Provincial Health Services Authority

Systemic Therapy Update

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For Health Professionals Who Care for Cancer Patients

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Editor's Choice

New Programs

Effective 01 September 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

Olaparib for BRCA-mutated, High-Risk Early Breast Cancer (UBRAJOLA) – The BC Cancer Breast Tumour Group is introducing adjuvant olaparib therapy for patients with **germline *BRCA*-mutated** (*see below for testing information*), HER2-negative, high-risk early breast cancer after neoadjuvant or adjuvant chemotherapy. In the phase III OlympiA study comparing to placebo, adjuvant olaparib was shown to improve the invasive disease-free survival (hazard ratio [HR] 0.63), distant disease-free survival (HR 0.61), and overall survival (HR 0.68). Olaparib was associated with manageable toxicities consistent with known safety profile.[3]

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Additional **germline *BRCA* testing** is approved for patients who require its confirmation to be eligible for adjuvant olaparib. Samples will be processed at the Cancer Genetics and Genomics Laboratory and tested at an external US site.

The **Hereditary Cancer Multi-Gene Panel Requisition** (accessed via www.bccancer.bc.ca/lab-services-site) must be used to request germline *BRCA* testing.

- The turnaround time (TAT) for result is 5 to 6 weeks
- For urgent cases, this must be indicated on the requisition
- **ALL** applicable indications for testing must be selected on the requisition, ***in addition to*** the indication **"Eligible for Olaparib"**
- Samples will routinely be sent to the US for testing. If the patient does not want their DNA sent to the US, this must be indicated in the text box on the requisition

Head and Neck

The BC Cancer Head and Neck Tumour Group is introducing **selpercatinib** for the treatment of advanced differentiated thyroid cancer and medullary thyroid cancer.

Selpercatinib for *RET* Fusion-Positive Differentiated Thyroid Cancer (HNOTDSEL) – Funding is for adult patients who are not amenable to surgery or radioactive iodine therapy, and after prior treatment with sorafenib and/or lenvatinib. In the phase I/II LIBRETTO-001 study, selpercatinib was associated with objective response rate of 77.3% and median duration of response of 18.43 months.[6] See under non-small cell lung cancer above for adverse events.

Selpercatinib for *RET*-Mutant Medullary Thyroid Cancer (HNOTMSEL) – Funding is for adult and pediatric patients older than 12 who have progressed on, or have intolerance or contraindication to vandetanib. In the phase I/II LIBRETTO-001 study, selpercatinib was associated with objective response rate of 81.0% and median duration of response was not evaluable after a median follow-up of 20.3 months.[6]. The most common adverse events included increase in ALT increase (23.8%), AST increase (21.4%), hypertension (42.9%), electrocardiogram QT prolongation (9.5%), dry mouth (>20%), and diarrhea (38.1%).[6] See under non-small cell lung cancer above for adverse events.

Focus panel testing to establish ***RET* fusion** status is available for all eligible patients through the Cancer Genetics and Genomics Lab, using the Cancer Genetics Solid Tumour Request Form - Molecular (accessed via www.bccancer.bc.ca/lab-services-site)

Lung

Atezolizumab for Adjuvant Treatment of Resected Non-Small Cell Lung Cancer (ULUAJATZ) – The BC Cancer Lung Tumour Group is introducing atezolizumab as adjuvant treatment of stage II to IIIA non-small cell lung cancer with PD-L1 ≥50% following complete resection and platinum based-chemotherapy. Patient must not have *EGFR* or *ALK* mutations and must start within 12 weeks of completing platinum-based chemotherapy. In the phase III IMpower010 study comparing to best supportive care (observation and regular scans), adjuvant atezolizumab was associated with improved disease-free survival (not reached vs. 35.3 mos, hazard ratio 0.47). Atezolizumab was associated with manageable toxicities consistent with known safety profile.[8]

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Selpercatinib for RET Fusion-Positive Advanced Non-Small Cell Lung Cancer (LUAVSEL) – The BC Cancer Lung Tumour Group is introducing selpercatinib for the treatment of patients with metastatic *RET* fusion-positive non–small cell lung cancer. In the phase I/II LIBRETTO-001 study, selpercatinib was associated with high objective response rates (ORR) and prolonged median duration of response (DOR) in both patients with prior treatments (ORR 61.1%, DOR 28.6 mos) or untreated patients (ORR 84.1%, DOR 20.2 mos). Most patients experienced either improvement in quality of life or their quality of life remained stable.[4] Adverse events from overall safety analysis include ALT increase (49.5%), AST increase (55%), hypertension (37.4%), drug hypersensitivity (5.2%) electrocardiogram QT prolongation (18.1%), dry mouth (26%), and diarrhea (40.4%).[5]

See under Head and Neck above on testing to establish ***RET* fusion** status.

Tumour Agnostic

Tumour Agnostic, also known as tissue-agnostic, is a new site for genomically-informed treatment regardless of anatomical or histological origin. The specific molecular alterations of the gene or protein are likely to predict response to a therapy and are found across a variety of cancers.

Two new treatments are available for **advanced solid tumours with *NTRK* gene fusion** in patients who have failed all standard treatments for their current tumour site. There are differences in their funded indications:

Therapy	Patient population	Types of solid tumours
Entrectinib	Adults only	Excluding primary brain tumours
Larotrectinib	Adults and children	Including primary brain tumours

Entrectinib (UTAAVENT) – In a pooled analysis of data from 3 open-label, single-arm studies, entrectinib was associated with an objective response rate of 61.2%. Grade 3 or 4 adverse events occurred in 69.4% of patients. Treatment interruptions or dosage modifications occurred in 54.4% and 26.9% of patients, respectively, with 14.5%.of permanent discontinuation.[1]

Larotrectinib (UTAAVLAR) – In a pooled analysis of data from 3 open-label, single-arm studies, larotrectinib was associated with an objective response rate of 73%. Grade 3 or 4 adverse events occurred in 15% or less of patients. Treatment interruptions or dosage modifications occurred in about 20% of the patients, with 5-8% of permanent discontinuation.[2]

***NTRK* testing** is already included on the Focus Panel (accessed via www.bccancer.bc.ca/lab-services-site), for patients who meet eligibility for this testing (i.e., patients with lung cancer, glioma, or melanoma).

Focus Panel testing eligibility is expanding to include **thyroid cancer** and **mammary analogue secretory carcinoma (MASC)** and for **pediatric patients with solid tumours** who meet eligibility for **Larotrectinib and/or Entrectinib.**

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Other eligible patients can be tested using Bayer's FastTRK Complimentary Testing Program: https://www.fasttrk.ca/en.

The **PREDiCTm clinical trial** remains open to enrollment for *NTRK* testing for patients with pancreatic, biliary tract, sarcoma, squamous head and neck cancer, thyroid and salivary cancer (requisition accessed via http://cancergeneticslab.ca/requisitions/).

References

1. CADTH Reimbursement Recommendation. Entrectinib (Rozlytrek): for the treatment of adults with unresectable locally advanced or metastatic extracranial solid tumours, including brain metastases, that have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion without a known acquired resistance mutation and with no satisfactory treatment options. November 2022.
2. CADTH Reimbursement Recommendation. Larotrectinib (Vitrakvi): solid tumours with NTRK gene fusion. November 2011.
3. CADTH Reimbursement Recommendation. Olaparib (Lynparza): for the adjuvant treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated, human epidermal growth factor receptor 2-negative high risk early breast cancer who have been treated with neoadjuvant or adjuvant chemotherapy. March 2023.
4. CADTH Reimbursement Recommendation. Selpercatinib (Retevmo): as monotherapy for the treatment of metastatic RET fusion-positive non-small cell lung cancer in adult patients. May 2022.
5. CADTH Reimbursement Review. Selpercatinib (Retevmo): RET fusion–positive non-small cell lung cancer. July 2022.
6. CADTH Reimbursement Recommendation. Selpercatinib (Retevmo): adult patients with rearranged during transfection (RET) fusion-positive differentiated thyroid carcinoma with advanced or metastatic disease (not amenable to surgery or radioactive iodine therapy) following prior treatment with sorafenib and/or lenvatinib. July 2022.
7. CADTH Reimbursement Recommendation. Selpercatinib (Retevmo): for the treatment of RET-mutant medullary thyroid cancer in adult and pediatric patients 12 years of age and older with unresectable advanced or metastatic disease. October 2022.
8. Felip E, Altorki N, Zhou C, et al. Adjuvant atezolizumab after adjuvant chemotherapy in resected stage IB-IIIA non-small-cell lung cancer (IMpower010): a randomised, multicentre, open-label, phase 3 trial. Lancet 2021;398(10308):1344-57.

New Supportive Care Protocol – Hepatitis B Virus Reactivation Prophylaxis (SCHBV)

The BC Cancer Provincial Systemic Therapy Program is introducing a new supportive care protocol SCHBV for the prophylaxis of hepatitis B virus reactivation in patients undergoing systemic therapy for lymphoid, plasma cell, and myeloid malignancies.

Lamivudine is currently recommended for the prophylaxis of hepatitis B virus (HBV) reactivation in all BC Cancer Lymphoma and Myeloma treatment protocols. Based on new practice guidelines[1-4] and discussion with PharmaCare with input from BMT/Leukemia, Liver Transplant and Transplant Infectious Disease:

- Entecavir and tenofovir will replace lamivudine when antiviral prophylaxis is indicated.
- Serology monitoring will replace lamivudine if the risks of reactivation is low.
- Different risk categories of HBV reactivation based on serology, immunosuppressive therapy, and underlying immunosuppression

Existing lymphoma and myeloma protocols, pre-printed orders, Cerner PowerPlans and Cancer Drug Manual monographs will be gradually revised to incorporate this change in practice. In the meantime, practice should follow the new supportive protocol SCHBV on antiviral prophylaxis for HBV reactivation, which outline the followings:

- Dosing and duration of antiviral therapy according to risk of HBV reactivation.
- Timing and types of serology tests required is outlined.
- Different risk categories of HBV reactivation based on serology, immunosuppressive therapy, and underlying immunosuppression.

Editor's Choice

New Programs

References

1. Coffin CS, et al. Management of hepatitis B virus infection: 2018 guidelines from the Canadian Association for the Study of the Liver (CASL) and Association of Medical Microbiology and Infectious Disease Canada (AMMI). Can Liver J 2018;1:156-217.
2. European Association for the Study of the Liver. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. J Hepatol 2017;67(2):370-398.
3. Lau G, et al. APASL clinical practice guideline on hepatitis B reactivation related to the use of immunosuppressive therapy. Hepatol Int 2021;15:1031-1048.
4. Hwang JP, et al. Hepatitis B virus screening and management for patients with cancer prior to therapy: ASCO Provisional Clinical Opinion Update. J Clin Oncol 2020;38:(31):3698-3715.

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 Monograph, Patient Handout, and Chemotherapy Preparation and Stability Chart entry is made available for reference only.

The **Tebentafusp Interim Monograph** has been expanded into a full **Monograph** and a **Patient Handout** has been developed. Expert review was provided by Dr. Alison Weppler (medical oncologist, BC Cancer Skin & Melanoma 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.* Tebentafusp is a bispecific T-cell engager that redirects T cells to target and kill glycoprotein 100 (gp100)-expressing melanoma cells. Tebentafusp is used in the treatment of uveal melanoma. Given weekly, the usual dosing begins with a dose escalation regimen of 20 mcg IV on day 1, 30 mcg IV on day 8, and 68 mcg IV on day 15, and then continues with 68 mcg IV weekly thereafter.

Highlights from these documents include:

- cytokine release syndrome (CRS) is commonly reported and typically occurs within the first three infusions
- acute skin reactions are common; presumably due to the recognition of gp100-expressing skin melanocytes by tebentafusp
- Hypo- and hyperpigmentation of the skin are frequently reported; hair and eyelash colour change may occur

Revised Documents

Atezolizumab Monograph and Patient Handout

Uses: deleted bladder cancer as no longer a Health Canada or FDA approved indication
Dosage Guidelines: updated dosing in hepatic impairment

Cancer Drug Manual©

Patient Handout: updated template wording to refer to healthcare team instead of oncologist

Entrectinib Monograph and Patient Handout

Dosage Guidelines: updated references to include BC Cancer protocol UTAAVENT; deleted statement referring user to Appendix for dose modification for myelosuppression

Patient Handout: updated language throughout to align with current template wording, including adding new language about dehydration and peripheral neuropathy

Larotrectinib Monograph and Patient Handout

Supply and Storage: updated information about oral solution per current product information

Dosage Guidelines: bolded and italicized BC Cancer standard dosing and added BC Cancer protocol UTAAVLAR to references; deleted statement referring user to Appendix for dose modification for myelosuppression

Dosage Guidelines (Children): added information about sodium benzoate toxicity

Patient Handout: updated header and footer

Olaparib Monograph and Patient Handout

Dosage Guidelines: updated references to include BC Cancer protocol UTAAVENT

Patient Handout: updated language throughout to align with current template wording, including adding new language about dehydration

Selpercatinib Monograph and Patient Handout

Dosage Guidelines: bolded and italicized BC Cancer dosing and added new protocols (HNOTSEL, HNOTMSEL, ULUAVSEL)

Patient Handout: updated header and footer

Tebentafusp Chemotherapy Preparation and Stability Chart

Product Stability column: included reminder to bring to room temperature before using

Extravasation Hazard Table

Trastuzumab deruxtecan: added as non-vesicant

Continuing Education

Family Practice Oncology Network Continuing Medical Education

The Family Practice Oncology Network (FPON) is pleased to announce a complimentary accredited webinar session on **'Opioid Prescribing for Cancer Pain in Primary Care**' on Thursday, 21 September, from 8 am to 9 am, as part of the Complimentary Accredited Webinar Series. The session will cover:

- Pain assessment approach for patients with cancer pain
- Opioid prescribing principles
- Opioid options, including methadone, and the clinical advantages of each opioid option.

For more information and links to registration, visit the FPON Continuing Medical Education site: https://ubccpd.ca/learn/learning-activities/course?eventtemplate=586-fpon-webinar-opioid-prescribing-for-cancer-pain-in-primary-care

Benefit Drug List

New Programs

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

Protocol Title	Protocol Code	Benefit Status
Treatment of BRCA-Mutated High-Risk Early Breast Cancer using **Olaparib**	**UBRAJOLA**	Restricted
Therapy of Advanced RET Fusion-Positive Differentiated Thyroid Cancer using **Selpercatinib**	**HNOTDSEL**	Class I
Treatment of Advanced RET-Mutant Medullary Thyroid Cancer using **Selpercatinib**	**HNOTMSEL**	Class I
Treatment of Resected Non-Small Cell Lung Cancer using **Atezolizumab**	**ULUAJATZ**	Restricted
Treatment of RET Fusion-Positive Advanced Non-Small Cell Lung Cancer (NSCLC) with **Selpercatinib**	**LUAVSEL**	Class I
Treatment of Tumours with Neurotrophic Tyrosine Receptor Kinase (NTRK) Fusion using **Entrectinib**	**UTAAVENT**	Restricted
Treatment of Solid Tumours with Neurotrophic Tyrosine Receptor Kinase (NTRK) Fusion using **Larotrectinib**	**UTAAVLAR**	Restricted
Treatment of Solid Tumours with Neurotrophic Tyrosine Receptor Kinase (NTRK) Fusion using **Larotrectinib**	**Pediatric**	Restricted

Benefit Drug List

Deleted Programs

Effective 01 September 2023, the following treatment program has been deleted from the BC Cancer Benefit Drug List:

Protocol Title	Protocol Code	Benefit Status
Adjuvant Therapy for High-Risk Breast Cancer using **Cyclophosphamide** (**oral**), **Methotrexate** and **Fluorouracil**	**BRAJCMFPO**	Class I

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, 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
UBRAJOLA	Treatment of BRCA-Mutated High-Risk Early Breast Cancer using Olaparib	☑	☑	--
GUBDDMVAC	Neoadjuvant Treatment of Urothelial Cancer using Dose-Dense Methotrexate, vinBLAStine, DOXOrubicin and CISplatin	--	--	☑
HNOTMSEL	Treatment of Advanced RET-Mutant Medullary Thyroid Cancer using Selpercatinib	☑	☑	--
HNOTDSEL	Therapy of Advanced RET Fusion-Positive Differentiated Thyroid Cancer using Selpercatinib	☑	☑	--
ULUAJATZ	Treatment of Resected Non-Small Cell Lung Cancer using Atezolizumab	☑	☑	--

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

Code	Protocol Title	Protocol	PPPO	Handout
LUAVSEL	Treatment of RET Fusion-Positive Advanced Non-Small Cell Lung Cancer (NSCLC) with Selpercatinib	☑	☑	--
SCHBV	Hepatitis B Virus Reactivation Prophylaxis	☑	--	--
UTAAVENT	Treatment of Solid Tumours with Neurotrophic Tyrosine Receptor Kinase (NTRK) Fusion using Entrectinib	☑	☑	--
UTAAVLAR	Treatment of Solid Tumours with Neurotrophic Tyrosine Receptor Kinase (NTRK) Fusion using Larotrectinib	☑	☑	☑

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

Code	Protocol Title	Protocol	PPPO	Handout
BR | Breast				
BRAJANAS	Neoadjuvant or Adjuvant Therapy for Breast Cancer using Anastrozole in Postmenopausal Women	*eligibility clarified*	--	--
BRAJCAP	Therapy of Adjuvant Breast Cancer using Capecitabine	*eligibility updated, exclusions and tests clarified*	--	--
BRAJEXE	Neoadjuvant or Adjuvant Therapy for Breast Cancer using Exemestane in Postmenopausal Women	*eligibility clarified*	--	--
BRAJLET	Neoadjuvant or Adjuvant Therapy for Breast Cancer using Letrozole in Postmenopausal Women	*eligibility clarified*	--	--
HN | Head and Neck				
HNAVPFPMB	First-Line Treatment of Advanced Squamous Cell Carcinoma of the Head and Neck Using Platinum, Fluorouracil and Pembrolizumab	--	*dose clarified*	--
HNAVPMBM	Maintenance Treatment of Advanced Squamous Cell Carcinoma of the Head and Neck with Pembrolizumab	*eligibility clarified*	--	--

REVISED Protocols, PPPOs and Patient Handouts *(revisions in respective columns)*				
Code	**Protocol Title**	**Protocol**	**PPPO**	**Handout**
HNAVPMBM6	Maintenance Treatment of Advanced Squamous Cell Carcinoma of the Head and Neck using 6-Weekly Pembrolizumab	*eligibility clarified*	--	--
HNOTLEN	Therapy for Locally Recurrent or Metastatic, RAI-refractory Differentiated Thyroid Cancer Using Lenvatinib	*eligibility, exclusions and tests updated*	--	--
HNOTVAN	Treatment for Locally Advanced or Metastatic Medullary Thyroid Cancer Using vanDETanib	*exclusions updated and tests clarified*	*tests clarified*	--
SM | Skin and Melanoma				
SMAJPEM	Adjuvant Treatment of Resected Stage IIB to IV NED Melanoma Using Pembrolizumab	*Eligibility 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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