Provincial Health Services Authority

Systemic Therapy Update

Volume 26 Issue 7
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For Health Professionals Who Care for Cancer Patients

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Editor's Choice

New Programs

Effective 01 July 2023, the BC Cancer Provincial Systemic Therapy Program has approved the following new treatment programs. The full details of these programs can be found on the BC Cancer website in the Chemotherapy Protocols section.

Breast

Sacituzumab Govitecan Therapy for Metastatic Triple Negative Breast Cancer (BRAVSG) — The BC Cancer Breast Tumour Group is introducing sacituzumab govitecan treatment for patients with recurrent inoperable or metastatic triple-negative breast cancer (TNBC). In the ASCENT phase III trial compared to single-agent chemotherapy (eribulin, vinorelbine, capecitabine, or gemcitabine), sacituzumab govitecan was associated with increased overall survival (12.1 vs. 6.7 mos, hazard ratio [HR] 0.48), progression-free

survival (5.6 vs. 1.7 mos, HR 0.41) and objective response (35% vs. 5%). Sacituzumab govitecan is an antibody-drug conjugate with the cytotoxic agent, SN-38, which is the active metabolite of irinotecan. The most significant toxicities include neutropenia/febrile neutropenia, infusion-related reactions, and diarrhea.[1] Cholinergic symptoms may occur during or shortly after infusion of sacituzumab govitecan, which should be treated with atropine. Patients should also be advised to obtain an adequate supply of loperamide with directions for the management of diarrhea. See BRAVSG protocol for more details.

Gynecological

Pembrolizumab for Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Endometrial Cancer (UGOENDAVP, UGOENDAVP6) — The BC Cancer Gynecological Tumour Group is introducing pembrolizumab therapy for patients with unresectable or metastatic MSI-H or dMMR endometrial cancer progressing after prior therapy and with no alternative treatment options. In the KEYNOTE-158 phase II trial after a median follow-up of 24.2 months, pembrolizumab was associated with median overall survival of 65.4 months and progression free survival of 13.1 months, with an objective response rate of 50%.[2,3] Pembrolizumab was associated with manageable toxicities consistent with known safety profile.

Lung

Treatment of Small Cell Lung Cancer (SCLC) using Platinum and Oral Etoposide for Extensive Stage Disease (LUSCPEPO) and with Radiation Therapy for Limited Stage (LUSCPEPORT) Disease — The BC Cancer Lung Tumour Group is introducing oral etoposide in combination with platinum chemotherapy for treatment of limited and extensive stage SCLC. These platinum combination treatment regimens have traditionally used intravenous etoposide to align with the clinical trials data. Although clinical studies comparing oral and intravenous etoposide kinetics have suggested similar patient outcomes with respect to overall survival and patient's preference for oral vs intravenous chemotherapy treatment,[4-8] the intravenous formulation of etoposide should remain the preferred treatment option for the majority of patients as oral etoposide bioavailability is variable.

Myeloma

Isatuximab for Multiple Myeloma in Combination with Carfilzomib and Dexamethasone (UMYISACARD) or with Pomalidomide and Dexamethasone (UMYISAPOMD) — The BC Cancer Myeloma Tumour Group is introducing the addition of isatuximab to carfilzomib with dexamethasone, and to pomalidomide with dexamethasone, for patients with relapsed multiple myeloma. In the IKEMA phase III trial, addition of isatuximab to carfilzomib with dexamethasone was associated with increased progression free survival (not reached vs. 19.15 mos, HR 0.531). Similarly, the addition of isatuximab to pomalidomide with dexamethasone was associated with increased progression free survival (11·5 vs 6·5 mos, HR 0·596). Isatuximab is associated with infusion-related reactions, neutropenia, febrile neutropenia, hypertension, pneumonia, and diarrhea. See Cancer Drug Manual monograph for more details on toxicities.

Editor's Choice

New Programs

Sarcoma

Regorafenib for Relapsed or Refractory Advanced Osteosarcoma (SAAVOR) – The BC Cancer Sarcoma Tumour Group is introducing regorafenib for patients with recurrent or metastatic osteosarcoma which has progressed after cytotoxic chemotherapy. In the randomized placebo-controlled phase II trial (REGOBONE), regorafenib was associated with increased overall survival (11.3 vs. 5.9 mos) and progression free survival (3.7 vs. 0.9 mos, HR 0.531). Regorafenib was associated with manageable toxicities consistent with known safety profile.[11]

Skin

Cetuximab for Locally Advanced or Metastatic Cutaneous Squamous Cell Carcinoma (SMAVCET) — The BC Cancer Skin Tumour Group is introducing cetuximab for patients with unresectable squamous cell carcinoma who are unable to receive first line cemiplimab or have progressed on cemiplimab and are still well enough to receive a second line systemic therapy. In three single-arm studies, anti-EGFR monoclonal antibody therapy was associated with an overall response rate (complete plus partial response) of about 28%, with a clinical benefit rate (response rate plus stable disease) of 69%. Cetuximab was associated with manageable toxicities consistent with known safety profile.[12-14]

References

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13. Reigneau M, Robert C, Routier E, et al. Efficacy of neoadjuvant cetuximab alone or with platinum salt for the treatment of unresectable advanced nonmetastatic cutaneous squamous cell carcinomas. Br J Dermatol 2015;173(2):527-34.
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Drug Update

Acalabrutinib Tablet Availability

Acalabrutinib is originally marketed as a capsule formulation. The tablet formulation is now available and the manufacturer will gradually phase out the capsule product. The tablet will be added to the Benefit List on 1 July 2023, and both tablet and capsule will be reimbursed during this transition period. Because of the high drug cost, the capsule should continue to be dispensed whenever possible until the inventory is exhausted. Once the capsule form is exhausted, the tablet form would be routinely dispensed for all acalabrutinib prescriptions.

Acalabrutinib capsule and tablet are bioequivalent, except the tablet is formulated with the maleate salt which allows complete drug dissolution of the tablet form regardless of gastrointestinal pH. Therefore, patients taking the tablet form do not need to avoid concurrent acid-reducing agents, and a separate patient information handout for acalabrutinib tablet will be available.

Molecular Testing Update

The Cancer Genetics and Genomics Lab (CGL) has recently expanded the following molecular testing:

Stage agnostic next generation sequencing (NGS) testing of non-small cell lung carcinoma (NSCLC)

- The CGL has expanded NGS testing from Stage IIIB to IV to include early stage NSCLC specimens of Stage IB to IIIA starting April 2023. All samples are eligible for "Illumina Focus amplicon NGS panel" testing which identifies targetable mutations such as *EGFR*, *KRAS*, *NRAS*, *ERBB2* and fusions including *ALK1*, *RET*, *ROS*, *METx14*, *NTRK1/2/3*.

***DPYD* screening**

- The CGL has expanded *DPYD* testing to the entire province for patients whose treatment plan includes fluorouracil or capecitabine starting March 2023.

Additional information on these tests are accessible at this link and the CGL will continue to update this page to inform on new assays or test indications.
http://cancergeneticslab.ca/updates/

Cancer Drug Manual©

All documents are available in the Cancer Drug Manual© on the BC Cancer website.

New Documents

Note that the following drug is not a BC Cancer Benefit Drug and requires application to the BC Cancer Compassionate Access Program (CAP). The corresponding Interim Monograph and Patient Handout are made available for reference only.

The **Selpercatinib Interim Monograph** and **Patient Handout** have been developed with expert review provided by Dr. Nicole Chau (medical oncologist, BC Cancer Head & Neck Tumour Group) and Megan Darbyshire (tumour group pharmacist, BC Cancer Provincial Pharmacy). Selpercatinib is a RET (REarranged during Transfection) tyrosine kinase inhibitor. It is used in the treatment of RET fusion-positive non-small cell lung cancer (NSCLC) and thyroid cancer. The usual dose is 120 or 160 mg orally twice daily.

Highlights from these documents include:

- pre-existing hypertension should be adequately controlled prior to starting treatment
- patients with severe hepatic impairment may require a reduced starting dose
- consider dose adjustment if concurrently used with a strong or moderate CYP 3A4 inhibitor
- increased gastric pH can decrease the absorption of selpercatinib; to prevent drug interactions between selpercatinib and drugs which reduce stomach acid, spacing the administration of antacids and H_2 antagonists is recommended

Selpercatinib has been added to the **Auxiliary Label List** and was previously evaluated for the **BC Health Authorities Provincial Hazardous Drug List.**

The **Sacituzumab govitecan Interim Monograph** has been expanded into a full **Monograph** and a **Patient Handout** has been developed. Expert review was provided by Dr. Nathalie Levasseur (medical oncologist, BC Cancer Breast Tumour Group) and Megan Darbyshire (tumour group pharmacist, BC Cancer Provincial Pharmacy). All monograph sections have been reviewed and updated. The following sections have been added or expanded: *Pharmacokinetics, Special Precautions, Side Effects, Interactions, and Dosage Guidelines.* Sacituzumab govitecan is an antibody drug conjugate (ADC) that targets Trop-2 expressed on the surface of cells. It is comprised of a monoclonal antibody component linked to SN-38 (topoisomerase I inhibitor) by a hydrolysable linker. Sacituzumab govitecan is used in the treatment of breast cancer. Usual dosing is 10 mg/kg IV given on days 1 and 8 of a 21 day cycle.

Highlights from these documents include:

- complications from severe diarrhea have been reported; prompt initiation of loperamide is recommended
- grade 3 or 4 neutropenia occurs frequently; filgrastim may be needed for secondary prophylaxis
- patients who are homozygous for UGT1A1*28 allele may be at increased risk of febrile neutropenia, neutropenia and anemia

Cancer Drug Manual©

The **Acalabrutinib Patient Handout (tablets)** has been created. There are now two formulations for acalabrutinib (acalabrutinib capsule and acalabrutinib maleate tablet). The tablet and capsule have bioequivalent pharmacokinetics, except when the capsule is administered with acid-reducing agents. **The tablet formulation has now** been added to the **Auxiliary Label List**.

Revised Documents

Acalabrutinib Monograph

Synonyms: added acalabrutinib maleate (salt for new tablet formulation)
Pharmacokinetics: updated oral absorption to include bioavailability of tablet formulation
Cautions: added statement about bioequivalency of tablet and capsule
Interactions table: updated interactions for acid-reducing agents to reflect differences between tablet and capsule formulation (no interaction for tablets)
Supply and Storage: added new tablet formulation

Acalabrutinib Patient Handout (capsules)

Header/Footer: added capsules to heading to differentiate from tablet formulation
Throughout: updated as per current template wording

Isatuximab Monograph

Caution: updated to include information about prophylaxis for herpes zoster reactivation
Caution (Breastfeeding): updated to include details about infant exposure
Side Effects (preamble): updated disclaimer
Side Effects table: added new side effects and updated incidence throughout
Parenteral Administration table: updated in-line filter information and added BC Cancer protocol UMYISACARD and UMYISACPOMD
Dosage Guidelines: bolded and italicized BC Cancer standard dosing and added BC Cancer protocol UMYISACARD and UMYISACPOMD

Isatuximab Patient Handout

Throughout: updated per current template wording

Sacituzumab govitecan Chemotherapy Preparation and Stability Chart

Product column: updated suggested bag volume range; deleted instruction to remove solution equal to bag volume prior to adding drug volume
Product stability column: updated with extended stability information

Benefit Drug List

New Programs

Effective 01 July 2023, the following new treatment programs have been added to the BC Cancer Benefit Drug List:

Protocol Title	Protocol Code	Benefit Status
Palliative Therapy for Metastatic Triple Negative Breast Cancer using **Sacituzumab Govitecan**	**BRAVSG**	Class I
Treatment of Microsatellite Instability-High or Mismatch Repair Deficient Endometrial Cancer using **Pembrolizumab**	**UGOENDAVP**	Restricted
Treatment of Microsatellite Instability-High or Mismatch Repair Deficient Endometrial Cancer using 6-Weekly **Pembrolizumab**	**UGOENDAVP6**	Restricted
Treatment of Extensive Stage Small Cell Lung Cancer with **Platinum** and **Oral Etoposide**	**LUSCPEPO**	Class I
Treatment of Limited Stage Small Cell Lung Cancer using **Platinum** and **Oral Etoposide** with Radiation Therapy	**LUSCPEPORT**	Class I
Therapy of Multiple Myeloma using **Carfilzomib** and **Dexamethasone** with **Isatuximab**	**UMYISACARD**	Restricted
Therapy of Multiple Myeloma using **Pomalidomide** and **Dexamethasone** with **Isatuximab**	**UMYISAPOMD**	Restricted
Treatment of Pediatric Patients with De Novo Acute Promyelocytic Leukemia using **Arsenic Trioxide** In Combination with **Tretinoin** and with or without **Idarubicin** and **Dexamethasone** on the COG AAML1331 Study	**Pediatric**	Class I
Treatment of Relapsed or Refractory Advanced Osteosarcoma using **Regorafenib**	**SAAVOR**	Class I
Treatment of Locally Advanced or Metastatic Cutaneous Squamous Cell Carcinoma using **Cetuximab**	**SMAVCET**	Class I

Highlights of New & Revised Protocols, PPPOs 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, with document revisions indicated in the respective columns. Protocol codes for treatment requiring BC Cancer Compassionate Access Program approval are prefixed with the letter **U**.

NEW Protocols, PPPOs and Patient Handouts *(new documents checked ☑)*

Code	Protocol Title	Protocol	PPPO	Handout
BRAVSG	Palliative Therapy For Metastatic Triple Negative Breast Cancer using Sacituzumab Govitecan	☑	☑	☐
UGOENDAVP	Treatment of Microsatellite Instability-High or Mismatch Repair Deficient Endometrial Cancer using Pembrolizumab	☑	☑	☐
UGOENDAVP6	Treatment of Microsatellite Instability-High or Mismatch Repair Deficient Endometrial Cancer using 6-Weekly Pembrolizumab	☑	☑	☐
UMYISAPOMD	Therapy of Multiple Myeloma using Pomalidomide and Dexamethasone with Isatuximab	☑	☑	☐
UMYISACARD	Therapy of Multiple Myeloma using Carfilzomib and Dexamethasone with Isatuximab	☑	☑	☐
LUSCPEPO	Treatment of Extensive Stage Small Cell Lung Cancer (SCLC) with Platinum and Oral Etoposide	☑	☑	☑
LUSCPEPORT	Treatment of Limited Stage Small Cell Lung Cancer using Platinum and Oral Etoposide with Radiation Therapy	☑	☑	☑
SAAVOR	Treatment of Relapsed or Refractory Advanced Osteosarcoma using **Regorafenib**	☑	☑	☐
SMAVCET	Treatment of Locally Advanced or Metastatic Cutaneous Squamous Cell Carcinoma using **Cetuximab**	☑	☑	☑

REVISED Protocols, PPPOs and Patient Handouts *(revisions in respective columns)*				
Code	**Protocol Title**	**Protocol**	**PPPO**	**Handout**
BR | Breast				
BRAVPALAI	Therapy of Advanced Breast Cancer using Palbociclib and Aromatase Inhibitor With or Without LHRH Agonist	*eligibility updated, exclusions clarified, tests updated, treatment and dose modifications clarified*	*prechemo metrics and tests updated, treatment clarified*	--
BRAVPBFLV	Therapy of Advanced Breast Cancer using Palbociclib and Fulvestrant With or Without LHRH Agonist	*eligibility and exclusions clarified, tests updated, treatment and dose modifications clarified*	*prechemo metrics and tests updated, treatment clarified*	--
BRAVRBFLV	Therapy of Advanced Breast Cancer using Ribociclib and Fulvestrant With or Without LHRH Agonist	*eligibility and exclusions clarified, tests updated, treatment clarified, dose modifications updated*	*prechemo metrics and tests updated, treatment clarified*	--
BRAVRIBAI	Therapy of Advanced Breast Cancer using Ribociclib and Aromatase Inhibitor With or Without LHRH Agonist	*title formatted, eligibility and exclusions clarified, tests updated, treatment and dose modifications clarified*	*prechemo metrics and tests updated, treatment clarified*	--
GI | Gastrointestinal				
GIFIRINOX	Palliative Combination Chemotherapy for Advanced Pancreatic Adenocarcinoma Using Irinotecan, Oxaliplatin, Fluorouracil and Leucovorin	--	*format changed*	--
GO | Gynecological				
GOOVCAG	Treatment of Advanced Ovarian Cancer in Patients Who Have Progressed or Recurred Following First-line Platinum-based Treatment Using CARBOplatin and Gemcitabine	*eligibility clarified, exclusions revised, tests and dose modifications clarified*	--	--
GOOVTAM	Therapy for Advanced Ovarian Cancer using Tamoxifen	*eligibility and exclusions updated, tests clarified, treatment formatted, reference added*	--	--
LK | Leukemia				

REVISED Protocols, PPPOs and Patient Handouts *(revisions in respective columns)*

Code	Protocol Title	Protocol	PPPO	Handout
ULKAMLAVEN	Therapy of Acute Myeloid Leukemia using azaCITIDine and Venetoclax	*tests updated, dose modifications revised, hepatitis B prophylaxis and precautions updated*	*tests updated*	--
MY | Myeloma				
UMYPOMDEX	Therapy of Multiple Myeloma Using Pomalidomide with Dexamethasone	*tumour group, contacts, and tests updated*	--	--
SM | Skin & Melanoma				
SMAVCEM	Treatment of Locally Advanced or Metastatic Cutaneous Squamous Cell Carcinoma using Cemiplimab	*exclusions updated*	--	--

Resources and Contact Information

Resource	Phone	Email / Toll Free / Fax
Systemic Therapy Update: www.bccancer.bc.ca/health-professionals/clinical-resources/systemic-therapy/systemic-therapy-update		
Systemic Therapy Update Editor	604-877-6000 x 672649	bulletin@bccancer.bc.ca
Oncology Drug Information Cancer Drug Manual Editor Pharmacy Oncology Certification Nurse Educators	604-877-6275 250-519-5500 x 693742 250-712-3900 x 686820 604-877-6000 x 672638	druginfo@bccancer.bc.ca nbadry@bccancer.bc.ca rxchemocert@bccancer.bc.ca nursinged@bccancer.bc.ca
CAP – Compassionate Access Program	604-877-6277	cap_bcca@bccancer.bc.ca fax 604-708-2026
OSCAR – Online System for Cancer Drugs Adjudication and Reimbursement	888-355-0355	oscar@bccancer.bc.ca fax 604-708-2051
Library/Cancer Information	604-675-8003	toll free 888-675-8001 x 8003 requests@bccancer.bc.ca
Library Document Delivery	604-675-8002	requests@bccancer.bc.ca
Pharmacy Professional Practice Professional Practice, Nursing Provincial Systemic Therapy Program	604-877-6000 x 672247 604-877-6000 x 672623 604-877-6000 x 672247	mlin@bccancer.bc.ca BCCancerPPNAdmin@ehcnet.phsa.ca mlin@bccancer.bc.ca
BC Cancer – Abbotsford BC Cancer – Kelowna BC Cancer – Prince George BC Cancer – Surrey BC Cancer – Vancouver BC Cancer – Victoria	604-851-4710 250-712-3900 250-645-7300 604-930-2098 604-877-6000 250-519-5500	toll free 877-547-3777 toll free 888-563-7773 toll free 855-775-7300 toll free 800-523-2885 toll free 800-663-3333 toll free 800-670-3322
Community Oncology Network (CON) sites: To update your contact information, please contact: bulletin@bccancer.bc.ca		

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