



## For Health Professionals Who Care For Cancer Patients

### Inside This Issue:

- **Editor's Choice** – **New Programs:** Ramucirumab with Paclitaxel for Gastric Cancer, Azacitidine with Sorafenib for Acute Myeloid Leukemia; **Revised Programs:** Breast Cancer Genomic Testing for Microscopic Disease
- **Benefit Drug List** – **New:** UGIGAVRAMT, ULKAMLAS
- **Cancer Drug Manual** – **New:** Ramucirumab, Atezolizumab **Revised:** Nivolumab, Pembrolizumab
- **List of New and Revised Protocols, Provincial Pre-Printed Orders and Patient Handouts:** **New:** UGIGAVRAMT, GUPDOCADT, ULKAMLAS; **Revised:** BRAVEVEX, CNBEV, CNTEM60, GOENDAI, GOOVDDCAT, GOOVDOC, GUAJPG, GUAVPG, GUEDPM, GUEP, GUEVER, GUMVAC, GUPMX, GUSCARB, GUSCPE, GUSCPERT, UGUTAXGEM, GUVEIP, GUVIP2, HLHETCSPA, HNOTTSH, LYCDA, LYCHOPRMTX, LYCODOXMR, LYGDP, LYGDPR, LYHDMRP, LYHDMTXP, LYHDMTXR, LYIVACR, UMYLDREL, UMYLENDEX, UMYLENMTN, SAHDMTX, USMAVDT, SMAVTMZ, SMCCNU, SMTAM
- **Website Resources and Contact Information**

## EDITOR'S CHOICE

### NEW PROGRAMS

Effective 1 May 2017, the BCCA Provincial Systemic Therapy Program has approved the following programs.

#### Gastrointestinal:

**Ramucirumab with Weekly Paclitaxel for Second-Line Treatment of Metastatic or Locally Advanced Gastric or Gastroesophageal Junction Cancer (UGIGAVRAMT)** – Patients with advanced gastric or gastroesophageal junction (GEJ) cancer whose disease progressed after first-line therapy were previously offered irinotecan or paclitaxel based therapy. Ramucirumab with paclitaxel is now approved as the standard second-line treatment and can be accessed through the BCCA Compassionate Access Program (CAP). In the phase 3 RAINBOW trial involving 665 patients, ramucirumab with paclitaxel demonstrated superior median overall survival (9.6 mo vs. 7.4 mo [HR 0.81, 95% CI 0.68-0.96]) and median progression-free survival (4.4 mo vs. 2.9 mo [HR 0.64, 95% CI 0.54-0.75]) when compared to paclitaxel alone. This treatment also resulted in improved quality of life particularly in the nausea and vomiting and emotional function domains, although it was associated with higher rates of grades 3 and 4 neutropenia, hypertension and fatigue. For further information about the toxicities and pharmacology of ramucirumab, please see the Cancer Drug Manual section below.

#### Reference:

Wilke H, et al. Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (RAINBOW): a double-blind, randomised phased 3 trial. *Lancet Oncol* 2014;15:1224-35.

## EDITOR'S CHOICE

### Leukemia:

**Azacitidine with Sorafenib as Salvage Therapy for Transplant Eligible Patients with Acute Myeloid Leukemia (AML) (ULKAMLAS)** – This combination treatment is now approved for patients with AML with FLT3 ITD mutation who are eligible for stem cell transplant (SCT) but have failed to achieve a complete remission (CR) on standard chemotherapy. FLT3 is a receptor tyrosine kinase expressed on most AML blasts and can be targeted by the multikinase inhibitor sorafenib. In a phase II study, the addition of sorafenib to azacitidine was associated with an overall response rate of 46%, including CR with incomplete count recovery in 27% and CR in 16% of patients. Maintenance with sorafenib for one year after SCT further reduces the risk of relapse. The most common severe toxicities are cytopenias. Azacitidine with sorafenib can be accessed through the BCCA Compassionate Access Program (CAP).

#### References:

1. Ravandi F, et al. Phase 2 study of azacitidine plus sorafenib in patients with acute myeloid leukemia and FLT-3 internal tandem duplication mutation. *Blood* 2013;121:4655-62.
2. Chen YB, et al. Phase 1 trial of maintenance sorafenib after allogeneic hematopoietic stem cell transplantation for Fms-like tyrosine kinase 3 internal tandem duplication acute myeloid leukemia. *Biol Blood Marrow Transplant* 2014;20:2042-8.

## REVISED PROGRAMS

### Breast:

**Genomic Testing for Single Lymph Node Microscopic Disease (0.3-2 mm deposit)** – This is now incorporated into the existing eligibility criteria on a permanent basis. Previously, the temporary coverage for this patient population was due to end in 15 April 2017. For more details on the genomic testing in this setting, see the August 2016 issue of the [Systemic Therapy Update](#).

## BENEFIT DRUG LIST

### NEW PROGRAMS

Effective 1 May 2017, the following BCCA treatment programs have been added to the BCCA [Benefit Drug List](#):

Protocol Title	Protocol Code	Benefit Status
Second-Line Therapy for Metastatic or Locally Advanced Gastric or Gastroesophageal Junction Cancer Using Weekly <i>PACLitaxel</i> and <i>Ramucirumab</i>	UGIGAVRAMT	Restricted
Therapy of Acute Myeloid Leukemia Using <i>azaCITIDine</i> and <i>SORafenib</i>	ULKAMLAS	Restricted

### NEW MONOGRAPHS AND PATIENT HANDOUTS

The **Ramucirumab Monograph and Handout** have been developed. Expert review was provided by Dr. Janine Davies (medical oncologist) and Jackie Buston (pharmacist) from the BCCA Gastrointestinal Tumour Group. Ramucirumab, a recombinant human IgG1 monoclonal antibody, is a vascular endothelial growth factor receptor (VEGFR)-2 antagonist that inhibits activation of the VEGF2 receptor and its downstream signalling pathways. The VEGF pathway mediates tumour angiogenesis and regulates tumour growth and metastatic spread. Due to its mechanism of action, ramucirumab has the potential for activity in many malignancies. Currently in Canada, ramucirumab is being used for the treatment of advanced or metastatic gastric cancer or gastroesophageal junction adenocarcinoma. Class effects of VEGF inhibitors include hypertension, proteinuria, bleeding, and impaired wound healing. The most common adverse reactions experienced with ramucirumab are diarrhea and hypertension. Serious side effects of ramucirumab include GI perforation and arterial thromboembolic events. Ramucirumab 8 mg/kg is given over 1 hour every two weeks as a single agent or in combination with paclitaxel (BCCA Protocol UGIGAVRAMT). Diphenhydramine premedication is recommended prior to each ramucirumab dose to prevent infusion related reactions. Blood pressure and proteinuria are monitored prior to each treatment; treatment delay and dose reduction may be required if elevated.

**Atezolizumab Interim Monograph** has been developed. Atezolizumab is a humanized IgG1 monoclonal antibody immune checkpoint inhibitor that binds to programmed death-ligand 1 (PD-L1) and blocks the interaction with PD-1 and B7-1 receptors on T-lymphocytes. Blocking these receptors restores anti-tumor T-cell activity. Recommended dose is a fixed dose of 1200mg administered IV once every three weeks. Like other immune checkpoint inhibitors, atezolizumab is associated with immune-mediated adverse events such as endocrinopathies, diarrhea/colitis, hepatitis, nephritis, pneumonitis and rash. Immune mediated reactions should be managed according to their severity; treatment interruption and/or corticosteroids may be indicated. Other highlights from this document:

- Mild to moderate infusion-related reactions may require temporary interruption of the infusion or reduced infusion rates. Atezolizumab should be permanently discontinued for grade 3-4 infusion reactions.
- Severe infections including sepsis, herpes encephalitis, pneumonia, and mycobacterial infection leading to retroperitoneal hemorrhage have been reported.

Atezolizumab has now been added to the **Chemotherapy Preparation and Stability Chart** and has been evaluated for the **Hazardous Drug List**.

### REVISED MONOGRAPHS AND PATIENT HANDOUTS

Highlights of key changes and/or updates to the Monographs and Patient Handouts are listed below:

#### **Nivolumab Monograph:**

- *Dosing:* addition of flat rate dosing

#### **Pembrolizumab Monograph and Handout:**

- *Side Effect table:* addition of Stevens-Johnson syndrome and toxic epidermal necrolysis
- *Handout:* addition of blisters to See Your Doctor section

## 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 treatment 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
UGIGAVRAMT	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Second-Line Therapy for Metastatic or Locally Advanced Gastric or Gastroesophageal Junction Cancer Using Weekly PACLitaxel and Ramucirumab
GUPDOCADT	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	First-Line Treatment of Castration Sensitive, Metastatic Prostate Cancer Using Docetaxel and Androgen Deprivation Therapy
ULKAMLAS	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Therapy of Acute Myeloid Leukemia Using azaCITIDine and SORafenib

### REVISED PROTOCOLS, PPPOs AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
BRAVEVEX	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Stomatitis prophylaxis added, references updated</i>	Therapy for Advanced Breast Cancer Using Everolimus and Exemestane
CNBEV	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Bevacizumab first dose infusion time clarified</i>	Palliative Therapy for Recurrent Malignant Gliomas Using Bevacizumab With or Without Concurrent Etoposide or Lomustine
CNTEM60	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Exclusions clarified</i>	Therapy for Newly Diagnosed Malignant Brain Tumours with MGMT Methylation in Elderly Patients using Temozolomide
GOENDAI	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Precautions clarified</i>	Advanced Therapy for Endometrial Cancer using an Aromatase Inhibitor
GOOVDDCAT	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<i>Total number of cycles clarified</i>	Treatment of Advanced Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Carcinoma Using CARBOplatin and Weekly PACLitaxel
GOOVDOC	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Tests clarified</i>	Treatment of Relapsed/Progressing Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Carcinoma Using DOCetaxel
GUAJPG	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Contact physician updated</i>	Adjuvant Therapy for Urothelial Carcinoma Using CISplatin and Gemcitabine
GUAVPG	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Contact physician updated</i>	Palliative Therapy for Urothelial Carcinoma Using CISplatin and Gemcitabine

**REVISED PROTOCOLS, PPPOs AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)**

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
GUEDPM	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Cisplatin administration guideline updated, filter size specified</i>	Treatment of Metastatic Adrenocortical Cancer with Etoposide, DOXOrubicin, CISplatin and Mitotane
GUEP	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Contact physician updated, filter size specified</i>	Etoposide-CISplatin Protocol for Germ Cell Cancers
GUEVER	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Stomatitis prophylaxis added to Precautions</i>	Therapy for Advanced Renal Cancer Using Everolimus
GUMVAC	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Contact physician updated</i>	Therapy for Transitional Cell Cancers of the Urothelium using Methotrexate, vinBLASStine, DOXOrubicin and CISplatin
GUPMX	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Contact physician updated, TALLman lettering formatted</i>	Palliative Therapy for Hormone Refractory Prostate Cancer Using mitoXANTRONE and predniSONE
GUSCARB	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Contact physician updated</i>	Adjuvant Therapy for Stage I High Risk Seminoma Using CARBOplatin
GUSCPE	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Prehydration added, filter size specified</i>	Palliative Therapy of Extensive Stage Genitourinary Small Cell Tumours with a Platinum and Etoposide
GUSCPERT	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Contact physician updated, filter size specified</i>	Therapy of Genitourinary Small Cell Tumors with a Platin and Etoposide with Radiation
UGUTAXGEM	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Contact physician updated</i>	Palliative Therapy for Germ Cell Cancers Using PACLitaxel and Gemcitabine
GUVEIP	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Contact physician updated</i>	BCCA Protocol Summary for Consolidation and Salvage Treatment for Germ Cell Cancer Using vinBLASStine, CISplatin, Ifosfamide and Mesna
GUVIP2	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Contact physician updated, filter size specified, protocol title clarified</i>	Consolidation and Salvage Therapy for Nonseminoma Using Etoposide, CISplatin, Ifosfamide, Mesna
HLHETCSPA	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Filter size specified, lab tests clarified</i>	Treatment of Hemophagocytic Lymphohistiocytosis with Etoposide, Dexamethasone and cycloSPORINE
HNOTTSH	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Eligibility updated</i>	Radioiodine Imaging and Treatment in Patients with Thyroid Cancer Using Thyrotropin Alpha
LYCDA	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Administration days and route clarified, precautions updated</i>	Treatment of Hairy Cell Leukemia with Cladribine

**REVISED PROTOCOLS, PPPOs AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)**

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
LYCHOPRMTX	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated, filter size specified</i>	Central Nervous System Prophylaxis with High Dose Methotrexate, CHOP and riTUXimab in Diffuse Large B-cell Lymphoma
LYCODOXMR	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Body weight for dosing clarified</i>	Treatment of Burkitt Lymphoma and Leukemia with Cyclophosphamide, vinCRiStine, DOXOrubicin, Methotrexate, Leucovorin and riTUXimab
LYGDP	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Dexamethasone dosing clarified</i>	Treatment of Lymphoma with Gemcitabine, Dexamethasone and CiSPlatin
LYGDP R	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Dexamethasone dosing clarified</i>	Treatment of Lymphoma with Gemcitabine, Dexamethasone and CiSPlatin with riTUXimab
LYHDMRP	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated</i>	Treatment of Primary Intracerebral Lymphoma with High Dose Methotrexate and riTUXimab
LYHDMTXP	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated</i>	Primary Intracerebral Lymphoma with High Dose Methotrexate
LYHDMTXR	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated</i>	Treatment of Leptomeningeal Lymphoma or Recurrent Intracerebral Lymphoma with High Dose Methotrexate
LYIVACR	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Body weight for dosing clarified, filter size specified</i>	Treatment of Burkitt Lymphoma and Leukemia with Ifosfamide, Mesna, Etoposide, Cytarabine and riTUXimab
UMYLDREL	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<i>Replacing UMYLENDEX</i>	Therapy of Relapsed Multiple Myeloma Using Lenalidomide with Dexamethasone
UMYLENDEX	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<i>Protocol code and title changed (replaced by UMYLDREL)</i>	Therapy of Multiple Myeloma Using Lenalidomide with Dexamethasone
UMYLENMTN	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Treatment section clarified</i>	Maintenance Therapy of Multiple Myeloma Using Lenalidomide
SAHDMTX	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Methotrexate serum level and contact physician updated</i>	Treatment of Osteosarcoma Using High Dose Methotrexate with Leucovorin Rescue
USMAVDT	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Tests clarified</i>	Treatment of BRAF V600 Mutation-Positive Unresectable or Metastatic Melanoma Using daBRAFeNIB and TrameTINIB
SMAVTMZ	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Dose modifications for hepatic dysfunction updated</i>	Palliative Therapy for Malignant Melanoma with Brain Metastases Using Temozolomide
SMCCNU	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Contact physician updated</i>	Palliative Therapy for Metastatic Melanoma Using Lomustine

**REVISED PROTOCOLS, PPPOs AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)**

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
SMTAM	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Contact physician updated	Palliative Therapy for Malignant Melanoma Using Tamoxifen

**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, 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
CON Pharmacy Educators	www.bccancer.bc.ca/health-professionals/professional-resources/pharmacy

CONTACT INFORMATION	PHONE	FAX	EMAIL
Systemic Therapy Update Editor			bulletin@bccancer.bc.ca
Provincial Systemic Therapy Program	604-877-6000 x 672247		mclin@bccancer.bc.ca
To update contact information of any CON sites, please contact:			
Oncology Drug Information	604-877-6275		druginfo@bccancer.bc.ca
Education Resource Nurse	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		mclin@bccancer.bc.ca
Nursing Professional Practice	604-877-6000 x 672623		ilundie@bccancer.bc.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 Chemotherapy Certification	250-712-3900 x 686741		rxchemocert@bccancer.bc.ca
BCCA-Abbotsford Centre	604-851-4710 Toll Free 877-547-3777		
BCCA-Centre for the North	250-645-7300 Toll Free 888-775-7300		
BCCA-Fraser Valley Centre	604-930-2098 Toll Free 800-523-2885		
BCCA-Sindi Ahluwalia Hawkins Centre for the Southern Interior	250-712-3900 Toll Free 888-563-7773		
BCCA-Vancouver Centre	604-877-6000 Toll Free 800-663-3333		
BCCA-Vancouver Island Centre	250-519-5500 Toll Free 800-670-3322		

**EDITORIAL REVIEW BOARD**

Mario de Lemos, PharmD, MSc (Oncol) (Acting Editor)  
 Caroline Lohrisch, MD  
 Robert Crisp, BScPT, MBA

Lorraine Leitz, MLS  
 Ava Hatcher, RN, BN CONc  
 Rob Watt, BSc(Pharm)