



Systemic Therapy Update

Volume 9, Number 10 *for health professionals who care for cancer patients* October 2006
Website access at <http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/stupdate.htm>

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EDITOR'S CHOICE

“RECOMMENDED LINKS” ON THE BC CANCER AGENCY WEBSITE

We live in a time when vast amounts of information are available at our fingertips through the internet. As a health care professional or patient, how do we know whether a particular website has reliable information or not? This article will highlight what information is available under the **“Recommended Links”** section of the BC Cancer Agency website.

The **Recommended Links** are located under the “Patient/Public Info” section of the BC Cancer Agency website at www.bccancer.bc.ca/PPI/RecommendedLinks. This section includes:

1. [Cancer and Health Related Websites](#)
2. [Inclusion/Removal Policy](#) – criteria used by the agency’s librarians to include or remove a link.
3. [Internet: Evaluating Websites](#) – various tools for self-evaluation of information from the internet.

1. Cancer and Health Related Websites

Many links have information directed to both health care professionals and patients, although they are located under the Patient/Public section. Currently, the links are broadly divided into either “cancer” or “health” related categories, although this may change over the next 6 months to have a more focused, user-friendly framework.

Cancer Websites

This section contains 49 sub-categories, ranging from “Advocacy” and “After Cancer” to “Thyroid” and “Waldenstrom’s Macroglobulinemia”. Specific tumour sites, medical news and newspapers, multilingual resources and diagnostics test are just some examples of the categories located in between. These sub-categories in turn contain anywhere from 1 to 26 links (e.g., Breast and Multilingual Resources sub-categories have 26 links each), so there are virtually hundreds of links located through this section. Some of the frequently recommended websites are listed in the table.

<i>For Patients</i>	<i>For Health Care Professionals</i>
<ol style="list-style-type: none"> 1. Under “General Cancer Websites”: <ul style="list-style-type: none"> ▪ American Cancer Society ▪ Canadian Cancer Society ▪ UptoDate Patient Information ▪ National Cancer Institute Publications Locator – NCI (US) 2. Diagnostic Tests 3. Smoking & Tobacco 4. Specific tumour sites, as requested 	<ol style="list-style-type: none"> 1. Clinical Trials 2. Conferences 3. Genetics 4. Medical News 5. Multilingual resources 6. Organizations 7. Statistics

Health Websites

This section contains 19 sub-categories, ranging from “Advocacy”, “Alternative Therapy” and “Chat Rooms” to “Prevention”, “Research Funding” and “Statistics”. These sub-categories may contain anywhere from 1 to 36 links. Many of them are also divided into “For Patients/Public” and “For Researchers/Clinicians”.

2. Inclusion/Removal Policy

This section outlines the criteria developed by the agency’s librarians to assess the suitability of a website for the Recommended Links section.

Inclusion Criteria

- provides information that supports the mission of the agency and is relevant to our clients
- provides accurate and reliable information
- clearly identifies the sources of information on its site
- identifies its mandate, scope, and objectives
- identifies its sources of funding and sponsorship
- exists primarily for informational or educational purposes and not to promote a product or service
- identifies the author or responsible organization and provides information about their credentials
- provides a way to contact the author, organization, or webmaster
- provides information that is reasonably current and is reviewed and updated regularly
- is well organized and easy to use
- provides unique information that is not easily found elsewhere

Using these criteria, the librarians critically review websites for their accuracy and dependability of information with the following process:

- A website is submitted by a patient, librarian or health care professional for consideration as a recommended link. Requests come in on a regular basis.
- BC Cancer Agency librarian prioritizes new prospects and selects top sites for review.
- Two librarians review the site using the inclusion criteria (see above):
 - If both agree that it is worthy of inclusion, the website is accepted. If one agrees and the other does not, a third librarian is asked for an opinion (“tie breaker”).
 - The opinion of an expert staff member may be sought in the case of a “tie breaker”, or if the site is particularly technical.
- Once the website is accepted, its category is determined based on feedback from reviewers.

A similar process exists for the removal of a link, involving two librarians. The links are reviewed periodically to determine whether the links continue to be appropriate for recommendation.

Removal Criteria

- is out of date and is no longer maintained
- contains numerous defunct links
- is found to contain inaccurate or misleading information
- is replaced by another site that provides superior coverage on the same topic

3. Internet: Evaluating Websites

Because many individuals “surf the web” for information, this section includes 11 different tools for finding and evaluating information on the internet. Each tool is slightly different, as each has a specific focus. For example, the US National Library of Medicine offers a 16-minute tutorial on evaluating internet health information and the Public Health Agency of Canada offers criteria on “How to find the most trustworthy health information websites”. For authors and users of consumer health information on treatment choices, “Discern” is a tool used to judge the quality of written information.

Summary

The Recommended Links section of the BC Cancer Agency website is a dependable source of reliable cancer related websites, evaluated through strict criteria by the BC Cancer Agency Librarians. There are literally hundreds of recommended links in this section. Health professionals and patients alike are encouraged to explore this extensive information resource provided by the agency.

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CANCER DRUG MANUAL

Tamoxifen Monograph and Patient Handout These have been completely updated. Expert review was provided by Dr. Caroline Lohrisch (Breast Tumour Group). Of particular interest, the Interaction and the Side Effects sections have been expanded.

Interactions

- an interaction with rifampin has been **added** to the tamoxifen handout. Though rarely encountered, there is strong clinical evidence to support this interaction.
- a potential interaction with antidepressants has been **deleted** from the tamoxifen handout. Some antidepressants may inhibit CYP2D6. The theoretical implications of this are discussed in the Interactions section of the tamoxifen monograph; however, the clinical significance of this interaction is unknown.
- a potential interaction with grapefruit juice has been **added** to the tamoxifen monograph. Grapefruit juice may decrease the bioavailability of tamoxifen and its active metabolites via inhibition of CYP3A4 in the intestinal wall; the clinical significance of a low rate of intestinal metabolism to active metabolites is unknown.

Please refer to the pharmacokinetic table and interaction table in the monograph for further details regarding the complex metabolism of tamoxifen.

Side Effects

In the monograph, the side effects table has been updated and includes the most recent data from the ATAC trial. Additionally, the side effects and management table in the handout has been modified to include:

- vaginal discharge, rash, increased blood pressure, risk of clot, weight change, hair thinning, changes in lipid levels, endometrial cancer, cataracts, and mood changes
- qualitative descriptors of incidence: common (>50%), sometimes (10-50%), rare (<10%), does not occur (0%)

In general, Cancer Drug Manual handouts list side effects in chronological order of onset. In this case, in an effort to deemphasize the transient stomach upset caused by tamoxifen, nausea has been listed after hot flashes and vaginal discharge.

Note that this handout provides general information on tamoxifen and is not specific to any particular cancer sites. There are protocol-specific handouts (BRAJTAM, BRAVTAM) which give more details on tamoxifen for breast cancer treatment.

Bevacizumab Monograph has been revised to include a more simplified infusion time (see **Protocol Highlights** in this issue of Update).

Erlotinib Monograph now includes compounding information for a suspension formulation. Stability and pharmacokinetic parameters have not been studied with this formulation, but it has been used in pivotal clinical trials, and may be an option for patients with enteral feeding tubes or those who are unable to swallow tablets.

Exemestane Patient Handout now advises patients that exemestane may be taken with or without food. The previous recommendation to take exemestane after breakfast was based on initial clinical trials. While it's true that absorption is increased after a high-fat meal, we now know that maximal estrogen suppression is achieved even under fasting conditions. Administration with food is not necessary.

Imatinib Monograph and Patient Handout Imatinib capsules are no longer available. The drug is now supplied as 100 mg and 400 mg tablets. This information has been added to the monograph, and the patient handout now says "tablet" rather than "capsule."

Rituximab Monograph The relative incidence of infusion-related reactions and fatal cytokine release syndrome has been clarified. Also, additional pediatric indications and dosing information (e.g., maintenance, in conjunction with radioimmunotherapy) have been incorporated.

FOCUS ON: ORAL CLODRONATE ADMINISTRATION – HOW SHOULD WE COUNSEL PATIENTS?

Recently, concerns have arisen regarding patient positioning after administration of clodronate. Clodronate is a bisphosphonate with poor oral absorption (1-3%)^{1,2} which may be reduced to almost nothing in the presence of food.³ Hence, patients are routinely counselled to take clodronate on an empty stomach. Since some oral bisphosphonates are associated with esophageal injury, patients may be told to sit up after taking clodronate. Conversely, some patients are counselled to lie down afterwards, in order to improve absorption. Is one position better than another in terms of absorption?

Clodronate absorption

Timing of food intake

By far, this is the most significant factor in clodronate absorption, as the presence of food significantly reduces clodronate absorption. Absorption is best when clodronate is taken **before** eating. Ideally, patients should take their dose and then wait 2 hours before eating. However, even waiting 30 minutes *before* eating would lead to better absorption than taking the clodronate 2 hours *after* eating (see graph next page)³.

Influence of positioning

No specific studies have been performed to address this issue. Studies with 10 ambulatory, healthy, male volunteers⁴ and 6 women with metastatic breast cancer in a recumbent position⁵ showed similar clearance, volume of distribution, and bioavailability (ambulatory, 2.2 ± 1.2 % vs. recumbent, 1.9 ± 0.4 %). The actual positioning was not well defined in the study with the breast cancer patients, who “remained recumbent” for 3 hours after dosing.⁵

The original manufacturer of clodronate (Hoffman-La Roche) does not recommend any specific positioning to improve absorption.⁶ In addition, large long-term efficacy studies (in multiple myeloma,⁷ breast cancer,^{8,9} and prostate cancer¹⁰ patients) made no mention of specific positioning after patients had taken their clodronate.

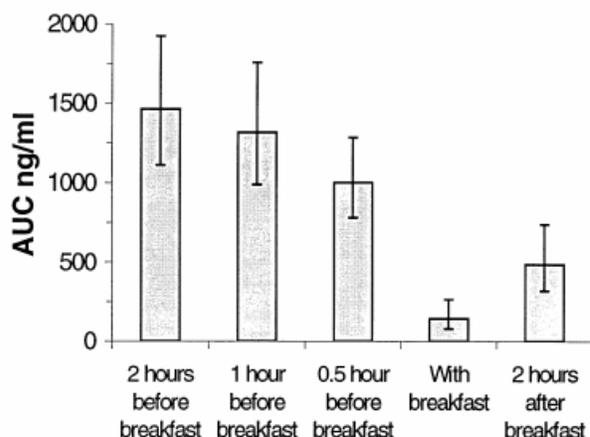


Figure 1. Median areas under serum concentration time curve in 24 h (AUC₀₋₂₄) during the five sessions. Vertical bars denote 95% CIs. AUC represents total amount of drug absorbed by the body. Used with permission from reference 3.

Bisphosphonates and GI irritation

Esophageal injury is most common with the aminobisphosphonates, so patients taking alendronate (FOSAMAX®) are most at risk.¹¹ These patients must not lie down for at least 30 minutes after dosing.¹² Patients taking risedronate (ACTONEL®) are at lower risk, but are also advised to sit or stand for 30 minutes after administration to minimize GI irritation.¹³ In contrast, patients experiencing GI discomfort with etidronate (DIDRONEL®) or clodronate are simply advised to divide the dose.^{1,14}

Conclusions

Patient position after clodronate administration has not been shown to cause esophageal injury or to affect clodronate absorption. The timing of food intake is of much greater importance, and this should continue to be emphasized in patient counselling. Whenever possible, patients should take clodronate before eating, rather than after eating. The Cancer Drug Manual patient handout has recently been revised to reflect these findings.

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HIGHLIGHTS OF PROTOCOL CHANGES

The **Gastrointestinal Tumour Group** has introduced a new *adjuvant protocol for high risk rectal cancer* (GIFURC) to replace two previous protocols (GIRLACF, GIRLAIFF). This new combined modality protocol involves the use of fluorouracil, leucovorin, capecitabine with radiotherapy. Other combined modality protocol that is currently in use is the infusional fluorouracil with radiotherapy (GIFUR).

Also, the infusion time for all *bevacizumab*-containing protocols has been revised (UGICIRB, UGICOXB, UGIFFIRB, UGIFFOXB). There are recent data to suggest that bevacizumab can be safely administered as a 30-minute infusion without the need for 90-minute or 60-minute initial infusions.

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**.

New protocol:

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

Revised protocols:

Code	Changes	Protocol Name
GIA	<i>Blood work requirements prior to treatments revised</i>	Palliative Therapy for Hepatoma using Doxorubicin
UGICIRB	<i>Infusion time revised</i>	Palliative combination chemotherapy for metastatic colorectal cancer using irinotecan, bevacizumab and capecitabine
UGICOXB	<i>Infusion time revised</i>	Palliative combination chemotherapy for metastatic colorectal cancer using oxaliplatin, capecitabine and bevacizumab
UGIFFIRB	<i>Infusion time revised</i>	Palliative combination chemotherapy for metastatic colorectal cancer using irinotecan, fluorouracil, folinic acid (leucovorin) and bevacizumab
UGIFFOXB	<i>Infusion time revised</i>	Palliative combination chemotherapy for metastatic colorectal cancer using oxaliplatin, 5-fluorouracil, folinic acid (leucovorin) and bevacizumab
GIFUR	<i>Exclusions added, Tests and Treatment sections clarified</i>	Combined Modality Adjuvant Therapy for High Risk Rectal Carcinoma using Fluorouracil, Folinic Acid (Leucovorin) and Radiation Therapy
GIRLACF	<i>Replaced by GIFURC</i>	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
GIRLAIFF	<i>Replaced by GIFURC</i>	Preoperative Concurrent Chemotherapy And Radiotherapy And Postoperative Chemotherapy For Locally-Advanced (Borderline Resectable Or Unresectable) Rectal Adenocarcinoma

Code	Changes	Protocol Name
HNTSH	<i>PET scan information added to Eligibility and Treatment</i>	Radioiodine Imaging in Patients with Thyroid Cancer using Thyrotropin Alpha

PROTOCOL-SPECIFIC PATIENT HANDOUT

The **BC Cancer Agency Protocol-Specific Patient Handout** are developed and revised on a periodic basis. New handout for this month is listed below:

New protocol:

Code	Protocol Name
BRAVTPC	Palliative Therapy for Metastatic Breast Cancer using Trastuzumab, Paclitaxel and Carboplatin as First-Line Treatment for Recurrent Breast Cancer

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.

Revised pre-printed orders:		
Code	Changes	Pre-Printed Order Name
BRAJCEF	<i>Blood work requirements prior to treatments revised</i>	Adjuvant Therapy for Breast Cancer Using Cyclophosphamide, Epirubicin and Fluorouracil
UGICIRB	<i>Infusion time revised</i>	Palliative combination chemotherapy for metastatic colorectal cancer using irinotecan, bevacizumab and capecitabine
UGICOXB	<i>Infusion time revised</i>	Palliative combination chemotherapy for metastatic colorectal cancer using oxaliplatin, capecitabine and bevacizumab
UGIFFIRB	<i>Infusion time revised</i>	Palliative combination chemotherapy for metastatic colorectal cancer using irinotecan, fluorouracil, folinic acid (leucovorin) and bevacizumab
UGIFFOXB	<i>Infusion time revised</i>	Palliative combination chemotherapy for metastatic colorectal cancer using oxaliplatin, 5-fluorouracil, folinic acid (leucovorin) and bevacizumab
GIFUR	<i>Changes to blood parameters. Separate parameters for infusional vs. bolus therapy</i>	Combined Modality Adjuvant Therapy for High Risk Rectal Carcinoma using Fluorouracil, Folinic Acid (Leucovorin) and Radiation Therapy
GUPNSAA	<i>Treatment section revised ("tablets" changed to "months", i.e. mitte _____ months)</i>	Non-Steroidal Treatment of Prostate Cancer

COMPASSIONATE ACCESS PROGRAM

The Undesignated Indications Request is now the **Compassionate Access Program (CAP)** and has a new e-mailbox. Questions and comments on CAP should be sent to cap_bcca@bccancer.bc.ca or to "CAP-BCCA" from the agency global directory. This mailbox is monitored on a daily basis. The old undesignated email box will continue to function until December 1st and all email redirected to CAP – BCCA mailbox until then.

CONTINUING EDUCATION

National Oncology Pharmacy Symposium (NOPS) 2006 will be held from **13-15 October, 2006** at the Hyatt Regency in Montréal, Quebec. The theme for 2006 is “*The Dollars and Sense of Quality Cancer Care*”. This symposium is presented by the Canadian Association of Pharmacy in Oncology (www.capho.org). Registration can be submitted online (www.meetingassistant.com/NOPS2006.) until 10 October 2006.

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: \$125 early bird (before 29 September), \$175 (after 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:

<u>Thursday, 23 November</u>	
<ul style="list-style-type: none">• Oral Oncology• Psychosocial Oncology	
<u>Friday, 24 November</u>	
<ul style="list-style-type: none">• Nutrition• Palliative Care	
<u>Saturday, 25 November</u>	
<ul style="list-style-type: none">• Pharmacy• Nursing• Surgical Oncology• Medical Oncology	<ul style="list-style-type: none">• Radiation Therapy• Family Practice• 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.

New Community Care Award

Do you know someone who has made a difference in caring for people with cancer?

The BC Cancer Agency is honouring our partners in the community who have made a difference in supporting the BC Cancer Agency and its patients with the first annual “**Community Care Award – working with our community care networks.**”

The BC Cancer Agency Community Care Award, sponsored by the BC Cancer Foundation, recognizes the value community partners provide to the BC Cancer Agency through outstanding contributions made by individuals in the community to the care of cancer patients in British Columbia. We invite you to nominate someone who has

gone above and beyond the call of duty, or went the extra mile, on behalf of others in the care of cancer patients. Deadline for nominations is October 10, 2006.

To make a nomination online, visit:

www.bccancer.bc.ca

For more information, please contact:

conference@bccancer.bc.ca or 604.877.6216
Toll free: 1.800.663.3333, ex 6216

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

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