Systemic Therapy Update



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For Health Professionals Who Care For Cancer Patients

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EDITOR'S CHOICE

New Programs

The BCCA Provincial Systemic Therapy Program has approved the following new programs effective 1 May 2016:

Lymphoma:

Obinutuzumab in Combination with Chlorambucil for Previously Untreated Chronic Lymphocytic Leukemia (CLL) (ULYOBCHLOR) – The BCCA Lymphoma Tumour Group is launching this new treatment program based on an open-label, three-armed, randomized controlled trial which evaluated patients who were previously untreated for CLL and were considered unsuitable for treatment with fludarabine. ¹ Compared to chlorambucil alone, the combination of chlorambucil with obinutuzumab was associated with significant improvement in median overall survival (hazard ratio [HR] 0.41, 95%CI 0.23-0.74), and progression-free survival (HR 0.18, 95% CI 0.13-0.24). Patients receiving obinutuzumab experienced higher rates of neutropenia and infusion-related reactions. Further information on the pharmacology of obinutuzumab can be found in the Cancer Drug Manual section below.

Currently, fludarabine-based therapy remains the standard initial therapy for CLL at the BCCA. However, in patients who are unsuitable for fludarabine, treatment with obinutuzumab and chlorambucil is to

EDITOR'S CHOICE

replace the use of chlorambucil with rituximab (LYCHLRR).

References:

1. Goede V, Fischer K, Busch R, et al. Obinutuzumab plus chlorambucil in patients with CLL and coexisting conditions. NEJM 2014;370(12): 1101-1110.

Supportive Care:

Inpatient Oxaliplatin Desensitization Protocol (SCOXRX) — A new desensitization protocol has been developed by the BCCA Gastrointestinal (GI) Tumour Group to manage oxaliplatin hypersensitivity reactions (HSRs). This protocol is indicated in the rare circumstance where the continued use of oxaliplatin is warranted despite a severe HSR. While the literature shows that various desensitization protocols have been used successfully in some patients, the GI Tumour Group cautions clinicians to weigh the benefit of continued oxaliplatin treatment against the risk of recurrent severe reactions when considering the use of the desensitization protocol. In fact, the oxaliplatin Canadian Product Monograph lists a history of severe HSRs as a contraindication to oxaliplatin rechallenge. Please note that information on oxaliplatin rechallenge for grades 1 or 2 HSRs, as well as for more severe reactions, have been updated under the *Precautions* section of all oxaliplatin-containing GI Protocols.

HIGHLIGHTS OF CHANGES IN PROTOCOLS, PPPOS AND PATIENT HANDOUTS

Gastrointestinal:

Oxaliplatin-Containing Gastrointestinal (GI) Protocols, PPPOs and Patient Handouts have been updated with the following changes:

- 1) Updated hypersensitivity and desensitization information in the *Precautions* section of the protocols based on availability of the new *Inpatient Oxaliplatin Desensitization Protocol (SCOXRX)*.
- 2) Added information on QT prolongation for health professionals and patients based on new information from the Canadian and US Product Monographs. The protocols and PPPOs now contain additional laboratory requirements (i.e. calcium and magnesium prior to every cycle) for all patients, and ECG monitoring for high-risk patients.
- 3) Standardized nomenclature for fluorouracil administration* "IV push" has replaced "IV bolus"
- 4) Added field under *Return Appointment Orders* for clinicians to indicate the reason for requesting *Weekly Nursing Assessment*.*

For all affected documents, please see the List of New and Revised Protocols, PPPOs and Patient Handouts section <u>below</u>.

PROVINCIAL SYSTEMIC THERAPY PROGRAM

REVISED POLICIES

The BCCA Provincial Systemic Therapy Program has revised the following policies effective 1 May 2016:

^{*}These items will be updated in other BCCA GI protocols and PPPOs in the near future.

PROVINCIAL SYSTEMIC THERAPY PROGRAM

Prevention and Management of Extravasation of Chemotherapy: (Policy III-20)

- Added information on patient education in the prevention of extravasation with peripheral and Central Venous Access Device (CVAD)
- Added information on patient monitoring post-ambulation for catheter or needle dislodgement, and for risk of extravasation
- Highlighted information on suspected and actual extravasation
- Added hyperlinks to Provincial Systemic Therapy Program Policies III-80 and C-252
- Revised "Flowsheet on Suspected/Actual Chemotherapy Extravasation" (Appendix 1) to include additional requirements for describing the extravasation event, and for completing a Patient Safety Learning System (PSLS) report

Physician Coverage for Medical Emergencies During Delivery of Selected Chemotherapy Drugs: (Policy III-60)

Added obinutuzumab – Infusion-related reactions are common with the first two doses of this drug.
 Therefore, physicians must remain on-site during the entire duration of the infusion plus one hour post-infusion for the first and second doses in cycle 1 of treatment.

CANCER DRUG MANUAL

New Monographs and Patient Handouts

The **Obinutuzumab Monograph** and **Patient Handout** have been developed with expert review provided by Dr. Laurie Sehn (Medical Oncologist) and Linda Hamata (Pharmacist) from the BCCA Lymphoma Tumour Group.

Obinutuzumab is a humanized recombinant type II anti-CD20 monoclonal antibody that targets CD20 transmembrane antigen on B-lymphocytes. Infusion-related reactions are common and patients with high tumour burden may be at an increased risk of severe reactions. The use of premedications and giving the first treatment dose over two days have been shown to reduce the incidence and severity of such reactions. Other side effects include neutropenia, thrombocytopenia, elevated transaminases and tumour lysis syndrome. All patients should be screened for Hepatitis B virus (HBV) infection prior to initiation of treatment, as HBV reactivation can occur. Live or attenuated vaccines are not recommended during treatment and until B-cell recovery has occurred after treatment.

REVISED MONOGRAPHS AND PATIENT HANDOUTS

Cyclosporine (PO) Patient Handout:

Added information on blood pressure monitoring

Everolimus Monograph and Patient Handout:

 Added information on the increased risk of angioedema when everolimus and ACE inhibitors are used concurrently

CANCER DRUG MANUAL

Oxaliplatin Patient Handout:

Added information on QT prolongation

BENEFIT DRUG LIST

New Programs

The following program has been added to the BCCA Benefit Drug List effective 1 May 2016:

Protocol Title	Protocol Code	Benefit Status
Treatment of Previously Untreated Chronic Lymphocytic Leukemia Using Obinutuzumab in Combination with Chlorambucil	ULYOBCHLOR	Restricted

REVISED PROGRAMS

The following programs have been revised on the BCCA Benefit Drug List effective 1 May 2016:

Protocol Title	Protocol Code	Benefit Status
Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Oxaliplatin, Bevacizumab and Capecitabine	GICOXB	Class II (Previously Restricted)
Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Oxaliplatin, Fluorouracil, Leucovorin, and Bevacizumab	GIFFOXB	Class II (Previously Restricted)

Systemic Therapy Update Editorial Board

FAREWELL TO BOARD MEMBER

The Systemic Therapy Update (STU) Editorial Board would like to bid farewell to long-time board member, Beth Morrison, as she embarks on a new journey in June 2016 – retirement!

Beth joined the BC Cancer Agency in November 1990 as a Reference Librarian. Over the course of her career, she has held various roles within the Agency and the Library, including the BCCA website coordinator and the Provincial Library Leader. Beth joined the STU Editorial Board in July 2002, and has made significant contributions to the STU over the years. The Editorial Board would like to thank Beth for her many years of service, and for sharing her knowledge, wisdom, and expertise with the Editorial Board. We wish her the very best in her retirement.

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 BCCA Compassionate Access Program approval are prefixed with the letter "U".

NEW Protocols, PPPOs and Patient Handouts (Affected Documents are Checked):					
CODE	Protocol	PPPO	Patient Handout	Protocol Title	
LULAPE2RT			\square	Treatment of Locally Advanced Non-Small Cell Lung Cancer using Alternative Dosing of Cisplatin and Etoposide with Radiation Therapy	
LULAPE2RT (Carboplatin Option)				Treatment of Locally Advanced Non-Small Cell Lung Cancer using Alternative Dosing of Cisplatin and Etoposide with Radiation Therapy	
ULUAVCRIZF			V	First-Line Treatment of ALK-Positive Advanced Non-Small Cell Lung Cancer (NSCLC) with Crizotinib	
ULYOBCHLOR	V	$\overline{\checkmark}$		Treatment of Previously Untreated Chronic Lymphocytic Leukemia Using Obinutuzumab in Combination with Chlorambucil	
SCOXRX	$\overline{\checkmark}$			Inpatient Treatment of Oxaliplatin Desensitization	

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED):						
CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title	
UBRAVERIB	Ø	Ø		Dose modification for renal dysfunction updated, TALLman lettering formatted	Palliative Therapy for Metastatic Breast Cancer using eriBULin	
CNAJTZRT	Ø			Eligibility updated	Concomitant (Dual Modality) and Adjuvant Temozolomide for Newly Diagnosed Malignant Gliomas with Radiation	
CNMODPCV	\square			Eligibility updated	Modified PCV Chemotherapy Of Brain Tumours Using Procarbazine, Lomustine (CCNU) and vinCRIStine	
GICAPOX	\square		$\overline{\checkmark}$	Eligibility updated	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Oxaliplatin and Capecitabine	
GICOXB	Ø	Ø	$\overline{\checkmark}$	Benefit status and eligibility updated	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Oxaliplatin, Bevacizumab and Capecitabine	

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED):					
CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
GIFFOXB	Ø			Benefit status and eligibility updated	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Oxaliplatin, Fluorouracil, Leucovorin, and Bevacizumab
GIFOLFOX				Eligibility updated	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Oxaliplatin, Fluorouracil and Leucovorin
UGUPRAD				Eligibility revised; dose and references updated	Therapy for Metastatic Castration Resistant Prostate Cancer Using Radium- 223
LYHDMRP				Contact physician updated	Treatment of Primary Intracerebral Lymphoma with High Dose Methotrexate and riTUXimab
LYHDMTXP	\square			Contact physician updated	Treatment of Primary Intracerebral Lymphoma with High Dose Methotrexate
LYHDMTXR				Contact physician updated	Treatment of Leptomeningeal Lymphoma or Recurrent Intracerebral Lymphoma with High Dose Methotrexate
SAAJGI				INR monitoring in patients receiving warfarin clarified	Adjuvant Treatment of C-Kit Positive High Risk Gastrointestinal Stromal Cell Tumours Using Imatinib
SAAVGI				INR monitoring in patients receiving warfarin clarified	Treatment of Advanced c-Kit Positive and c-Kit Negative Gastrointestinal Stromal Cell Tumors (GISTs) using Imatinib
SAAVGIDD				INR monitoring in patients receiving warfarin clarified	Treatment of Advanced c-Kit Positive Gastrointestinal Stromal Cell Tumors (GIST's) using 800 mg Dosing of Imatinib
SADTIC	\square			Removed D5W option as infusion solution for dacarbazine	High Dose Single Agent Dacarbazine (DTIC) for Metastatic Soft Tissue Sarcoma

The following BCCA Oxaliplatin-Containing Gastrointestinal Protocols, PPPOs and Patient Handouts have been updated to reflect one or more of the following updates:

- Include information on QT-prolongation
- Include information on oxaliplatin hypersensitivity reactions and desensitization
- Standardize nomenclature for fluorouracil "IV push" administration
- Create field in PPPOs to indicate reason for requesting Weekly Nursing Assessment

CODE	Protocol Title
GIAJCAPOX	Adjuvant Combination Chemotherapy for Stage III and Stage IIB Colon Cancer Using Oxaliplatin and Capecitabine

CODE	Protocol Title
GIAJFFOX	Adjuvant Combination Chemotherapy for Stage III and Stage IIB Colon Cancer Using Oxaliplatin, Fluorouracil and Leucovorin
GICAPOX	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Oxaliplatin and Capecitabine
GIFOLFOX	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Oxaliplatin, Fluorouracil and Leucovorin
GIRAJCOX	Adjuvant Combination Chemotherapy for Stage III Rectal Cancer Using Oxaliplatin and Capecitabine
GIRAJFFOX	Adjuvant Combination Chemotherapy for Stage III Rectal Cancer Using Oxaliplatin, Fluorouracil and Leucovorin
GICOXB	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Oxaliplatin, Bevacizumab and Capecitabine
GIFFOXB	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Oxaliplatin, Fluorouracil, Leucovorin and Bevacizumab
UGIFIRINOX	Palliative Combination Chemotherapy for Advanced Pancreatic Adenocarcinoma Using Irinotecan, Oxaliplatin, Fluorouracil and Leucovorin

Website Resources and Contact Information			
WEBSITE RESOURCES	www.bccancer.bc.ca		
Systemic Therapy Update	www.bccancer.bc.ca/health-professionals/professional-resources/systemic-therapy/systemic-therapy-update		
Reimbursement & Forms: Benefit Drug List, Class II, Compassionate Access Program	www.bccancer.bc.ca/health-professionals/professional-resources/systemic-therapy		
Cancer Drug Manual	www.bccancer.bc.ca/health-professionals/professional-resources/cancer-drug-manual		
Cancer Management Guidelines	www.bccancer.bc.ca/health-professionals/professional-resources/cancer-management-guidelines		
Cancer Chemotherapy Protocols, Pre-printed Orders, Protocol Patient Handouts	www.bccancer.bc.ca/health-professionals/professional-resources/chemotherapy-protocols		
Systemic Therapy Program Policies	www.bccancer.bc.ca/health-professionals/professional-resources/systemic-therapy		
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