BC Cancer Agency

Systemic Therapy Update

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

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IN TOUCH phone list is provided if additional information is needed.

EDITOR'S CHOICE

MAINTENANCE RITUXIMAB THERAPY – COMMONLY ASKED QUESTIONS

QUESTION:

The infusion rate for the maintenance rituximab protocol (ULYRMTN) is the same whether or not patients have had prior rituximab (i.e. infuse over 90 minutes). Given that some of the ULYRMTN patients might never have had rituximab, should their treatment be given over 90 minutes or should the infusion be longer (e.g. over 3-8 hours as in the LYRITUX protocol) so that the potential for allergic reactions are minimized?

RESPONSE:

Prior exposure would be an issue if the rituximab infusion reaction were an allergic reaction. However, the rituximab reaction is *not* an allergic reaction but rather is due to cytokines released from the malignant B cells (i.e. a "cytokine release reaction"). The size of the neoplastic B cell population determines the likelihood of a reaction to rituximab, not whether the patient is rituximab-naive. Very few patients on the ULYRMTN protocol will be rituximab-naïve. Even those who are rituximab-naïve will, by definition, have had some recent chemotherapy and be maintaining a good response to that chemotherapy. Therefore, they would also have a very low neoplastic B cell population. Patients will maintain a low B cell count throughout the two years of maintenance because of the rituximab and so should have a very low likelihood of a rituximab reaction.

QUESTION:

There are different rates of rituximab infusion for LYCVPR, LYFLUDR, and LYRITUX. What is the rationale for the different infusion rates in these protocols? Is there a reason why the rate of infusion for rituximab is not standardized in these protocols?

ANSWER:

When rituximab is being given to an individual with *increased numbers of malignant B cells* we give it in a prolonged infusion to avoid a cytokine release reaction. This is the situation for the first doses in LYCVPR, LYCHOPR and LYFLUDR and all doses in LYRITUX. The reason that we do not use rapid infusion for *any* dose in LYRITUX is that, in at least half of the patients, the rituximab does not lead to a reduction in malignant B cells. In theory we could use rapid infusion for the good responders and not for the poor responders. However, that is too difficult to specify so we avoid rapid infusion for all patients on LYRITUX.

When the rituximab is being given at a time *when the malignant B cells have been largely eliminated, or at least severely damaged, by chemotherapy* and no longer able to release large amounts of cytokines, we can use rapid infusion. This is the situation with second and subsequent dose rituximab in LYCVPR, LYCHOPR and LYFLUDR and all doses in ULYRMTN.

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CANCER DRUG MANUAL

Grapefruit Juice Interaction Standard information has been added to the monographs and handouts for several oral cancer drugs (**busulfan**, **flutamide**, **letrozole**, **ondansetron**). This completes the revisions on all grapefruit juice interactions with the oral cancer drugs in the Cancer Drug Manual. For more general information on this drug-food interaction, see the February issue of the Systemic Therapy Update.

Irinotecan monograph has been updated to include storage and stability information for a new generic formulation, as well as a drug interaction with bevacizumab. There appears to be a pharmacokinetic interaction between bevacizumab and irinotecan, such that plasma levels of the active metabolite of irinotecan (SN-38) are increased. The mechanism of this interaction is currently unknown. Since this interaction may be synergistic in improving overall efficacy while increasing the risk of irinotecan toxicity, initial doses of irinotecan should *not* be decreased when given with bevacizumab. Rather, clinicians should follow dosing guidelines in the UGIFFIRB protocol, monitor patients for severe diarrhea or neutropenia, and adjust doses as per the protocol if such toxicities occur.

Imatinib monograph The interaction with acetaminophen has been removed from the Interaction Table and replaced with a short paragraph on the theoretical potential. This change has been made because the manufacturer has replaced with the more restrictive warning ("….*to avoid or restrict the use of over-the-counter and prescription medicines containing acetaminophen*") with a general caution ("*caution is recommended*").

The caution on acetaminophen use was related to one fatality due to acute liver failure. This occurred in a patient taking high doses (unspecified) of acetaminophen while receiving imatinib for acute phase chronic myeloid leukemia. *In vitro*, imatinib can interfere with the normal detoxification of acetaminophen by inhibiting glucuronidation. However, no specific human studies have been performed and no other cases of clinical interaction have been published.

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
HNAVPG	Treatment of locoregionally recurrent and/or metastatic nasopharyngeal cancer with cisplatin and gemcitabine

Revised protocols:

Code	Changes	Protocol Name
GIGAI	*timing of cycle 2 chemotherapy clarified*	Combined modality adjuvant therapy for completely resected gastric adenocarcinoma using fluorouracil + folinic acid (leucovorin) + radiation therapy
GOCXRADC	*hydration regimen revised*	Treatment of high risk squamous cell carcinoma of cervix with concurrent cisplatin and radiation
UMYBORTEZ	*eligibility revised*	Treatment of Multiple Myeloma with Bortezomib
MYTHALID	*prior use of bortezomib added to eligibility criteria*	Therapy of multiple myeloma using thalidomide

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
HNAVPG	Treatment of locoregionally recurrent and/or metastatic nasopharyngeal cancer with cisplatin and gemcitabine

Revised pre-printed orders:

Code	Changes	Protocol Name
UBRAJTAC	*Undesignated Class II approved clause added to the top of the PPO*	Adjuvant Therapy for Breast Cancer using Cyclophosphamide, Doxorubicin and Docetaxel
GIGAI	*Timing of cycle 2 chemotherapy clarified*	Combined modality adjuvant therapy for completely resected gastric adenocarcinoma using fluorouracil + folinic acid (leucovorin) + radiation therapy
GIFOLFIRI	*Timing of bloodwork parameter changes from 24 hours to within 72 hours*	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Irinotecan, Fluorouracil and Folinic Acid (Leucovorin)
GIFUC	*Timing of bloodwork parameter changes from 24 hours to within 48 hours*	Palliative therapy for gastric cancer using Fluorouracil and Cisplatin (rounding off fluorouracil dose)
GIPGEM	*Timing of bloodwork parameter changes from 24 hours to within 48 hours*	Palliative therapy for pancreatic adenocarcinoma cancer using Gemcitabine
UGIAJFFOX	*Timing of bloodwork parameter changes from 24 hours to within 72 hours*	ADJUVANT Combination Chemotherapy for Stage III Colon Cancer Using Oxaliplatin, 5-Fluorouracil and Folinic Acid (Leucovorin)
UGIFFIRB	*Timing of bloodwork parameter changes from 24 hours to within 72 hours*	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Irinotecan, Fluorouracil, Folinic Acid (Leucovorin) and Bevacizumab
UGIFFOXB	*Timing of bloodwork parameter changes from 24 hours to within 72 hours*	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Oxaliplatin, 5-Fluorouracil, Folinic Acid (Leucovorin) and Bevacizumab

Revised pre-printed orders:

Code	Changes	Protocol Name
UGIFOLFOX	*Timing of bloodwork parameter changes from 24 hours to within 72 hours*	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Oxaliplatin, 5-Fluorouracil and Folinic Acid (Leucovorin)
GOCXRADC	*Hydration regimen revised*	Treatment of high risk squamous cell carcinoma of cervix with concurrent cisplatin and radiation
MYTHALID	*Prior use of bortezomib added to eligibility criteria*	Therapy of multiple myeloma using thalidomide

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, 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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