BC CANCER
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 April 2019, the BC Cancer Provincial Systemic Therapy Program has approved the following treatment program:

Skin/Melanoma:

Ipilimumab-Nivolumab Combination Therapy for Metastatic Melanoma (USMAVIPNI) – The BC Cancer Skin/Melanoma Tumour Group is introducing combination checkpoint blockade with ipilimumab (CTLA-4 inhibitor) and nivolumab (PD-1 inhibitor) as first-line immunotherapy for metastatic melanoma patients regardless of BRAF status. Patients may have received first-line BRAF/MEK inhibitor therapy. As the availability of this new treatment program affects the eligibility criteria of other existing advanced immunotherapy regimens for metastatic melanoma, please refer to the chemotherapy protocols for information on these changes.

A phase III randomized, 3-arm trial (CheckMate 067) compared this combination to ipilimumab monotherapy and nivolumab monotherapy.[1] Compared to ipilimumab monotherapy, combination therapy improved progression-free survival (mPFS 11.5 mo vs. 6.9 mo, HR 0.43, 95% CI 0.35-0.52) and overall survival (mOS not yet reached vs. 19.9 mo, HR 0.55, 95% CI 0.42-0.72). Although the study was not powered to compare combination therapy with nivolumab monotherapy, combination therapy resulted in numerically improved survival. Combination therapy resulted in higher rates of grades 3 to 4 adverse events as expected (59% [combination] vs. 21% [nivolumab] vs. 28% [ipilimumab]), but quality of life measures were no different between the treatment groups. Management of immune-related adverse events will follow the SCIMMUNE protocol.

EDITOR'S CHOICE

References:
1. Wolchok JD, Chiarion-Sileni A, Gonzalez R, et al. Overall survival with combination nivolumab and ipilimumab in advanced melanoma. N Engl J Med 2017;377:1345-1356.

DRUG UPDATE

CHLORMETHINE HYDROCHLORIDE TO REPLACE DISCONTINUED MECHLORETHAMINE

Mechlorethamine injectable has been used in the compounded ointment preparation for the treatment of mycosis fungoides. This injectable was discontinued by the manufacturer in December 2018. Available supplies at BC Cancer have a product expiry of 31 March 2019. The Provincial Systemic Therapy Program has approved the coverage of mechlorethamine topical gel (marketed as **chlormethine hydrochloride [LEDAGA®]** in Europe or **mechlorethamine [VALCHLOR®]** in the United States).[1] It is only available via the Health Canada Special Access Programme (SAP) but does not require a request to the BC Cancer Compassionate Access Program (CAP).

Unfortunately, the SAP supply will not be available until around June 2019. In the interim, **topical carmustine 0.4% white petrolatum (LYCARTOP)** can be used as a treatment alternative to mechlorethamine topical ointment. Please note that associated protocols and pre-printed orders for chlormethine hydrochloride are currently under development and will be available May 2019.

References:
1. Lessin SR, Duvic M, Guitart J et al. Topical Chemotherapy in Cutaneous T-cell Lymphoma. Positive Results of a Randomised, Controlled, Multicenter Trial testing the efficacy and safety of a novel mechlorethamine 0.02% gel in Mycosis Fungoides. JAMA Dermatol. 2013;149(1):25-32.

MEDICAL PATIENT ASSISTANCE PROGRAMS UPDATED

The listing of oncology medical patient assistance programs offered by pharmaceutical companies has been updated and can be found at: www.bccancer.bc.ca/mpap.*

*Located on the BC Cancer Systemic Therapy website under Health Professionals > Systemic Therapy > Reimbursement & Forms

BENEFIT DRUG LIST

NEW PROGRAMS

Effective 01 April 2019, the following treatment program has been added to the BC Cancer Benefit Drug List:

Protocol Title	Protocol Code	Benefit Status
Treatment of Unresectable or Metastatic Melanoma using Ipilimumab and Nivolumab	USMAVIPNI	Restricted

CANCER DRUG MANUAL

NEW MONOGRAPHS AND PATIENT HANDOUTS

The following drugs are NOT BC Cancer Benefit Drugs and require application to the BC Cancer Compassionate Access Program (CAP). Their corresponding Interim Monographs are made available for reference only and can be accessed on the Cancer Drug Manual Drug Index.

Cemiplimab Interim Monograph has been developed and added to the **Chemotherapy Preparation and Stability Chart** and the **Hazardous Drug List**. Cemiplimab is a recombinant human IgG monoclonal antibody immune checkpoint inhibitor that binds to programmed death receptor-1 (PD-1) on T cells and blocks the interaction with its ligands, PD-L1 and PD-L2. Inhibition of the receptor/ligand signaling restores the anti-tumour immune response. Cemiplimab is only available through the Health Canada Special Access Programme (SAP). Cemiplimab is recommended at a fixed dose of 350 mg IV given every 3 weeks. As with other checkpoint inhibitors, immune-related adverse events have been reported and can affect many organ systems.

Highlights from the Monograph include:

- The most common adverse reactions (≥ 20%) are fatigue, rash and diarrhea.
- The most common grade 3 or 4 events (≥ 2%) are cellulitis, sepsis, hypertension, pneumonia, musculoskeletal pain, skin infection, urinary tract infection and fatigue.
- Uveitis, iritis, and other immune-mediated ocular toxicities are rare but some cases have been associated with retinal detachment. Varying degrees of visual impairment, including blindness, can occur.
- Severe infusion-related reactions have been reported in less than 1% of patients. Reactions can be managed by interrupting or slowing the rate of infusion, although permanent discontinuation of cemiplimab may be necessary.

Cancer Drug Manual

Tocilizumab Interim Monograph has been developed and added to the **Chemotherapy Preparation and Stability Chart**. It is a humanized anti-human IL-6 receptor antibody used in the treatment of multi-centric Castleman's disease to alleviate the symptoms and biochemical abnormalities associated with the disease. It is dosed at 8 mg/kg IV every two weeks.

Highlights from the Monograph include:

- Infusion reactions are usually transient and mild, and symptoms may include hypertension, headache, nausea, rash, pruritus and urticaria.
- Anaphylaxis and anaphylactoid reactions are rare, but fatalities have been reported.
- Serious infections have been report; avoid use in patients with active infection (including chronic and localized infections).
- Screening for active and latent tuberculosis (TB) and viral hepatitis prior to treatment is recommended as reactivation of TB and hepatitis B and C have been reported.
- Gastrointestinal perforation is rare, but has been reported primarily as a complication of diverticulitis; patients with a history of gastrointestinal ulceration or diverticulitis may be at higher risk.

Revised Monographs and Patient Handouts

Highlights of key changes and/or updates to the Monographs, Patient Handouts and Chemotherapy Preparation and Stability Chart (CPSC) are listed below:

Palbociclib Monograph:

- *Dosing* – renal dosing updated

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. Protocol codes for treatment requiring BC Cancer Compassionate Access Program approval are prefixed with the letter "U".

New Protocols, PPPOs and Patient Handouts (Affected Documents are Checked)

CODE	Protocol	PPPO	Patient Handout	Protocol Title
USMAVIPNI	☑	☑	☑	Treatment of Unresectable or Metastatic Melanoma using Ipilimumab and Nivolumab

Revised Protocols, PPPOs and Patient Handouts (Affected Documents are Checked)

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
BRAJZOL2	☑	☑	☐	*Eligibility and dosing clarified*	Adjuvant Treatment of Post-Menopausal Women using 3-Monthly Zoledronic Acid
BRAJZOL5	☑	☑	☐	*Eligibility and dosing clarified*	Adjuvant Treatment of Post-Menopausal Women using 6-Monthly Zoledronic Acid
UBRAVPALAI	☑	☑	☐	*Dispensing quantity, renal dosing clarified*	Therapy of Advanced Breast Cancer using Palbociclib and Aromatase Inhibitor with or without LHRH Agonist
CNAJTZRT	☑	☐	☐	*Precautions clarified*	Concomitant (Dual Modality) and Adjuvant Temozolomide for Newly Diagnosed Malignant Gliomas with Radiation
CNELTZRT	☑	☐	☐	*Precautions clarified*	Treatment of Elderly Newly Diagnosed Glioma Patient with Concurrent and Adjuvant Temozolomide and Radiation Therapy
UGILAN	☑	☑	☑	*Dosing clarified*	Symptomatic Management of Functional Carcinoid and Neuroendocrine Tumors of the GI Tract using Lanreotide (SOMATULINE AUTOGEL)
GOCXCAD	☑	☐	☐	*Contact Physician, Pharmacist and Institution name updated*	Treatment of Advanced/Recurrent Non-Small Cell Cancer of the Cervix with Carboplatin and Docetaxel in Ambulatory Care Settings
GOOVCADX	☑	☐	☐	*Contact Physician, Pharmacist and Institution name updated*	Primary Treatment of Visible Residual (Extreme Risk) Invasive Epithelial Ovarian Cancer using Carboplatin and Docetaxel
ULYOBBEND	☑	☑	☐	*Minor typo corrected*	Treatment of Rituximab-Refractory Follicular Lymphoma (FL) with Obinutuzumab in combination with Bendamustine
ULYRICE	☑	☑	☐	*Premedication clarified*	Treatment of Relapsed or Refractory Advanced Stage Aggressive B-Cell Non-Hodgkin's Lymphoma with Ifosfamide, Carboplatin, Etoposide and Rituximab
UMYCARLD	☑	☐	☐	*Exclusions clarified*	Therapy of Multiple Myeloma using Carfilzomib, Lenalidomide with Dexamethasone
UMYDARBD	☑	☑	☐	*Tests updated*	Treatment of Relapsed and Refractory Multiple Myeloma with Daratumumab in Combination with Bortezomib and Dexamethasone with or without Cyclophosphamide
UMYDARLD	☑	☑	☐	*Tests updated*	Treatment of Relapsed and Refractory Multiple Myeloma with Daratumumab in Combination with Lenalidomide and Dexamethasone
MYZOL	☐	☑	☐	*Dosing clarified*	Treatment of Multiple Myeloma with Zoledronic Acid

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)					
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Changes**	**Protocol Title**
USATEMBEV	☐	☑	☐	*Lab tests clarified*	Therapy for Advanced Solitary Fibrous Tumours and Hemangiopericytoma using Temozolomide and Bevacizumab
SAVDC	☑	☑	☐	*Treatment option revised*	Adjuvant Therapy for Rhabdomyosarcoma using Vincristine, Dactinomycin and Cyclophosphamide
SCIMMUNE	☑	☐	☐	*Prednisone dosing for enterocolitis clarified*	Management of Immune-Mediated Adverse Reactions to Checkpoint Inhibitors Immunotherapy
USMAVFIPI	☑	☐	☐	*Eligibility and institutional name updated*	First-Line Treatment of Unresectable or Metastatic Melanoma using Ipilimumab
USMAVIPI	☑	☐	☐	*Eligibility and institutional name updated*	Treatment of Unresectable or Metastatic Melanoma using Ipilimumab
USMAVNIV	☑	☐	☐	*Eligibility updated*	Treatment of Unresectable or Metastatic Melanoma using Nivolumab
USMAVNIV4	☑	☐	☐	*Eligibility updated*	Treatment of Unresectable or Metastatic Melanoma using 4-Weekly Nivolumab
USMAVPEM	☑	☐	☐	*Eligibility updated*	Treatment of Unresectable or Metastatic Melanoma using Pembrolizumab

Website Resources and Contact Information

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Oncology Drug Information	604-877-6275		druginfo@bccancer.bc.ca
Nurse Educators	604-877-6000 x 672638		nursinged@bccancer.bc.ca
Library/Cancer Information	604-675-8003 Toll Free 888-675-8001 x 8003		requests@bccancer.bc.ca
Pharmacy Professional Practice	604-877-6000 x 672247		mlin@bccancer.bc.ca
Provincial Professional Practice Nursing			BCCancerPPNAdmin@ehcnet.phsa.ca
OSCAR	888-355-0355	604-708-2051	oscar@bccancer.bc.ca
Compassionate Access Program (CAP)	604-877-6277	604-708-2026	cap_bcca@bccancer.bc.ca
Pharmacy Oncology Certification	250-712-3900 x 686820		rxchemocert@bccancer.bc.ca
BC Cancer-Abbotsford	604-851-4710 Toll Free 877-547-3777		
BC Cancer-Prince George (Centre for the North)	250-645-7300 Toll Free 888-775-7300		
BC Cancer-Surrey	604-930-2098 Toll Free 800-523-2885		
BC Cancer-Kelowna	250-712-3900 Toll Free 888-563-7773		
BC Cancer-Vancouver	604-877-6000 Toll Free 800-663-3333		
BC Cancer-Victoria	250-519-5500 Toll Free 800-670-3322		

Editorial Review Board