

# **Systemic Therapy Update**

June 2019 ♦ Vol. 22 ♦ No. 6

# For Health Professionals Who Care For Cancer Patients

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## **EDITOR'S CHOICE**

#### **New Programs**

Effective 01 June 2019, the BC Cancer Provincial Systemic Therapy Program has approved the following treatment program:

#### Leukemia/BMT:

Inotuzumab Ozogamicin for Acute Lymphoblastic Leukemia (ALL) (ULKINOZ) – The BC Cancer Leukemia/BMT Tumour Group is introducing inotuzumab ozogamicin for relapsed or refractory B-cell precursor ALL following induction chemotherapy. Previous treatment options in this setting typically involved combination salvage induction chemotherapy to achieve remission with the hope of proceeding to potentially curative hematopoietic stem cell transplantation (HSCT). Patients whose disease fails re-induction or for whom HSCT is not feasible have poor prognosis. Blinatumomab was recently made available in the relapsed/refractory setting at BC Cancer; BC Cancer will only fund one of blinatumomab or inotuzumab ozogamicin. Current funding is also restricted to treatments prescribed by the Leukemia/BMT physicians and delivered at the Vancouver General Hospital.

Inotuzumab ozogamicin is a humanized monoclonal antibody-drug conjugate that targets the CD22 receptor in CD22-positive B-cell precursor ALL. A phase III randomized controlled trial (INO-VATE) compared inotuzumab ozogamicin to standard salvage chemotherapy. Inotuzumab ozogamicin demonstrated a higher complete response rate (80.7% vs. 29.4%, p<0.001) and a greater likelihood of proceeding to HSCT (41% vs 11%, p<0.001). Overall survival for patients who went on to receive HSCT was not statistically different between the treatment arms. The overall incidence of serious adverse effects was also similar, although inotuzumab ozogamicin was associated with a higher incidence of veno-occlusive disease (11% vs 1%), with HSCT patients at the highest risk. More information about the adverse effects and pharmacology of inotuzumab ozogamicin can be found in the Cancer Drug Manual

## **EDITOR'S CHOICE**

section of the February 2019 issue of the Systemic Therapy Update.

#### References:

- pan-Canadian Oncology Drug Review (pCODR) Expert Review Committee (pERC). Final recommendation for inotuzumab ozogamicin (Besponsa<sup>®</sup>) for acute lymphoblastic leukemia (ALL). 06July2018.
- 2. Kantarjian HM, DeAngelo DJ, Stelljes M, et al. Inotuzumab ozogamicin versus standard therapy for acute lymphoblastic leukemia. N Engl J Med 2016;375:740-753.

#### **DRUG UPDATE**

## **BC Cancer Magic Mouthwash: Clarifications & Updates**

The **BC Cancer Magic Mouthwash Protocol (SCMMW)** was implemented in May 2019 along with a **Frequently Asked Questions** document and **Prescription Templates**. Since then, Provincial Drug Information has received a number of requests for clarifications and to improve the ease of use of the electronic prescription templates.

In response to the above, the following changes have been made:

- SCMMW Protocol clarified language around BC PharmaCare coverage and Special Authority exemption in the Eligibility section, and the expiry date in the Evidence Review section
- **FAQ Document** added information about the expiry date and the use of Sterile Water for Irrigation in the compounding process
- **BC Cancer Prescription Templates** added fillable fields to provide clinicians the option to complete the prescription electronically

The above documents can be found on the <u>BC Cancer Supportive Care Chemotherapy Protocol</u> website. For more information about the BC Cancer Magic Mouthwash, please see the <u>May 2019</u> issue of the Systemic Therapy Update.

#### BENDAMUSTINE DOSING IN CLL PROTOCOLS CLARIFIED

In March 2019, the BC Cancer Protocol for **bendamustine and rituximab** for previously untreated Chronic Lymphocytic Leukemia (CLL) **(LYCLLFBR)** was revised to reflect evidence-based dosing. As this dosing does not match the bendamustine dosing in the refractory setting (LYCLLBENDR), the BC Cancer Lymphoma Tumour Group would like to clarify the rationale for the intentional dosing discrepancy.

- LYCLLFBR Bendamustine dosing in previously untreated CLL is 90 mg/m² IV on days 1 and 2 based on the phase III randomized controlled trial (CLL10) that established this treatment in the first-line setting.¹ This was updated in March 2019, which originally had a starting dose of 70 mg/m², with the option to increase to 90 mg/m² as tolerated by the patient.
- LYCLLBENDR Bendamustine dosing in the relapsed/refractory setting is 70 mg/m² based on supportive evidence from a phase II trial.²

## **DRUG UPDATE**

#### References:

- 1. Eichhorst B, Fink A, Bahlo J, et al. First-line chemoimmunotherapy with bendamustine and rituximab versus fludarabine, cyclophosphamide, and rituximab in patients with advanced chronic lymphocytic leukaemia (CLL10): an international, open-label, randomised, phase 3, non-inferiority trial. Lancet Oncol 2016;17:928–942.
- 2. Fischer K, Cramer P, Busch R, et al. Bendamustine combined with rituximab in patients with relapsed and/or refractory chronic lymphocytic leukemia: a multicenter phase II trial of the German chronic lymphocytic leukemia study group. J Clin Oncol 2011;29:3559-3566.

## **MEDICAL PATIENT ASSISTANCE PROGRAMS UPDATED**

The listing of oncology medical patient assistance programs offered by pharmaceutical companies has been updated and can be found at: <a href="https://www.bccancer.bc.ca/mpap">www.bccancer.bc.ca/mpap</a>.\*

\*Located on the BC Cancer Systemic Therapy website under Health Professionals > Systemic Therapy > Reimbursement & Forms

#### **BENEFIT DRUG LIST**

## **New Programs**

Effective 01 June 2019, the following treatment program has been added to the BC Cancer <u>Benefit Drug</u> List:

Protocol Title	Protocol Code	Benefit Status
Treatment of Relapsed or Refractory Pre-B-Cell Acute Lymphoblastic Leukemia with Inotuzumab Ozogamicin	ULKINOZ	Restricted

## **REVISED PROGRAMS**

Effective 01 June 2019, tretinoin has been added to the following treatment program on the BC Cancer Benefit Drug List:

Protocol Title	Protocol Code	Benefit Status
Induction and Consolidation Therapy of Relapsed Acute Promyelocytic Leukemia using Arsenic Trioxide and Tretinoin (All-Trans Retinoic Acid)	LKATOR	Class I

#### **CANCER DRUG MANUAL**

#### **New Monographs and Patient Handouts**

The following drug is <u>NOT</u> a BC Cancer Benefit Drug and requires application to the BC Cancer Compassionate Access Program (CAP). Its corresponding Interim Monograph and Patient Handout are made available for reference only. All BC Cancer drug monographs and patient handouts can be accessed on the Cancer Drug Manual <u>Drug Index</u>.

The **Cabozantinib Interim Monograph** and **Patient Handout** have been developed with expert review provided by Dr. Daniel Khalaf (medical oncologist) and Victoria Kletas (pharmacist) of the BC Cancer Genitourinary Tumour Group. Cabozantinib is an inhibitor of multiple tyrosine kinases, including hepatocyte growth factor receptor protein (MET), vascular endothelial growth factor (VEGF), and fms-like tyrosine kinase-3 (FLT3). Cabozantinib is used in the treatment of advanced renal cell carcinoma. The usual dose is 60 mg orally once daily, on an empty stomach.

Highlights of these documents include:

- Hypertension is commonly observed; blood pressure should be well controlled prior to starting treatment.
- Impaired wound healing has been reported; it is recommended to hold cabozantinib for at least 28 days prior to surgery, including dental surgery.
- Rare, but serious, adverse effects include arterial and venous thromboembolism, gastrointestinal
  perforation and fistula, hemorrhage, hepatotoxicity, hypertensive crisis, osteonecrosis of the jaw,
  and reversible posterior leukoencephalopathy syndrome.

#### **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:

#### **EPOCH-R CPSC:**

Deleted recommendation to protect infusion bag from light during storage and administration

#### **Everolimus Monograph:**

Supply and Storage: discontinued 7.5 mg tablet

#### **Mechlorethamine CPSC:**

Deleted injectable formulation as no longer marketed in Canada

## **Olaparib Monograph:**

 Supply and Storage: updated requirement for refrigeration for capsule formulation only; storage requirements for tablet formulation remain unchanged

#### **Olaparib Patient Handout (Tablets):**

Storage bullets: added recommendation to store tablets in original container with desiccant

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

**BC Cancer 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 treatment requiring BC Cancer Compassionate Access Program approval are prefixed with the letter "U".

New Protocols, PPPOs and Patient Handouts (Affected Documents are Checked)					
CODE	E Protocol PPPO Patient Handout Protocol Title				
ULKINOZ	$\overline{\checkmark}$		Treatment of Relapsed or Refractory Pre-B-Cell Acute Lymphoblastic Leukemia with Inotuzumab Ozogamicin		
LYFCR			Treatment of Chronic Lymphocytic Leukemia (CLL) or Prolymphocytic Leukemia with Fludarabine, Cyclophosphamide and Rituximab		

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)						
CODE	Protocol PPPO Patient Handout Changes		Changes	Protocol Title		
GIAJCAPOX			V	Dose modifications and baseline tumour marker clarified	Adjuvant Combination Chemotherapy for Stage III and Stage IIB Colon Cancer using Oxaliplatin and Capecitabine	
GIAJFFOX	Ø		Ø	Treatment updated  Nutrition supportive care document information updated in Patient Handout	Adjuvant Combination Chemotherapy for Stage III and Stage IIB Colon Cancer using Oxaliplatin, Fluorouracil, and Leucovorin	
GIAJFL	<b>V</b>		V	GI Systemic Therapy Chair contact number updated Nutrition supportive care document information updated in Patient Handout	Adjuvant Therapy of Colon Cancer using Fluorouracil Injection and Infusion and Leucovorin Infusion	

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)						
CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title	
UGIAJRALOX	V	V	V	Institutional name, Tests, Treatment, Dosage Modifications, GI Systemic Therapy Chair contact number updated Nutrition supportive care document information updated in Patient Handout Oxaliplatin protocols, PPOs harmonized for CST	Adjuvant Combination Chemotherapy for Node Positive Colon Cancer using Oxaliplatin and Raltitrexed in Patients Intolerant to Fluorouracil or Capecitabine	
GIENACTRT	V		Ø	Premedications and Precautions updated	Neoadjuvant Treatment of Esophageal and Gastroesophageal Carcinomas using Carboplatin, Paclitaxel and Radiation Therapy	
UGIFFOXPAN	$\square$			Oxaliplatin protocols harmonized for CST	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer using Oxaliplatin, Fluorouracil, Leucovorin, and Panitumumab	
GIGAJCOX	<b>V</b>		<b>V</b>	Tests, Treatment and Dosage Modifications updated Nutrition supportive care document information updated in Patient Handout	Adjuvant Chemotherapy of Gastric Cancer Patients with D2 Resection (Node Negative) or Ineligible for Adjuvant Chemoradiation using Oxaliplatin and Capecitabine	
GIGAJFFOX	<b>V</b>		V	Treatment and GI Systemic Therapy Chair contact number updated Nutrition supportive care document information updated in Patient Handout	Adjuvant Chemotherapy of Gastric Cancer Patients with D2 Resection (Node Negative) or Ineligible for Adjuvant Chemoradiation using Oxaliplatin, Fluorouracil, and Leucovorin	
GIGFLODC	<b>I</b>	<b>4</b>		Oxaliplatin protocols, PPOs harmonized for CST	Perioperative Treatment of Resectable Adenocarcinoma of the Stomach, Gastroesophageal Junction or Lower 1/3 Esophagus using Docetaxel, Oxaliplatin, Infusional Fluorouracil, and Leucovorin	

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)						
CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title	
GIGFOLFIRI	Ø		Ø	GI Systemic Therapy Chair contact number updated Nutrition supportive care document information updated in Patient Handout	Second-Line Palliative Combination Chemotherapy for Metastatic Gastric or Esophageal Adenocarcinoma using Irinotecan, Fluorouracil and Leucovorin	
GIIR	<b></b>	<b></b>	<b>I</b>	Institutional name and logo, Tests and GI Systemic Therapy Chair contact number updated Nutrition supportive care document information updated in Patient Handout	Palliative Chemotherapy for Metastatic Colorectal Cancer using Irinotecan	
GIRAJCOX	Ø	<b>V</b>	Ø	Tests, Treatment, Dosage Modification, Precautions, and GI Systemic Therapy Chair contact number updated	Adjuvant Combination Chemotherapy for Stage III Rectal Cancer using Oxaliplatin and Capecitabine	
GIRAJFFOX	<b>4</b>		Ø	Tests, Treatment and Precautions updated Nutrition supportive care document information updated in Patient Handout	Adjuvant Combination Chemotherapy for Stage II Rectal Cancer using Oxaliplatin, Fluorouracil, and Leucovorin	
GIRINFRT	$\square$			Treatment updated	Combined Modality Adjuvant Therapy for High Risk Rectal Carcinoma using Capecitabine, Infusional Fluorouracil and Radiation Therapy	
UGOOVOLAPM				Dispensing quantity clarified	Maintenance Treatment of Relapsed, BRCA- mutated, Platinum-Sensitive and Responsive Epithelial Ovarian Cancer using Olaparib	
LKATOR	Ø			Title, Tests, Treatment and Premedications revised	Induction and Consolidation Therapy of Relapsed Acute Promyelocytic Leukemia using Arsenic Trioxide and Tretinoin (All-Trans Retinoic Acid)	
ULUAVNIV	V		V	Premedications updated	Advanced Non-Small Cell Lung Cancer using Nivolumab	
ULUAVNIV4	$\overline{\checkmark}$		V	Premedications updated	Advanced Non-Small Cell Lung Cancer using 4- Weekly Nivolumab	

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)						
CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title	
ULUAVPMB	$\square$	$\overline{\square}$		Premedications updated	Advanced Non-Small Cell Lung Cancer using Pembrolizumab	
ULUAVPMBF	$\square$	$\overline{\checkmark}$	$\overline{\checkmark}$	Premedications updated	First-Line Treatment of Advanced Non-Small Cell Lung Cancer using Pembrolizumab	
LULACATRT			$\overline{\mathbf{A}}$	Contact Physician, Institutional Name, and Tests updated	Locally Advanced Non-Small Cell Lung Cancer using Carboplatin and Paclitaxel with Radiation Therapy	
LUMMPG			V	Contact Physician, Institutional Name, and Tests updated	Treatment of Malignant Mesothelioma with Platinum and Gemcitabine	
LUOTPE			V	Contact Physician, Institutional Name, and Tests updated	Treatment of Thymoma with Cisplatin and Etoposide	
LUSCPI				Contact Physician, Institutional Name, and Tests updated	Second-Line Treatment of Extensive Stage Small Cell Lung Cancer (SCLC) with Irinotecan with or without Platinum	
LYCHOPRMTX				Treatment and Dose Modifications updated	Central Nervous System Prophylaxis with High Dose Methotrexate, CHOP and Rituximab in Diffuse Large B-Cell Lymphoma	
LYEPOCHR	Ø			Recommendation to protect infusion bag from light removed	Treatment of Lymphoma with Dose-Adjusted Etoposide, Doxorubicin, Vincristine, Cyclophosphamide, Prednisone and Rituximab with Intrathecal Methotrexate	
USMMCCAVE				Administration filter clarified	Second-Line Treatment of Recurrent or Metastatic Merkel Cell Carcinoma using Avelumab	
SCMMW				Eligibility and product expiry clarified	Treatment of Oral Mucositis using BC Cancer Magic Mouthwash	

## Website Resources and Contact Information

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Oncology Drug Information	604-877-6275		druginfo@bccancer.bc.ca
Nurse Educators	604-877-6000 x 672638		nursinged@bccancer.bc.ca
Library/Cancer Information	604-675-8003 Toll Free 888-675-8001 x 8003		requests@bccancer.bc.ca
Pharmacy Professional Practice	604-877-6000 x 672247		mlin@bccancer.bc.ca
Provincial Professional Practice Nursing			BCCancerPPNAdmin@ehcnet.phsa.ca
OSCAR	888-355-0355	604-708-2051	oscar@bccancer.bc.ca
Compassionate Access Program (CAP)	604-877-6277	604-708-2026	cap bcca@bccancer.bc.ca
Pharmacy Oncology Certification	250-712-3900 x 686820		rxchemocert@bccancer.bc.ca
BC Cancer-Abbotsford	604-851-4710 Toll Free 877-547-3777		
BC Cancer-Prince George (Centre for the North)	250-645-7300 Toll Free 888-775-7300		
BC Cancer-Surrey	604-930-2098 Toll Free 800-523-2885		
BC Cancer-Kelowna	250-712-3900 Toll Free 888-563-7773		
BC Cancer-Vancouver	604-877-6000 Toll Free 800-663-3333		
BC Cancer-Victoria	250-519-5500 Toll Free 800-670-3322		

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