Provincial Health Services Authority

Systemic Therapy Update

Volume 24 Issue 11
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For Health Professionals Who Care for Cancer Patients

Inside This Issue:

Editor's Choice

Updated: Influenza Vaccine Recommendations

The updated **BC Cancer Influenza Vaccine Recommendations for Adults with Cancer** are available on the BC Cancer website in the Supportive Care section of the Cancer Management Guidelines and on the Immunotherapy and Supportive Care pages in the Chemotherapy Protocols section.

As in the previous flu season, patients should be offered an age-appropriate **inactivated influenza vaccine**.

Updates for the 2021-2022 flu season include:

- The influenza vaccine may be administered at the same time as the COVID-19 vaccine, or at any time before or thereafter
- It is recommended that patients on CTLA-4 inhibitor monotherapy or combination therapy should not receive the influenza vaccine within 4 weeks of either starting treatment or the last dose (revised from 4-6 weeks)

New Programs

The BC Cancer Provincial Systemic Therapy Program has approved the following new treatment programs effective 01 November 2021. Full details of all treatment programs are available in the Chemotherapy Protocols section of the BC Cancer website.

Genitourinary

High-Dose Bicalutamide for Prostate Cancer (GUPHDBIC) — The BC Cancer Genitourinary Group is implementing high-dose bicalutamide (150 mg daily) for patients with **localized high-risk prostate cancer**

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with intolerance of, or have contraindications to, LHRH agonists or antagonists. In addition, these patients must have been treated with curative intent radiotherapy, or experienced biochemical relapse post-prostatectomy treated with curative intent salvage radiotherapy, or where treatment with high-dose bicalutamide is an alternative to watchful waiting in patients with localized high-risk prostate cancer. Patients with localized *low-risk* prostate cancer, who would otherwise undergo active surveillance or watchful waiting, are not eligible for this treatment program, as high-dose bicalutamide in this setting is associated with increased mortality.

Approval for high-dose bicalutamide is based on evidence from a series of randomized trials. The Early Prostate Cancer (EPC) trial program[1] demonstrated that overall survival was significantly longer in patients with localized high-risk prostate cancer treated with curative intent radiotherapy and high-dose bicalutamide compared with patients receiving radiotherapy alone (HR 0.65, 95% CI 0.44-0.95). In patients with localized high-risk prostate cancer who declined or had contraindications to local therapy, there was a trend to improved overall survival in patients treated with high-dose bicalutamide as compared to watchful waiting (HR 0.81, 95% CI 0.66-1.01). In a trial from the NRG Oncology Radiation Therapy Oncology Group, 12-year overall survival was significantly improved in patients with localized high-risk prostate cancer with biochemical relapse post-prostatectomy and treated with high-dose bicalutamide and curative intent salvage radiotherapy as compared with radiotherapy alone (76.3% vs 71.3%, HR 0.77, 95% CI 0.59-0.99).[2] Cardiovascular history and risk factors should be considered prior to initiation of high-dose bicalutamide. Gynecomastia and breast pain or tenderness are more common with high-dose bicalutamide monotherapy than with bicalutamide given at standard 50 mg dosing in combination with LHRH agonists or antagonists; these effects are related to the unopposed action of circulating estrogen during monotherapy, in contrast to the reduced circulating levels of testosterone and estrogen in combination therapy. Treatment to mitigate these side effects should be considered when high-dose bicalutamide is used.

Lymphoma

Alitretinoin for Cutaneous T-Cell Lymphoma (LYALIT) — The BC Cancer Lymphoma and Myeloma Tumour Group is introducing alitretinoin for use in cutaneous T-cell lymphoma (CTCL) including mycosis fungoides (MF) and Sézary syndrome (SS). Eligibility for alitretinoin includes disease that is not responsive to topical steroids, mechlorethamine, or phototherapy, or patients that have no access to phototherapy. The eligibility for LYMFBEX (bexarotene for treatment of CTCL) has been updated to restrict treatment to patients with advanced, progressive or refractory disease that has not been controlled by alitretinoin (LYALIT) and at least one prior systemic chemotherapy agent.

Two retrospective analyses of patients with MF and SS CTCL subtypes found that the majority of patients achieved a complete or partial response, or stable disease, during treatment with alitretinoin alone or in combination with standard treatment.[3,4] Alitretinoin was well tolerated, with hypertriglyceridemia the most commonly observed adverse effect. For more details on the pharmacology of alitretinoin, please see the *Cancer Drug Manual* section below.

References

1. McLeod DG, Iversen P, See WA, et al. Bicalutamide 150 mg plus standard care vs standard care alone for early prostate cancer. *BJU International* 2005;97:247-254. https://doi.org/10.1111/j.1464-410X.2005.06051.x
2. Shipley WU, Seiferheld W, Lukka HR, et al. Radiation with or without antiandrogen therapy in recurrent prostate cancer. *N Engl J Med* 2017;376(5):417-428. https://doi.org/10.1056/NEJMoa1607529
3. Kapser C, Herzinger T, Ruzicka T, et al. Treatment of cutaneous T-cell lymphoma with oral alitretinoin. *J Eur Acad Dermatol Venereol* 2015;29:783-788. https://doi.org/10.1111/jdv.12684
4. Alhusayena R, Vu TT, Almuhanna N, et al. Evaluation of alitretinoin for the treatment of mycosis fungoides and Sézary syndrome. *Dermatology* 2021;237:479–485. https://doi.org/10.1159/000512484

Provincial Systemic Therapy Program

All policies and procedures are on the Shared Health Organizations Portal (SHOP) BC Cancer page.

Updated: Compassionate Access Program (CAP) Policy

Policy III-45: Compassionate Access Program has been updated and replaced by two separate documents: **Compassionate Access Program Policy** and **Compassionate Access Program Application Procedure**. While these documents have also been updated to meet current documentation standards, it is important to note that their content remains essentially unchanged.

Cancer Drug Manual©

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

New Documents

The **Alitretinoin Monograph** and **Patient Handout** have been developed with expert review provided by Dr. Vincent Ho (BC Cancer Skin and Melanoma Tumour Group) and Winnie Cheng (BC Cancer Provincial Pharmacy). Alitretinoin is retinoid which binds to retinoic acid receptor (RAR) and retinoid X receptor (RAX). It is used in the treatment of cutaneous T-cell lymphoma at the usual dose of 30 mg orally once daily. For more information on the new alitretinoin protocol (LYALIT), please see the *Editor's Choice* section above.

Highlights from these documents include:

- alitretinoin is a known teratogen and is contraindicated in pregnancy; when prescribing for a female of childbearing potential, physicians must follow the TOCTINO® Pregnancy Prevention Program
- hypertriglyceridemia has been reported; serum cholesterol and triglyceride levels should be monitored frequently
- benign intracranial hypertension may rarely occur; symptoms include headache, nausea and vomiting, visual disturbances and papilloedema

Alitretinoin has been added to the **Auxiliary Label List** and has been evaluated for the **BC Cancer Hazardous Drug List**.

The **Bicalutamide Monograph** and **Patient Handout** have been completely revised with expert review provided by Victoria Kletas (pharmacist) of the BC Cancer Genitourinary Tumour Group. Bicalutamide is a first-generation non-steroidal anti-androgen used in the treatment of prostate cancer.

Highlights from these documents include:

- updated *Side Effect* table, including reactions documented through postmarketing reporting, and where available, dose-dependent incidence of specific side effects
- updated *Cautions*, including risk of cardiovascular disease and QTc prolongation associated with androgen deprivation therapy in men

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Cancer Drug Manual©

- updated *Dosage Guidelines*, including high-dose bicalutamide (i.e., 150 mg orally daily); for more information on the new high-dose bicalutamide protocol (GUPHDBIC), please see the *Editor's Choice* section above

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 Chemotherapy Preparation and Stability Chart entry are made available for reference only.

The **Trastuzumab Deruxtecan Interim Monograph** has been developed. Trastuzumab deruxtecan is an antibody-drug conjugate directed against the HER2 protein. After the conjugate is internalized by the tumour cell, the topoisomerase inhibitor deruxtecan is cleaved from trastuzumab and able to cause apoptotic cell death of the tumour cell. Trastuzumab deruxtecan is used in the treatment of breast cancer. It is typically administered as 5.4 mg/kg IV once every three weeks.

Highlights from this document include:

- trastuzumab deruxtecan is not interchangeable with trastuzumab or trastuzumab emtansine
- left ventricular ejection fraction (LVEF) decrease has been observed; some patients may be asymptomatic
- fatal cases of interstitial lung disease/pneumonitis have occurred
- the product must be protected from light during all steps of preparation and the infusion bag must be covered for administration

Trastuzumab deruxtecan has been added to the **Chemotherapy Preparation and Stability Chart** and has been evaluated for the **BC Cancer Hazardous Drug List.**

Upcoming Treatment Program Funding *(new section)*

Select treatment programs anticipating BC Cancer funding in the near future are outlined below.

December 2021

Apalutamide and **enzalutamide** have been evaluated for patients with metastatic castrate-sensitive prostate cancer (mCSPC), and funding through BC Cancer is anticipated as of 01 December 2021. BC Cancer funding will allow for transitioning of a number of patients – who previously accessed apalutamide or enzalutamide through a manufacturer patient assistance program – to BC Cancer centre pharmacies for their medication supply. Patients will be transitioning via the BC Cancer Compassionate Access Program (CAP) between 01 December 2021 and 01 February 2022.

Niraparib has been evaluated for the first-line maintenance of platinum-responsive ovarian cancer and for the second- and subsequent-line maintenance of relapsed platinum-sensitive or -responsive ovarian cancer, irrespective of BRCA mutation status. Funding through BC Cancer is anticipated as of 01 December 2021, and CAP approval will be required.

Benefit Drug List

New Programs

The following new treatment programs have been added to the BC Cancer Benefit Drug List effective 01 November 2021:

Protocol Title	Protocol Code	Benefit Status
Treatment of Prostate Cancer with **High-Dose Bicalutamide**	**GUPHDBIC**	Class I
Treatment of Cutaneous T-Cell Lymphoma (Mycosis Fungoides/Sézary Syndrome) with **Alitretinoin**	**LYALIT**	Class I

Deleted Programs

The following treatment program has been deleted from the BC Cancer Benefit Drug List effective 01 November 2021:

Protocol Title	Protocol Code	Benefit Status
Primary Adjuvant Treatment of Adenocarcinoma/Adenosquamous Cancer of the Cervix with **Carboplatin** and **Paclitaxel** Preceding or Following Irradiation with or without **Cisplatin**	**GOCXAJCAT**	Deleted

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

Protocol Code	Protocol Title	Protocol	PPPO	Handout
GUPHDBIC	Treatment of Prostate Cancer with High-Dose Bicalutamide	☑	☑	☐
LYALIT	Treatment of Cutaneous T-Cell Lymphoma (Mycosis Fungoides/Sézary Syndrome) with Alitretinoin	☑	☑	☐

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 (CAP) approval are prefixed with the letter **U.**

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

Protocol Code	Protocol Title	Protocol	PPPO	Handout
GI | Gastrointestinal				
GIGAVCCT	Palliative Treatment of Metastatic or Locally Advanced Gastric, Gastroesophageal Junction or Esophageal Adenocarcinoma using Cisplatin, Capecitabine and Trastuzumab	*Dose Modifications updated*	-----	-----
GIGAVCFT	Palliative Treatment of Metastatic or Inoperable, Locally Advanced Gastric or Gastroesophageal Junction Adenocarcinoma using Cisplatin, Infusional Fluorouracil and Trastuzumab	*Dose Modifications updated*	-----	-----
GIGAVCOXT	Palliative Treatment of Metastatic or Locally Advanced Gastric, Gastroesophageal Junction or Esophageal Adenocarcinoma using Capecitabine, Oxaliplatin and Trastuzumab	*Dose Modifications updated*	-----	-----
GIGAVTR	Continuation of Palliative Treatment of Metastatic or Inoperable, Locally Advanced Gastric or Gastroesophageal Junction Adenocarcinoma using Trastuzumab	*Treatment duration, Dose Modifications and GI ST physician and contact information updated*	-----	-----
GO | Gynecologic				
GOCXAJCAT	Primary Adjuvant Treatment of Adenocarcinoma/ Adenosquamous Cancer of the Cervix with Carboplatin and Paclitaxel Preceding or Following Irradiation with or without Cisplatin	*Deleted*	*Deleted*	-----
GU | Genitourinary				
GUBEP	Curative Therapy for Germ Cell Cancer using Bleomycin, Etoposide and Cisplatin	*Lab tests updated*	*Lab tests updated*	-----
GUCABO	Therapy for Metastatic Renal Cell Carcinoma using Cabozantinib	*Eligibility updated*	-----	-----
LY | Lymphoma				
LYMFBEX	Treatment of Cutaneous T-Cell Lymphoma (Mycosis Fungoides/Sézary syndrome) with Bexarotene	*Eligibility updated*	-----	-----
SM| Skin and Melanoma				
SMMCCAVE	Second-Line Treatment of Recurrent or Metastatic Merkel Cell Carcinoma using Avelumab	-----	*Premedications revised*	-----

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
Manufacturer Patient Assistance Programs: http://www.bccancer.bc.ca/mpap		
Library/Cancer Information	604-675-8003	requests@bccancer.bc.ca toll free 888-675-8001 x 8003
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		

Editorial Review Board