

Systemic Therapy Update

Volume 25 Issue 7 July 2022

For Health Professionals Who Care for People with Cancer

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Resources and Contact Information

Editor's Choice

New Programs

BC Cancer Provincial Systemic Therapy has approved the following new treatment programs effective 01 July 2022. Full details of all treatment programs are available in the Chemotherapy Protocols section of the BC Cancer website.

Gastrointestinal

First-Line Treatment of Locally Advanced or Metastatic Gastroesophageal Cancer — The BC Cancer Gastrointestinal Tumour Group is introducing two first-line options with combination chemotherapy and immune checkpoint inhibitor for patients with locally advanced or metastatic gastroesophageal cancer. Eligibility includes HER-2-negative esophageal carcinoma (adenocarcinoma or squamous cell carcinoma) or gastroesophageal junction (GEJ) adenocarcinoma, irrespective of PD-L1 status/CPS score.

• Oxaliplatin, Capecitabine and Pembrolizumab (GIGAVCOXP):

Cycle Oxaliplatin		Capecitabine	Pembrolizumab	
3 weeks	130 mg/m ²	days 1-14	2 mg/kg	

Oxaliplatin, Fluorouracil, Leucovorin and Pembrolizumab (GIGAVFFOXP):

Cycle Oxaliplatin		Fluorouracil/Leucovorin	Pembrolizumab
6 weeks	85 mg/m² every 2 weeks	5-FU/leucovorin bolus plus 5-FU infusion every 2 weeks	4 mg/kg

Editor's Choice

Standard first-line chemotherapy for this patient population has typically included a platinum- and fluoropyrimidine-based regimen. The addition of pembrolizumab to standard first-line chemotherapy has demonstrated, for the first time, survival exceeding 12 months. For both treatment protocols, the chemotherapy portion is continued until disease progression or unacceptable toxicity. Pembrolizumab continues until disease progression, unacceptable toxicity or to a maximum of 2 years of treatment.

Approval of these treatment programs is supported by the randomized, controlled phase III KEYNOTE-590 trial, which compared first-line chemotherapy (cisplatin and fluorouracil) plus pembrolizumab with chemotherapy alone in advanced esophageal and GEJ cancers. At a median follow-up of 22.6 months, a significant overall survival (OS) and progression-free survival (PFS) benefit was reported in all patients randomized to the pembrolizumab group (OS: 12.4 months vs. 9.8 months, HR 0.73 95% CI 0.62-0.86; PFS: 6.3 months vs. 5.8 months, HR 0.65, 95% CI 0.55-0.76). No new safety signals were reported. The pembrolizumab group reported a higher incidence of immune-mediated adverse events (AEs) and infusion reactions (25.7% vs. 11.6%), hypothyroidism (10.8% vs. 6.5%), hyperthyroidism (5.7% vs. 0.8%), pneumonitis (6.2% vs. 0.5%) and discontinuation due to treatment-related AEs (19.5% vs. 11.6%).

While the KEYNOTE-590 trial used cisplatin and fluorouracil as the chemotherapy backbone, pERC agreed in their review that pembrolizumab could be added to other chemotherapy backbones used in the first-line setting such as oxaliplatin and capecitabine or fluorouracil (e.g., GIGAVCOX or GIGAVFFOX).²

References

- Sun J-M, Shen L, Shah MA, et al. Pembrolizumab plus chemotherapy versus chemotherapy alone for first-line treatment of advanced oesophageal cancer (KEYNOTE-590): a randomised, placebo-controlled, phase 3 study. *Lancet* 2021;398(10302):759-771. https://doi.org/10.1016/S0140-6736(21)01234-4
- 2 CADTH Reimbursement Recommendation. Pembrolizumab (Keytruda®). *Canadian Journal of Health Technologies* 2021;1(12): 1-19. https://www.cadth.ca/sites/default/files/DRR/2021/PC0250%20Keytruda%20-%20CADTH%20Final%20Rec.pdf

Provincial Systemic Therapy

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

Updated: Holding Anticoagulants Prior to Intrathecal Drug Administration

Procedure III-50: Administration of High Alert Medications by the Intrathecal Route via Lumbar Puncture or Ommaya Reservoir has been updated effective 01 July 2022. Administration of an intrathecal drug while a patient is anticoagulated can result in bleeding and negative patient outcomes. Several lymphoma treatment protocols have recently been updated to ensure consistent language around the practice of holding anticoagulants prior to intrathecal drug administration. The following statement has been added to Procedure III-50 to align with the updated protocols: "Ensure anticoagulants were held prior to intrathecal administration as per local guidelines for anticoagulation management."

Cancer Drug Manual®

All documents are available in the <u>Cancer Drug Manual</u>[©] 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 **Larotrectinib Interim Monograph** and **Patient Handout** have been developed with expert review provided by Dr. Ursula Lee (medical oncologist) of the BC Cancer Sarcoma Tumour Group and Dr. Jennifer Kendrick (clinical pharmacy specialist) of BC Children's Hospital. **Larotrectinib** is an inhibitor of Tropomyosin Receptor Kinase and is used in the treatment of Neurotrophic Tyrosine Receptor Kinase (*NTRK*) gene fusion-positive solid tumours. The usual dose is 100 mg orally twice daily.

Highlights from these documents include:

- larotrectinib is supplied as capsules and as an oral solution, which may be used interchangeably
- the oral solution requires refrigeration and expires 30 days after opening
- neurologic/psychiatric side effects are common and can include dizziness, cognitive impairment, mood disorders and sleep disturbances
- rare but serious side effects include sepsis, encephalopathy, brain edema and cerebrovascular accident

Larotrectinib has been added to the **Auxiliary Label List**, and has been evaluated for the **BC Health Authorities Provincial Hazardous Drug List**.

Revised Documents

Amivantamab Chemotherapy Preparation and Stability Chart

Added marketed brand (Janssen)

Product Stability and Special Precautions (for SAP supply): updated instructions for protect from light

Capecitabine Patient Handout

Side Effects: updated nausea/vomiting and diarrhea sections in table to include new messaging about dehydration

Fluorouracil IV Patient Handout

Side Effects: updated diarrhea section in table to include new messaging about dehydration

Irinotecan Patient Handout

Side Effects: updated nausea/vomiting and diarrhea sections in table to include new messaging about dehydration

Lurbinectedin Monograph and Chemotherapy Preparation and Stability Chart

Supply and Storage: added marketed brand (Jazz)

Solution Preparation and Compatibility (Additional information): added information pertaining to peripheral and central line administration and incompatibility with nylon in-line filters

Chemotherapy Preparation and Stability Chart: added marketed brand (Jazz)

Cancer Drug Manual[©]

Oxaliplatin Patient Handout

Side Effects: updated nausea/vomiting and diarrhea sections in table to include new messaging about dehydration; updated neuropathy information to include new messaging about balance and walking

Ruxolitinib Monograph

Uses: updated to myelodysplastic neoplasms

Cautions: added information pertaining to monitoring for lipid disorders; updated *Pregnancy* and *Breastfeeding* sections (deleted outdated FDA Pregnancy Category; added new details)

Dosage Guidelines: updated platelet count parameters in Starting Dose table

Trastuzumab Emtansine Monograph

Cautions: updated Pregnancy section (deleted outdated FDA Pregnancy Category; added new details) Parenteral Administration table: deleted information pertaining to length of observation period (refer to protocol); added information pertaining to in-line filter

Dosage Guidelines: deleted Dose Reduction Levels table (refer to protocol)

CDM Editorial Board Changes

The Cancer Drug Manual[©] Editorial Review Board would like to bid farewell to **Sanna Pellatt, CON Pharmacy Educator,** BC Cancer – Victoria. Thank you, **Sanna**, for your many contributions to the Cancer Drug Manual[©] board over the years. We wish you all the best in your retirement and future endeavours.

BC Cancer Benefit Drug List

New Programs

The following treatment programs have been added to the **Benefit Drug List** effective 01 July 2022:

Protocol Title	Protocol Code	Benefit Status
First-Line Treatment of Locally Advanced or Metastatic Gastroesophageal Cancer using Oxaliplatin, Capecitabine and Pembrolizumab	GIGAVCOXP	Class I
First-Line Treatment of Locally Advanced or Metastatic Gastroesophageal Cancer using Oxaliplatin, Fluorouracil, Leucovorin and Pembrolizumab	GIGAVFFOXP	Class I
Dinutuximab : in combination with irinotecan , temozolomide and sargramostim for high-risk neuroblastoma in first relapse or determination of refractory disease	Pediatric	Class I

BC Cancer Benefit Drug List

Revised Programs

The following treatment programs have been revised on the **Benefit Drug List** effective 01 July 2022:

Protocol Title	Protocol Code	Benefit Status
Dinutuximab : in combination with aldesleukin , tretinoin and sargramostim for high-risk neuroblastoma with a response to prior first-line multi-agent, multimodal therapy	Pediatric	Class I (previously Restricted)

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
GIGAVCOXP	First-Line Treatment of Locally Advanced or Metastatic Gastroesophageal Cancer using Oxaliplatin, Capecitabine and Pembrolizumab		$\overline{\checkmark}$	Ø
GIGAVFFOXP	First-Line Treatment of Locally Advanced or Metastatic Gastroesophageal Cancer using Oxaliplatin, Fluorouracil, Leucovorin and Pembrolizumab	\square	\square	V

REVISED Protocols, PPPOs and Patient Handouts (revisions in respective columns)						
Protocol Code	Protocol Title	Protocol	PPPO	Handout		
BR Breast	BR Breast					
BRAJLHRHAI	Neoadjuvant or Adjuvant Ovarian Suppression and Aromatase Inhibitor in Premenopausal Women with High-Risk Early Stage Breast Cancer	Eligibility updated				
CN Neuro-Oncology						
CNBEV	Summary for Palliative Therapy for Recurrent Malignant Gliomas using Bevacizumab with or without Concurrent Etoposide or Lomustine	Tests clarified	Tests clarified			

REVISED Protocols, PPPOs and Patient Handouts (revisions in respective columns)				
Protocol Code	Protocol Title	Protocol	PPPO	Handout
GI Gastrointe	estinal			
GICPART	Curative Combined Modality Therapy for Carcinoma of the Anal Canal using Cisplatin, Capecitabine and Radiation Therapy	Eligibility and Exclusion updated		
GIEFFOXRT	Combined Modality Therapy for Locally Advanced Esophageal Cancer using Oxaliplatin, Fluorouracil, Leucovorin and Radiation Therapy	Precautions clarified		
GIFIRINOX	Palliative Combination Chemotherapy for Advanced Pancreatic Adenocarcinoma using Irinotecan, Oxaliplatin, Fluorouracil and Leucovorin	Eligibility updated	Chemotherapy section: 'immediately followed by' removed	
GIFUART	Curative Combined Modality Therapy for Carcinoma of the Anal Canal using Mitomycin, Infusional Fluorouracil and Radiation Therapy	Exclusion and Dose Modification updated		
GIFUPART	Curative Combined Modality Therapy for Carcinoma of the Anal Canal using Cisplatin, Infusional Fluorouracil and Radiation Therapy	Eligibility, Exclusion and Dose Modification updated; Precautions clarified		
GIGFLODOC	Perioperative Treatment of Resectable Adenocarcinoma of the Stomach, Gastroesophageal Junction or Lower ¼ Esophagus using Docetaxel, Oxaliplatin, Infusional Fluorouracil and Leucovorin	Filgrastim dose and contact information updated		
GIGFOLFIRI	Second-Line Palliative Combination Chemotherapy for Metastatic Gastric or Esophageal Adenocarcinoma using Irinotecan, Fluorouracil and Leucovorin	CAP statement removed		
GIPAJFIROX	Adjuvant Chemotherapy for Resected Pancreatic Adenocarcinoma using Irinotecan, Oxaliplatin, Fluorouracil and Leucovorin		Chemotherapy section: 'immediately followed by' removed	
GIPAJGEM	Adjuvant Chemotherapy for Pancreatic Adenocarcinoma using Gemcitabine	Treatment clarified		
GIYTT	Yttrium-90 for Transarterial Radioembolisation (TARE)	Treatment site added		
GU Genitour	inary			
GUFUPRT	Combined Modality Therapy for Squamous Cell Cancer of the Genitourinary System using Fluorouracil and Cisplatin with Radiation	Precautions clarified		

REVISED P	REVISED Protocols, PPPOs and Patient Handouts (revisions in respective columns)					
Protocol Code	Protocol Title	Protocol	PPPO	Handout		
GUVIP2	Consolidation and Salvage Therapy for Nonseminoma using Etoposide, Cisplatin, Ifosfamide and Mesna	Precautions updated				
HN Head and	Neck					
HNAVPC	Treatment for Unresectable, Locoregionally Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck using Paclitaxel and Cisplatin or Carboplatin	Carboplatin dose clarified				
LU Lung						
LUAVPCIPNI	First-Line Treatment of Advanced Squamous Non- Small Cell Lung Cancer with Paclitaxel, Carboplatin, Ipilimumab and Nivolumab	Treatment schedule clarified; ipilimumab infusion time revised	Treatment schedule clarified; ipilimumab infusion time revised Cycle 1-2 & Cycle 3+ PPPOs	Treatment schedule clarified		
LUAVPPIPNI	First-Line Treatment of Advanced Non-Squamous Non-Small Cell Lung Cancer with Platinum, Pemetrexed, Ipilimumab and Nivolumab	Treatment schedule clarified; ipilimumab infusion time revised	Treatment schedule clarified; ipilimumab infusion time revised Cycle 1-2 & Cycle 3+ PPPOs	Treatment schedule clarified		
LUMMIPNI	Treatment of Malignant Mesothelioma using Ipilimumab and Nivolumab	Ipilimumab infusion time revised	Ipilimumab infusion time revised	Ipilimumab infusion time revised		
LY Lymphoma	a					
LYABVD	Treatment of Hodgkin Lymphoma with Doxorubicin, Bleomycin, Vinblastine and Dacarbazine	Precautions updated				
LYCHOP	Treatment of Lymphoma with Doxorubicin, Cyclophosphamide, Vincristine and Prednisone	Recommendation for CNS prophylaxis with IT chemo removed; HBV DNA monitoring revised				
LYCHOPR	Treatment of Lymphoma with Doxorubicin, Cyclophosphamide, Vincristine, Prednisone and Rituximab	Recommendation for CNS prophylaxis with IT chemo removed; HBV DNA monitoring revised				
LYCVPPABO	Treatment of Hodgkin Lymphoma with Cyclophosphamide, Vinblastine, Procarbazine, Prednisone, Doxorubicin, Vincristine and Bleomycin	Precautions updated				
LYOBBEND	Treatment of Rituximab-Refractory Follicular Lymphoma (FL) with Obinutuzumab in Combination with Bendamustine		Return Appointment Orders updated			

REVISED Protocols, PPPOs and Patient Handouts (revisions in respective columns)					
Protocol Code	Protocol Title	Protocol	PPPO	Handout	
ULYROMI	Treatment of Relapsed or Refractory Peripheral T-Cell Lymphoma (PTCL) with Romidepsin	Treatment duration updated			
LYVENETOR	Treatment of Relapsed/Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma using Venetoclax and Rituximab		Lab test clarified Post ramp-up PPPO		
SA Sarcoma					
KSVB	Palliative Therapy for Kaposi's Sarcoma using Vinblastine Alternating with Vincristine	Precautions updated			

Resources and Contact Information					
Resource	Phone	Email / Toll Free / Fax			
$Systemic \ The rapy \ Update: \ \underline{www.bccancer.bc.ca/health-professionals/clinical-resources/systemic-therapy/systemic-therapy-update}$					
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.c	a/mpap			
Library/Cancer Information	604-675-8003	requests@bccancer.bc.ca toll free 888-675-8001 x 8003			
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