

## For Health Professionals Who Care for People with Cancer

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### Editor's Choice

#### New Programs

BC Cancer Provincial Systemic Therapy has approved the following new treatment program effective 1 February 2023. Full details of all treatment programs are available in the [Chemotherapy Protocols](#) section of the BC Cancer website.

#### Breast

**Neoadjuvant Pembrolizumab and Chemotherapy Followed by Adjuvant Pembrolizumab for Triple Negative Breast Cancer (BRPCATC, BRPCWTAC, BRAJPEM)** — The BC Cancer Breast Tumour Group is introducing pembrolizumab for high risk early triple negative breast cancer (TNBC) with negative staining of estrogen, progesterone and HER-2 receptors. Patients would be treated with two options of neoadjuvant protocols, followed by one adjuvant protocol:

##### Neoadjuvant

BRPCTAC: Pembrolizumab concurrent with 3-weekly carboplatin AUC 5 and weekly paclitaxel followed by doxorubicin and cyclophosphamide (AC), or

BRPCWTAC: Pembrolizumab concurrent with weekly carboplatin AUC 1.5 and weekly paclitaxel, followed by AC

##### Adjuvant

BRAJPEM: Adjuvant pembrolizumab monotherapy after resection

### New Programs

These patients are currently treated with neoadjuvant chemotherapy followed by potentially adjuvant chemotherapy based on the pathological response. The addition of the immune checkpoint inhibitor pembrolizumab to chemotherapy is supported by the randomized, placebo-controlled phase III KEYNOTE-522 study. In the fourth interim analysis, the addition of pembrolizumab was associated with increased event-free survival (84.5% vs. 76.8% at 36 months, hazard ratio 0.63) and pathological complete response (63% vs. 55%). Pembrolizumab was associated with manageable toxicities consistent with known safety profile and its addition to chemotherapy did not seem to affect the quality of life.<sup>1,2</sup>

#### Gastrointestinal

**Yttrium-90 for Transarterial Radioembolisation for Locally Advanced Cholangiocarcinoma or Gallbladder Carcinoma (GIBYTT)** — The BC Cancer Gastrointestinal Tumour Group is introducing yttrium-90 as transarterial radioembolisation (TARE) therapy for locally advanced cholangiocarcinoma or gallbladder carcinoma not amenable for surgical resection. These patients are currently offered chemoembolization with cisplatin, which requires inpatient admission, whereas TARE can be delivered as outpatient treatment. TARE has been shown to provide local control and delay requirement for chemotherapy, consolidate response from chemotherapy and facilitate a treatment break, and increase overall survival.<sup>3-6</sup>

#### Lung

**Adjuvant Osimertinib for EGFR Mutation Positive Non-Small Cell Lung Cancer (LUAJOSI)** — The BC Cancer Lung Tumour Group is introducing osimertinib as an adjuvant therapy for non-small cell lung cancer with EGFR exon 19 deletion and/or exon 21 L858R substitution, i.e., the most common sensitizing EGFR mutations. These patients are currently offered adjuvant platinum doublet chemotherapy, which is associated with modest benefit in overall survival.

The use of oral tyrosine kinase inhibitor, osimertinib, in this patient population is supported by the randomized, placebo-controlled phase III ADAURA study. Adjuvant osimertinib was associated with increased disease-free survival in the overall study population (median not reached vs. 27.5 mos, HR 0.20) and in the primary analysis population (median not reached vs. 19.6 mos, HR 0.17). This benefit was observed regardless of whether patients were also treated with adjuvant chemotherapy. Osimertinib was associated with manageable toxicities consistent with known safety profile.<sup>7</sup> Note that adjuvant osimertinib does not replace adjuvant chemotherapy and patients may or may not be also treated with adjuvant chemotherapy.

#### Melanoma

**Alternative Ipilimumab and Nivolumab Dosing Regimen for Unresectable or Metastatic Melanoma (SMAVALIPNI)** — The BC Cancer Melanoma Tumour Group is introducing an alternative dosing regimen of ipilimumab and nivolumab for unresectable or metastatic melanoma. This alternative regimen can be used in patients with tolerability or toxicity concerns associated with the standard dosing regimen (SMAVIPNI).

**SMAVIPNI (Standard dosing)**

4 cycles of:

- Nivolumab 1 mg/kg every 3 weeks, and
- Ipilimumab 3 mg/kg every 3 weeks

Followed by Nivolumab maintenance.

**SMAVALIPNI (Alternative dosing)**

4 cycles of:

- Nivolumab 3 mg/kg every 3 weeks, and
- Ipilimumab 1 mg/kg every 3 weeks

Followed by Nivolumab maintenance.

## Editor's Choice

### New Programs

This alternative dosing regimen is supported by the randomized, double-blind phase IIIb/IV CheckMate 511 study. Compared to standard dosing, the use of higher nivolumab dose with lower ipilimumab dose was associated with reduced incidence of grades 3 and 4 treatment-related adverse events (33.3% vs. 48.3%), and treatment discontinuation due to these events (16.7% vs. 27.5%). The efficacy of the alternative dosing regimen seems to be overall comparable (objective response rate 45.6% vs. 50.6%, complete response 15.0% vs. 13.5%, median progression-free survival 9.9 vs. 8.9 mos).<sup>8</sup>

#### References

1. Schmid P, Cortes J, Pusztai L, et al. Pembrolizumab for early triple-negative breast cancer. *N Engl J Med* 2020;382(9):810-21.
2. Schmid P, Cortes J, Dent R, et al. Event-free survival with pembrolizumab in early triple-negative breast cancer. *N Engl J Med* 2022;386(6):556-67.
3. Buettner S, Braat A, Margonis GA, et al. Yttrium-90 radioembolization in intrahepatic cholangiocarcinoma: a multicenter retrospective analysis. *J Vasc Interv Radiol* 2020;31(7):1035–1043.e2.
4. Jia Z, Paz-Fumagalli R, Frey G, Sella DM, McKinney JM, Wang W. Resin-based yttrium-90 microspheres for unresectable and failed first-line chemotherapy intrahepatic cholangiocarcinoma: preliminary results. *J Cancer Res Clin Oncol* 2017;143(3):481–9.
5. Hoffmann RT, Paprottka PM, Schön A, et al. Transarterial hepatic yttrium-90 radioembolization in patients with unresectable intrahepatic cholangiocarcinoma: factors associated with prolonged survival. *Cardiovasc Intervent Radiol* 2012;35(1):105–16.
6. Swinburne NC, Biederman DM, Besa C, et al. Radioembolization for unresectable intrahepatic cholangiocarcinoma: review of safety, response evaluation criteria in solid tumors 1.1 imaging response and survival. *Cancer Biother Radiopharm* 2017;32(5):161–8.
7. Wu YL, Tsuboi M, He J, et al. Osimertinib in resected EGFR-mutated non-small-cell lung cancer. *N Engl J Med* 2020;383(18):1711-23.
8. Lebbé C, Meyer N, Mortier L, et al. Evaluation of two dosing regimens for nivolumab in combination with ipilimumab in patients with advanced melanoma: results from the phase IIIb/IV CheckMate 511 trial. *J Clin Oncol* 2019;37(11):867-75.

## Febrile Neutropenia Assessment and Treatment Guidance

The BC Cancer guidance document of **Febrile Neutropenia for Adults with Solid Tumour and Lymphoma Protocol** has been updated and is available on the BC Cancer website in the Supportive Care section of the Cancer Management Manual, under [Febrile Neutropenia](#), and on [SHOP](#). This guidance document supports prescribers, pharmacists and nurses with the assessment and inpatient/outpatient management of febrile neutropenia in adults with solid tumour/lymphoma at BC Cancer centres. The key updates include:

- Consolidated assessment and treatment recommendations of febrile neutropenia
- Updated high risk treatment recommendations:
  - updated treatment alternatives for beta-lactam allergy
  - clarified indications for antimicrobial selection
  - updated duration of antimicrobial therapy
  - updated vancomycin trough target levels
- Updated low risk treatment recommendations:
  - consider omitting ciprofloxacin if no previous infection history with *Pseudomonas aeruginosa*
  - updated treatment alternatives for beta-lactam allergy
  - updated treatment alternative for low risk patients who do not meet all outpatient criteria

## Provincial Systemic Therapy Policies

**V-40 Vinca Alkaloid Preparation and Administration policy** has been updated with new labelling requirements

## Cancer Drug Manual<sup>®</sup>

All documents are available in the [Cancer Drug Manual<sup>®</sup>](#) on the BC Cancer website.

### Revised Documents

#### **Bendamustine Chemotherapy Preparation and Stability Chart**

*All brands (Product column):* updated recommended bag size range to include new lower limit

#### **Carboplatin Monograph**

*Uses:* updated off-label indications and confirmed Health Canada approved indications

*Cautions:* updated *Carcinogenicity, Mutagenicity, Fertility, and Pregnancy* sections

*Side Effects (table):* added dysgeusia, encephalopathy, posterior reversible encephalopathy syndrome (PRES) to table and updated emetogenicity per current SCNAUSEA protocol

*Side Effects (paragraphs):* added paragraph for *Encephalopathy* and updated *Neurotoxicity* paragraph

*Supply and Storage:* updated with current Canadian brands

*Dosage Guidelines:* added weekly dosing for adults to align with protocol BRPCWTAC and updated dosing with concurrent radiation to align with protocol HNLACART

#### **Ipilimumab Monograph**

*Cautions:* updated *Pregnancy* section

*Side effects paragraphs:* deleted paragraph regarding administration over 30 minute

*Parenteral Administration table:* updated administration time to 30 minutes to align with protocols SMAVALPNI, SMAVIPI, SMAVFIPI, SMAVIPNI

#### **Pembrolizumab Monograph**

*Uses:* updated with new indications

#### **Pemetrexed Chemotherapy Preparation and Stability Chart**

*Dr Reddy's brand:* added room temperature storage to *Vial Stability* and *Product Stability* columns

### Editorial Board Changes

The Cancer Drug Manual<sup>®</sup> writing team and Editorial Review Board would like to welcome Amy Lim, clinical pharmacist (BC Cancer - Abbotsford) as the new CDM writer. Welcome Amy!

## BC Cancer Benefit Drug List

### New Programs

The following treatment programs have been added to the [Benefit Drug List](#) effective 01 February 2023:

Protocol Title	Protocol Code	Benefit Status
Adjuvant Treatment of Resected Triple Negative Breast Cancer using <b>Pembrolizumab</b>	BRAJPEM	Class I
NEOAdjuvant Therapy for Triple Negative Breast Cancer using <b>Pembrolizumab</b> with <b>CARBOplatin</b> and Weekly <b>PACLitaxel</b> , Followed by <b>DOXOrubicin</b> and <b>Cyclophosphamide</b>	BRPCTAC	Class I
NEOAdjuvant Therapy for Triple Negative Breast Cancer using <b>Pembrolizumab</b> , Weekly <b>CARBOplatin</b> and Weekly <b>PACLitaxel</b> , Followed by <b>DOXOrubicin</b> and <b>Cyclophosphamide</b>	BRPCWTAC	Class I
<b>Yttrium-90</b> for Transarterial Radioembolisation (TARE) for Locally Advanced Cholangiocarcinoma or Gallbladder Carcinoma Not Amenable for Surgical Resection	GIBYTT	Class I
Adjuvant Treatment of Epidermal Growth Factor Receptor (EGFR) Mutation-Positive Non-Small Cell Lung Cancer (NSCLC) with <b>Osimertinib</b>	LUAJOSI	Class I
Treatment of Unresectable or Metastatic Melanoma Using Alternative Dosing Regimen of <b>Ipilimumab</b> and <b>Nivolumab</b>	SMAVALIPNI	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 (CAP) approval are prefixed with the letter **U**.

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

Protocol Code	Protocol Title	Protocol	PPPO	Handout
<b>BRAJPEM</b>	Adjuvant Treatment of Resected Triple Negative Breast Cancer using Pembrolizumab	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<b>BRPCTAC</b>	NEOAdjuvant Therapy for Triple Negative Breast Cancer using Pembrolizumab with CARBOplatin and Weekly PACLitaxel Followed by DOXOrubicin and Cyclophosphamide	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>

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

Protocol Code	Protocol Title	Protocol	PPPO	Handout
<b>BRPCWTAC</b>	NEOAdjuvant Therapy for Triple Negative Breast Cancer using Pembrolizumab, Weekly CARBOplatin and Weekly PACLitaxel, Followed by DOXOrubicin and Cyclophosphamide	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<b>GIBYTT</b>	Yttrium-90 for Transarterial Radioembolisation (TARE) for Locally Advanced Cholangiocarcinoma or Gallbladder Carcinoma Not Amenable for Surgical Resection	<input checked="" type="checkbox"/>	-	-
<b>LUAJOSI</b>	Adjuvant Treatment of Epidermal Growth Factor Receptor (EGFR) Mutation-Positive Non-Small Cell Lung Cancer (NSCLC) with Osimertinib	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<b>SMAVALIPNI</b>	Treatment of Unresectable or Metastatic Melanoma Using Alternative Dosing Regimen of Ipilimumab and Nivolumab	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>

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

Protocol Code	Protocol Title	Protocol	PPPO	Handout
<b>GI   Gastrointestinal</b>				
<b>GIYTT</b>	Yttrium-90 for Transarterial Radioembolisation (TARE) for Hepatocellular Cancer or Neuroendocrine Tumours with Hepatic Disease	<i>Title, exclusions and treatment clarified, eligibility updated, contact physician revised</i>	-	-
<b>LU   Lung</b>				
<b>LUAVOSI</b>	Treatment of EGFR T790M Mutation-Positive Advanced Non-Small Cell Lung Cancer (NSCLC) with Osimertinib	<i>Exclusions clarified</i>	-	<i>Side effects and management updated</i>
<b>LUAVOSIF</b>	First-Line Treatment of Epidermal Growth Factor Receptor (EGFR) Mutation-Positive Advanced Non-Small Cell Lung Cancer (NSCLC) with Osimertinib	<i>Eligibility and exclusions clarified</i>	-	<i>Side effects and management updated</i>
<b>SM   Skin and Melanoma</b>				
<b>SMAVFIPI</b>	First-Line Treatment of Unresectable or Metastatic Melanoma Using Ipilimumab	<i>Ipilimumab infusion time updated</i>	<i>Ipilimumab infusion time updated, tests clarified</i>	<i>Ipilimumab infusion time updated</i>
<b>SMAVIPI</b>	Treatment of Unresectable or Metastatic Melanoma Using Ipilimumab	<i>Ipilimumab infusion time updated</i>	<i>Ipilimumab infusion time updated, tests clarified</i>	<i>Ipilimumab infusion time updated</i>
<b>SMAVIPNI</b>	Treatment of Unresectable or Metastatic Melanoma Using Ipilimumab and Nivolumab	<i>Eligibility, tests and ipilimumab infusion time updated</i>	<i>Ipilimumab infusion time updated</i>	<i>Ipilimumab infusion time updated</i>

## Resources and Contact Information

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

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