BC Cancer Agency centres and in the Communities Oncology Network, as well as family doctors prescribing chemotherapy should remember that 17 is the maximum number of cycles. Their pharmacy staff is encouraged to remind them. The BC Cancer Agency Provincial Pharmacy will endeavor to alert community cancer centres when their patients are approaching the total number of cycles. Please advise all existing and new patients that 1 year of trastuzumab comprises a total of 17 treatments.

The Breast Tumour Group is also working on developing an optional protocol based on the Finnish study of chemotherapy followed by 3 months of adjuvant trastuzumab for clinicians to consider as an alternative for selected patients. You will be updated regarding this option shortly.

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CANCER DRUG MANUAL

Alemtuzumab Monograph and Patient Handouts This is a new monograph and a revised handout, with additional review provided by Dr. Joseph Connors (Lymphoma Tumour Group), Dr. Dawn Warkentin (Leukemia/BMT Group) and Rongrong Karim (Pharmacy, Vancouver Centre-BCCA). Due to significant differences in the side effect profile of alemtuzumab when given subcutaneously (SC) vs. intravenously (IV), two handouts have been developed. IV administration of alemtuzumab is usually accompanied by transient infusion-related side effects that manifest as flu-like symptoms. SC administration of alemtuzumab reduces infusion-related symptoms; fever and transient grade 1 or 2 local skin reaction frequently occur. Hematological and infectious complications are independent of the route of administration.

Thyrotropin alfa Monograph and Patient Handout This is a new monograph and a revised handout. Expert review was provided by Dr. John Hay (Head and Neck Tumour Group). The new documents coincide with changes to the HNTSH protocol. Thyrotropin alfa can now be given with or without radioiodine or PET scan. For example, patients found to have a thyrotropin alfa-stimulated thyroglobulin serum level < 2 ng/mL may not require an iodine or PET scan. Thyrotropin alfa has been added to the *Chemotherapy Preparation and Stability Chart*.

Rituximab Monograph The section on vitals monitoring during infusion has been revised to be consistent with the protocols (see also under **LIST OF REVISED PROTOCOLS** in this issue).

Trastuzumab Monograph The infusion time has been revised for 3-weekly dosing. The loading dose remains the same (over 90 minutes) while the second dose can now be given over 60 minutes, with subsequent doses over 30 minutes if no adverse reactions (see also under **LIST OF REVISED PROTOCOLS** in this issue).

CANCER MANAGEMENT GUIDELINES

Management of Prostate Cancer has been revised for the sections on low and intermediate risk of recurrence (*www.bccancer.bc.ca/HPI/CancerManagementGuidelines/Genitourinary/Prostate/Management*). The main change relates to the option of systematic monitoring (active surveillance) for selected patients with low risk prostate cancer. Treatment is recommended if their tumours show significant growth characteristics, at a time when treatment remains potentially curative.

Active surveillance is distinct from watchful waiting. The latter refers to situations where treatment is deferred even if the opportunity for cure is lost, with possible palliative treatment in the future or delayed palliation for tumours which are too advanced for cure at diagnosis.

FOCUS ON: ORAL ANTI-CANCER DRUGS, DIARRHEA, AND LACTOSE INTOLERANCE

Diarrhea is a side effect associated with some oral anti-cancer drugs. However, these agents may be only one of a multitude of causes of diarrhea for a particular patient. For example, other medications, surgery, infections, and lactose intolerance may also cause diarrhea. This article lends insight into the association between the lactose content in oral chemotherapy preparations and diarrhea in susceptible individuals.

Lactose intolerance
Lactose intolerance is the inability to digest significant amounts of lactose, a disaccharide found in milk and other dairy products, caused by a shortage of the intestinal enzyme lactase (beta-galactosidase).[1] People with insufficient lactase may feel very uncomfortable after digesting dairy products. Common symptoms caused by lactose maldigestion range from mild to severe, and may include nausea, cramps, bloating, gas and diarrhea.

Anti-cancer drugs and lactose
Many BCCA drug information monographs and patient handouts list diarrhea as a potential side effect. Note that handouts for some drugs like *capecitabine* and *anastrozole*, for example, contain lactose and may cause gastric upset and/or diarrhea in persons who are lactose intolerant. The Compendium of Pharmaceuticals and Specialities (CPS) lists selected lactose-containing oral products based on information from the manufacturers. The capecitabine handout suggests that lactase enzyme (LACTAID® and many generic formulations) may be taken prior to the oral chemotherapy dose.

A capecitabine (XELODA®) 150 mg tablet contains 15.6 mg of lactose, whereas the 500 mg tablet contains 52 mg of lactose.[2] Thus a patient taking a capecitabine dose of 2000 mg will ingest approximately 200 mg of lactose, roughly the same amount of lactose as is contained in *one teaspoon of milk* (see below). A 1 mg table of anastrozole (ARIMIDEX®) contains just under 100 mg of lactose.[3] Therefore, although these amounts are unlikely to be of clinical relevance to many patients, determining an individual patient's lactose tolerance may give an idea of the patient's ability to tolerate the lactose content of oral anti-cancer agents or other oral medications.

Why lactose?
Why do oral drugs contain lactose? Lactose is a frequently-used filler in tablets and capsules. Without fillers, tablets and capsules would be extremely tiny, making it much more difficult to ensure the proper mixing of ingredients and to maintain consistency between batches of tablets or capsules.

How much lactose?
How much lactose is too much? People vary widely in their degree of lactase deficiency, so it is impossible to predict how much lactose a person can tolerate before developing the symptoms of lactose intolerance. Below is a short list outlining the lactose content of various dairy products[1]:

Dairy product (quantity)	***Amount of lactose***
Yogurt (1 cup)	5 grams
Milk (1 cup)	11 grams
Hard cheese (e.g. Swiss) (30 grams)	1 gram
Ice cream (1/2 cup)	6 grams
Cottage cheese (1/2 cup)	2-3 grams

Management
If a patient taking lactose-containing anti-cancer drug is found to have a low threshold for lactose-containing dairy products, and other causes of diarrhea have been ruled out (see also *Chemotherapy-Induced Diarrhea Guidelines*), a trial with lactase enzyme may be warranted. The LACTAID® monograph (or other generic products) states that three regular strength tablets should be swallowed or chewed just before eating a meal that contains lactose.[4] However, because the dosage is dependent on the amount of lactose contained in the food that is to be consumed, one LACTAID® tablet may suffice for patients prior to taking lactose-containing medications, owing to the smaller lactose content.

Food Ideas to Help with Diarrhea during Chemotherapy and *Nutritional Guidelines for Symptom Management: Diarrhea* are useful BCCA handouts available on our website for healthcare professionals when advising

patients who are experiencing or anticipating anti-cancer drug-induced diarrhea. *Low Lactose Guidelines* is another BCCA handout which outlines management suggestions for patients with lactose intolerance, and gives examples of low, medium, and high lactose containing dairy products.

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References

1. Sibley E. Lactose Intolerance. National Institutes of Health, 2006. Available from http://digestive.niddk.nih.gov/ddiseases/pubs/lactoseintolerance/. Accessed 8 September, 2006.
2. L. Cesario. Personal communication. Medical Information, Hoffmann-La Roche; 26 May 2005.
3. F. Jaffer. Personal communication. Medical Information, AstraZeneca; 10 October 2006.
4. McNeil Consumer Healthcare. Lactaid product monograph. Guelph, Ontario; 2006.

BENEFIT DRUG LIST

Dexrazoxane for pediatric osteosarcoma has been revised. The previous class II indication for study protocol COG AOST0212 has been replaced by COG AOST0331.

LIST OF NEW AND REVISED PROTOCOLS

The **BC Cancer Agency Protocol Summaries** are revised on a periodic basis. New and revised protocols for this month are listed below. Protocol codes for treatments requiring "Undesignated Indication" approval are prefixed with the letter **U**.

Revised protocols:

Code	Changes	Protocol Name
BRAJACTT	*Maximum number of cycles revised to 17, infusion time shortened*	Adjuvant Therapy for Breast Cancer using Doxorubicin and Cyclophosphamide followed by Paclitaxel and Trastuzumab
BRAJACTTG	*Maximum number of cycles revised to 17, infusion time shortened*	Adjuvant Therapy for Breast Cancer using Dose Dense Therapy: Doxorubicin and Cyclophosphamide followed by Paclitaxel and Trastuzumab
BRAJTR	*Maximum number of cycles revised to 17, infusion shortened*	Adjuvant Therapy for Breast Cancer using Trastuzumab following the Completion of Chemotherapy (Sequential)
BRAVTPC	*Infusion shortened*	Palliative Therapy for Metastatic Breast Cancer using Trastuzumab (HERCEPTIN®), Paclitaxel and Carboplatin as First-Line Treatment for Advanced Breast Cancer
BRAVTR	*Infusion shortened*	Palliative Therapy for Metastatic Breast Cancer using Trastuzumab
BRAVTRAD	*Infusion shortened*	Palliative Therapy for Metastatic Breast Cancer using Trastuzumab (HERCEPTIN®) and Docetaxel as First-Line Treatment for Recurrent Breast Cancer
BRAVTRAP	*Infusion shortened*	Palliative Therapy for Metastatic Breast Cancer using Trastuzumab (HERCEPTIN®) and Paclitaxel as First-Line Treatment for Recurrent Breast Cancer
LYCHOPR	*Clarified vital signs monitoring*	Treatment of Lymphoma with Doxorubicin, Cyclophosphamide, Vincristine, Prednisone and Rituximab

Code	Changes	Protocol Name
LYCVPR	*Clarified volume of preparation for Rituximab, clarified vital signs monitoring*	Treatment of Advanced Indolent Lymphoma using Cyclophosphamide, Vincristine, Prednisone and Rituximab (CVP-R)
LYFLUDR	*Clarified vital signs monitoring*	Treatment of Chronic Lymphocytic Leukemia or Prolymphocytic Leukemia with Fludarabine and Rituximab
ULYRICE	*Clarified eligible histologies, dosing of ifosfamide and mesna and vital signs monitoring*	Treatment of Advanced Stage Large B-Cell Non-Hodgkin's Lymphoma with Ifosfamide, Carboplatin, Etoposide and Rituximab
LYRITUX	*Clarified volume of preparation for Rituximab, clarified vital signs monitoring*	Treatment of Lymphoma with Single Agent Rituximab
LYRITZ	*Clarified vital signs monitoring*	Palliative Therapy For Lymphoma Using Radioimmunotherapy: Rituximab-Priming for Ibritumomab ^{90}Y
ULYRMTN	*Clarified vital signs monitoring*	Maintenance Rituximab for Indolent Lymphoma

LIST OF NEW AND REVISED PRE-PRINTED ORDERS

The **INDEX to BC Cancer Agency Pre-printed Orders** are revised on a periodic basis. The revised pre-printed orders for this month are listed below.

New pre-printed orders:

Code	Protocol Name
GIFURC (replacing GIRLACF, GIRLAIFF)	Combined Modality Adjuvant Therapy for High Risk Rectal Carcinoma using Fluorouracil, Folinic Acid (Leucovorin), Capecitabine and Radiation Therapy

Revised pre-printed orders:

Code	Changes	Pre-Printed Order Name
BRAJTR	*Maximum number of cycles revised to 17, infusion shortened*	Adjuvant Therapy for Breast Cancer using Trastuzumab following the Completion of Chemotherapy (Sequential)
BRAVTPC	*Infusion shortened*	Palliative Therapy for Metastatic Breast Cancer using Trastuzumab (HERCEPTIN®), Paclitaxel and Carboplatin as First-Line Treatment for Advanced Breast Cancer
BRAVTR	*Infusion shortened*	Palliative Therapy for Metastatic Breast Cancer using Trastuzumab
BRAVTRAD	*Infusion shortened*	Palliative Therapy for Metastatic Breast Cancer using Trastuzumab (HERCEPTIN®) and Docetaxel as First-Line Treatment for Recurrent Breast Cancer
BRAVTRAP	*Infusion shortened*	Palliative Therapy for Metastatic Breast Cancer using Trastuzumab (HERCEPTIN®) and Paclitaxel as First-Line Treatment for Recurrent Breast Cancer
GIRLACF	*Replaced by GIFURC*	Pre-Operative Combined Modality Therapy With Radiation And Capecitabine And Post Operative Chemotherapy Using Fluorouracil, Folinic Acid (Leucovorin) For Locally Advanced (Borderline Resectable Or Unresectable) And Low Rectal Adenocarcinoma

Revised pre-printed orders:		
Code	**Changes**	**Pre-Printed Order Name**
GIRLAIFF	*Replaced by GIFURC*	Preoperative Concurrent Chemotherapy And Radiotherapy And Postoperative Chemotherapy For Locally-Advanced (Borderline Resectable Or Unresectable) Rectal Adenocarcinoma
HNAVPG	*Antiemetics clarified*	Treatment of Locoregionally Recurrent and/or Metastatic Nasopharyngeal Cancer with Cisplatin and Gemcitabine
ULYRICE	*Clarified eligible histologies, dosing of ifosfamide and mesna and vital signs monitoring*	Treatment of Advanced Stage Large B-Cell Non-Hodgkin's Lymphoma with Ifosfamide, Carboplatin, Etoposide and Rituximab
LYRITUX	*Clarified volume of preparation for Rituximab, clarified vital signs monitoring*	Treatment of Lymphoma with Single Agent Rituximab
LYRITZ	*Clarified vital signs monitoring*	Palliative Therapy For Lymphoma Using Radioimmunotherapy: Rituximab-Priming for Ibritumomab ^{90}Y
ULYRMTN	*Clarified vital signs monitoring*	Maintenance Rituximab for Indolent Lymphoma

PROTOCOL-SPECIFIC PATIENT HANDOUT

The **INDEX to BC Cancer Agency Protocol-Specific Patient Handouts** are revised on a periodic basis. The revised patient handouts for this month are listed below.

New patient handouts:	
Code	**Handout Name**
BRAJACTT	Adjuvant Therapy for Breast Cancer using Doxorubicin and Cyclophosphamide followed by Paclitaxel and Trastuzumab
BRAJACTTG	Adjuvant Therapy for Breast Cancer using Dose Dense Therapy: Doxorubicin and Cyclophosphamide followed by Paclitaxel and Trastuzumab

Revised patient handouts:		
Code	**Changes**	**Handout Name**
BRAJTR	*Number of treatment cycles.*	Adjuvant Therapy for Breast Cancer using Trastuzumab following the Completion of Chemotherapy (Sequential).

CONTINUING EDUCATION

BC Cancer Agency Annual Cancer Conference 2006 You can now register for this year's conference, which will be held from **23-25 November, 2006** at the Westin Bayshore Resort and Marina in Vancouver. Registration fees are: $175 (29 September through 23 November) and $200 onsite (23-25 November).

The theme of this year will be **"***Partners in Research and Care – BC & the World***",** which will create the framework for the exploration of how the BC Cancer Agency encourages collaboration between researchers, scientists, clinicians and community resource professionals, within the provincial system of cancer control, as well as with organizations around the world.

The *Partners in Cancer Care* meeting and the BC Cancer Agency Research Centre *Scientific Meeting* will be held respectively on Thursday, 23 November. The *Clinical Scientific Symposium* will be held on Friday, 24

November. This is open to all healthcare professionals and is an academic, evidence-based exploration of new scientific insights that hold potential to advance cancer care. In addition, there will be *Provincial Oncology Professionals* education and business meetings held on selected dates (preliminary) on 23-25 November for the following disciplines:

THURSDAY, 23 NOVEMBER	FRIDAY, 24 NOVEMBER	SATURDAY, 25 NOVEMBER
o Oral Oncology o Psychosocial Oncology	o Nutrition o Palliative Care	o Pharmacy o Nursing o Surgical Oncology o Medical Oncology o Radiation Therapy o Family Practice o Pediatric Oncology

Other programs will include the *Poster Presentation and Awards Banquet* (24 November) and the *Community Cancer Forum* (25 November).

For more information on the conference registration, please visit the BC Cancer Agency website www.bccancer.bc.ca.

WEBSITE RESOURCES

The following are available on the BC Cancer Agency website (www.bccancer.bc.ca) under the Health Professionals Info section:

Reimbursement and Forms: Benefit Drug List, Class II, Compassionate Access Program (Undesignated Indication)	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	www.bccancer.bc.ca/ChemoProtocols
Cancer Chemotherapy Pre-Printed Orders	www.bccancer.bc.ca/ChemoProtocols under the index page of each tumour site
Systemic Therapy Program Policies	www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Policies
Unconventional Cancer Therapies Manual	under Patient/Public Info, Unconventional Therapies

IN TOUCH	www.bccancer.bc.ca	bulletin@bccancer.bc.ca
BC Cancer Agency	(604) 877-6000	Toll-Free 1-(800) 663-3333
Communities Oncology Network	Ext 2744	jvenkate@bccancer.bc.ca
Education Resource Nurse	Ext 2638	nursinged@bccancer.bc.ca
Nursing Professional Practice	Ext 2623	ilundie@bccancer.bc.ca
Pharmacy Professional Practice	Ext 2247	gconcon@bccancer.bc.ca
Provincial Systemic Therapy Program	Ext 2247	gconcon@bccancer.bc.ca
Communities Oncology Network Pharmacist	Ext 6277	lkovacic@bcancer.bc.ca
Drug Information	Ext 6275	druginfo@bccancer.bc.ca
Library/Cancer Information	1-888-675-8001 Ext 8003	requests@bccancer.bc.ca
OSCAR Help Desk	1-888-355-0355 Fax (604) 708-2051	oscar@bccancer.bc.ca
Compassionate Access Program office (formerly Undesignated Drug Application office)	Ext 6277 Fax (604) 708-2026	cap_bcca@bccancer.bc.ca
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Centre for the Southern Interior (CCSI)	(250) 712-3900	Toll-Free 1-(888) 563-7773
Fraser Valley Centre (FVCC)	(604) 930-2098	Toll-Free 1-(800) 523-2885
Vancouver Centre (VCC)	(604) 877-6000	Toll-Free 1-(800) 663-3333
Vancouver Island Centre (VICC)	(250) 519-5500	Toll-Free 1-(800) 670-3322