Systemic Therapy Update

BC Cancer Agency
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For Health Professionals Who Care For Cancer Patients

Inside This Issue:

EDITOR'S CHOICE

NEW PROGRAMS

The BCCA Provincial Systemic Therapy Program has approved the following new programs effective 1 February 2017:

Lymphoma:

Brentuximab Vedotin for Adjuvant Treatment Post-Transplantation for Hodgkin Lymphoma (ULYAJBV) – Previously, relapse of Hodgkin Lymphoma (HL) following autologous stem cell transplant (ASCT) was generally managed by palliative care. Less than 20% of patients survive beyond 5 years, and less than 5% are ultimately cured of their lymphoma. In a recent randomized, phase III trial (AETHERA), brentuximab vedotin demonstrated superior median progression-free survival (42.9 mo vs. 24.1 mo [HR 0.57, 95% CI 0.40-0.81]) in 329 patients given high-dose chemotherapy and ASCT for relapsed HL.[1] At 2 years, 65% of patients who received brentuximab vedotin were disease-free, compared to 45% in the placebo arm. This benefit was sustained through 4 years of follow-up, and signifies the curative potential of brentuximab vedotin in a disease that was previously deemed largely incurable.[2] Overall, this treatment was well tolerated, with the most frequent grade 3 or higher adverse effects being peripheral neuropathy and neutropenia. Patients eligible for treatment will require a BCCA Compassionate Access Program (CAP) approval.

Romidepsin for Relapsed or Refractory Peripheral T-Cell Lymphoma (ULYROMI) – Peripheral T-Cell Lymphoma (PTCL) is a rare and aggressive form of non-Hodgkin lymphoma. Previously, patients with

EDITOR'S CHOICE

relapsed or refractory disease would be offered high-dose chemotherapy and autologous stem cell transplant (ASCT), or palliative care. Romidepsin is now available as another treatment option after failing at least one line of chemotherapy. In two open-label, phase II, single-arm trials involving 131 and 47 patients, respectively, romidepsin was associated with overall response rates between 25% and 38%, a median duration of response ranging from 9 to 28 months, and a median progression-free survival of 4 months.[3-4] Romidepsin was associated with significant toxicities, with 47% of patients requiring dose interruptions and 11% requiring dose reductions.[5] The most common toxicities included nausea, vomiting, diarrhea, fatigue and myelosuppression. For further information about the pharmacology and toxicities of romidepsin, please see the Cancer Drug Manual section below. Patients eligible for treatment will require a BCCA Compassionate Access Program (CAP) approval.

Melanoma:

Imatinib for the Treatment of Advanced C-Kit Positive Melanoma (USMAVI) – Approximately 40% to 60% of advanced melanoma are BRAF mutation-positive. In non-BRAF mutated tumours, a subset may carry the c-Kit mutation. C-Kit mutations occur in about 30% of patients with the following three subtypes of melanoma – chronic sun damage, acral and mucosal; they are not seen in patients with non-chronic sun damage melanoma.

BCCA now offers c-Kit mutation testing in patients with advanced BRAF mutation-negative melanoma as part of The OncoPanel Pilot (TOP) study. Those testing positive for c-Kit aberrations are eligible to receive imatinib which targets multiple tyrosine kinase receptors including c-kit. In several studies, imatinib resulted in a disease control rate of 36% to 53%, a median progression-free survival of 4 to 9 months, and a median overall survival of 10 to 15 months.[6-8] Patients eligible for treatment will require a BCCA Compassionate Access Program (CAP) approval.

References:

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3. Coiffier B, Pro B, Prince HM, et al. Romidepsin for the treatment of relapsed/refractory peripheral T-cell lymphoma: pivotal study update demonstrates durable responses. J Hematol Oncol 2014;7:11.
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5. Coiffier B, Pro B, Prince M, et al. Results from a pivotal, open-label, phase II study of romdepsin in relapsed or refractory peripheral T-cell lymphoma after prior systemic therapy. J Clin Oncol 2012;30:631-636.
6. Carvajal RD, Antonescu CR, Wolchok JD, et. al. KIT as a therapeutic target in metastatic melanoma. JAMA 2011;305:2327-2334.
7. Guo J, Si L, Kong Y, et. al. Phase II, open-label, single-arm trial of imatinib mesylate in patients with metastatic melanoma harboring a c-Kit mutation or amplification. J Clin Oncol 2011;29:2904-2909.
8. Hodi FS, Corless CL, Giobbie-Hurder A, et al. Imatinib for melanomas harboring mutationally activated or amplified KIT arising on mucosal, acral, and chronic sun damaged skin. J Clin Oncol 2013;31:3182-3190.

DRUG UPDATE

FILGRASTIM BIOSIMILAR (GRASTOFIL®) – NEW BC PHARMACARE BENEFIT

Effective January 31st, BC PharmaCare has approved the biosimilar formulation of filgrastim (GRASTOFIL®) as a benefit drug through the Special Authority program. GRASTOFIL® is biologically similar to the reference

DRUG UPDATE

product, NEUPOGEN®, but the two products are NOT interchangeable. Indications for PharmaCare coverage will remain the same. Only GRASTOFIL® will be funded for all new approvals and re-approvals of filgrastim. Hence, physicians must specify either "filgrastim" or "Grastofil" on the prescription, not "Neupogen". Patients who had previously received a Special Authority approval for filgrastim prior to January 31st will continue to receive coverage for NEUPOGEN® until the Special Authority coverage expiry date. PharmaCare will also cover GRASTOFIL® for these patients should they choose to switch to the biosimilar agent (a new Special Authority submission is not required).

The *BCCA Filgrastim (G-CSF) Usage Form* previously found on the BCCA Systemic Therapy website is no longer in effect. It has been replaced by a link to the PharmaCare Special Authority website from which clinicians can now access the new *Filgrastim Special Authority Request Form*. In addition, patients may now be enrolled into the **Apobiologix ANSWERS™ Program** for additional coverage of GRASTOFIL®, which has replaced the Amgen VICTORY® Program previously used for NEUPOGEN® coverage. For further information about the PharmaCare coverage of GRASTOFIL®, please see the PharmaCare Special Authority website.

For inpatient usage of filgrastim, BCCA will allow a transition period of 3 months within which both GRASTOFIL® and NEUPOGEN® will be covered. This transition period will allow centres to utilize their existing stock of NEUPOGEN®. Thereafter, BCCA will exclusively cover GRASTOFIL® for the same indications approved by PharmaCare.

MEDICATION SAFETY CORNER

REVISED: BCCA PATIENT HANDOUTS FOR SAFE HANDLING IN THE HOME

The BCCA Provincial Systemic Therapy Program has revised two Safe Handling Patient Handouts titled – Guidelines for Disposal of Sharp Medical Supplies and Guidelines for Handling Cancer Drugs and Body Fluids in the Home. The impetus for the revisions was to align BCCA recommendations with existing safe handling standards from various regulatory bodies, and to address frequently asked questions from cancer patients and caregivers. The revised handouts are intended to optimize safe handling practices in the home setting in order to reduce the risk of unintended cancer drug exposure while minimizing unnecessary anxiety for patients, family members and caregivers.

Key updates to the **Guidelines for Disposal of Sharp Medical Supplies (Sharps)** include:

- All sharp medical supplies must be discarded in sharps disposal containers – previous suggestion to use household plastic containers has been removed
- Sharps disposal containers must be labelled as CYTOTOXIC, HAZARDOUS or CHEMOTHERAPY if the supplies were used to administer cancer drugs
- Sharps disposal containers can no longer be discarded in regular household garbage

Key updates to the **Guidelines for Handling Cancer Drugs and Body Fluids in the Home** include:

- Specific instructions for patients, family members and caregivers in the handling of cancer drugs and body fluids, and in managing accidental exposure
- Recommendation that patients are no longer required to wear gloves when handling cancer drugs and

Medication Safety Corner

body fluids as they have already been exposed to the drug

- New recommendation on requiring safe handling precautions only during the "special handling period" (usually 48 hours after exposure to cancer drugs)
  - The 48-hour window has been established by various regulatory bodies, including the Occupational Safety and Health Administration, as the recommended precautionary period to be followed in an institutional setting. This timeframe has been adopted for the home setting in the current BCCA Patient Handout because no regulatory standards are currently established for the non-institutional care setting.
- Information on safe bodily contacts such as hugging, kissing and intercourse

Submitted by:
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Cancer Drug Manual

New Monographs and Patient Handouts

The **Romidepsin** Interim Monograph has been expanded to a **Full Monograph**, and a new **Patient Handout** has been created. Expert review was provided by Dr. Kerry Savage (medical oncologist) and Linda Hamata (pharmacist) of the BCCA Lymphoma Tumour Group. Romidepsin is a bicyclic peptide which acts as a potent and selective inhibitor of class I and II histone deacetylase (HDAC). HDAC inhibitors induce acetylation of histones and other proteins, resulting in tumour suppressor gene transcription, growth inhibition, cell cycle arrest and apoptosis.

Highlights in the Monograph and Patient Handout include:

- Infections have been reported during and up to 30 days following treatment. Reactivation of hepatitis B, cytomegalovirus, and Epstein-Barr infections has also been reported.
- In animal studies, romidepsin was embryocidal and teratogenic. Females of childbearing potential are advised to use contraception during treatment and for 8 weeks after discontinuation of treatment. Because romidepsin binds to estrogen receptors and may reduce the effectiveness of estrogen-containing contraceptives, patients should be advised to use alternate methods of contraception.

Revised Monographs and Patient Handouts

Highlights of key changes and/or updates to the Monographs and Patient Handouts are listed below:

Filgrastim Monograph:

- *Common Trade Name, Cautions*, and *Supply and Storage* sections – added information related to the new biosimilar formulation (GRASTOFIL®)

Pegylated Liposomal Doxorubicin Monograph:

- *Parenteral Administration* table: updated infusion rate

Cancer Drug Manual

The following M**onographs** have been updated to include the maximum cumulative dose of *mitoxantrone* in the *Cumulative Dose* table under the *Side Effects* section:

- **Daunorubicin**
- **Doxorubicin**
- **Epirubicin**
- **Idarubicin**
- **Mitoxantrone**

Benefit Drug List

New Programs

Effective 1 February 2017, the following BCCA treatment programs have been added to the BCCA Benefit Drug List:

Protocol Title	Protocol Code	Benefit Status
Adjuvant Therapy Post-Autologous Stem Cell Transplant (ASCT) for Hodgkin Lymphoma Using Brentuximab Vedotin	ULYAJBV	Restricted
Treatment of Relapsed or Refractory Peripheral T-Cell Lymphoma (PTCL) with Romidepsin	ULYROMI	Restricted
Treatment of Advanced C-Kit Positive Melanoma Using iMAtinib	USMAVI	Restricted

List of New and Revised Protocols, Pre-Printed Orders and Patient Handouts

BC Cancer Agency 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 BCCA 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
ULYAJBV	☑	☑	☐	Adjuvant Therapy Post-Autologous Stem Cell Transplant (ASCT) for Hodgkin Lymphoma Using Brentuximab Vedotin
ULYROMI	☑	☑	☐	Treatment of Relapsed or Refractory Peripheral T-Cell Lymphoma (PTCL) with Romidepsin

NEW PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)				
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Protocol Title**
USMAVI	☑	☑	☐	Treatment of Advanced C-Kit Positive Melanoma Using iMAtinib

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)					
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Changes**	**Protocol Title**
BRAJACTG	☐	☐	☑	*Brand name of filgrastim (NEUPOGEN®) deleted*	Adjuvant Therapy for Breast Cancer Using Dose Dense Therapy: DOXOrubicin and Cyclophosphamide Followed by PACLitaxel
BRAJACTTG	☐	☐	☑	*Brand name of filgrastim (NEUPOGEN®) deleted*	Adjuvant Therapy for Breast Cancer Using Dose Dense Therapy: DOXOrubicin and Cyclophosphamide Followed by PACLitaxel and Trastuzumab
UBRAJDAC	☐	☐	☑	*Brand name of filgrastim (NEUPOGEN®) deleted*	Adjuvant Therapy for Breast Cancer Using Cyclophosphamide, DOXOrubicin and DOCEtaxel
BRAJDC	☐	☐	☑	*Brand name of filgrastim (NEUPOGEN®) deleted*	Adjuvant Therapy for Breast Cancer Using DOCEtaxel and Cyclophosphamide
BRLAACD	☐	☐	☑	*Brand name of filgrastim (NEUPOGEN®) deleted*	Treatment of Locally Advanced Breast Cancer Using DOXOrubicin and Cyclophosphamide Followed by DOCEtaxel
UGISORAF	☑	☐	☐	*TALLman lettering formatted*	Therapy for Advanced Hepatocellular Carcinoma Using SORAfenib
GOENDCAT	☑	☐	☐	*Eligibility clarified*	Treatment of Primary Advanced or Recurrent Endometrial Cancer using CARBOplatin and PACLitaxel
GOOVDDCAT	☑	☐	☐	*Hepatic dose adjustment modified*	Treatment of Advanced Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Carcinoma Using CARBOplatin and Weekly PACLitaxel
GOTDEMACO	☑	☑	☐	*Use of in-line filter specified*	Therapy for High-Risk Gestational Trophoblastic Neoplasia (GTN) Using Etoposide, Methotrexate, Leucovorin (Folinic Acid), DACTINomycin, Cyclophosphamide and vinCRIStine
GOTDLR	☑	☐	☐	*Urine pH test frequency specified*	Therapy for Low-Risk Gestational Trophoblastic Neoplasia (GO 94 02) Using Methotrexate, Leucovorin and Actinomycin D
UGUSORAF	☑	☐	☐	*TALLman lettering formatted*	Palliative Therapy for Renal Cell Carcinoma Using SORAfenib

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)					
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Changes**	**Protocol Title**
UHNLADCF	☐	☑	☑	*Brand name of filgrastim (NEUPOGEN®) deleted*	Treatment of Locally Advanced Squamous Cell Carcinoma of the Head and Neck with DOCEtaxel, CISplatin and Infusional Fluorouracil
LYABVD	☐	☐	☑	*Brand name of filgrastim (NEUPOGEN®) deleted*	Treatment of Hodgkin's disease with DOXOrubicin, Bleomycin, vinBLAStine and Dacarbazine
LYCHOPR	☐	☐	☑	*Brand name of filgrastim (NEUPOGEN®) deleted*	Treatment of Lymphoma with DOXOrubicin, Cyclophosphamide, vinCRIStine, predniSONE and riTUXimab

Website Resources and Contact Information

Website Resources	WWW.BCCANCER.BC.CA
Systemic Therapy Update	www.bccancer.bc.ca/health-professionals/professional-resources/systemic-therapy/systemic-therapy-update
Reimbursement & Forms: Benefit Drug List, Class II, Compassionate Access Program	www.bccancer.bc.ca/health-professionals/professional-resources/systemic-therapy
Cancer Drug Manual	www.bccancer.bc.ca/health-professionals/professional-resources/cancer-drug-manual
Cancer Management Guidelines	www.bccancer.bc.ca/health-professionals/professional-resources/cancer-management-guidelines
Cancer Chemotherapy Protocols, Pre-Printed Orders, Protocol Patient Handouts	www.bccancer.bc.ca/health-professionals/professional-resources/chemotherapy-protocols
Systemic Therapy Program Policies	www.bccancer.bc.ca/health-professionals/professional-resources/systemic-therapy
CON Pharmacy Educators	www.bccancer.bc.ca/health-professionals/professional-resources/pharmacy

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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
Nursing Professional Practice	604-877-6000 x 672623		ilundie@bccancer.bc.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 Chemotherapy Certification	250-712-3900 x 686741		rxchemocert@bccancer.bc.ca
BCCA-Abbotsford Centre	604-851-4710 Toll Free 877-547-3777		
BCCA-Centre for the North	250-645-7300 Toll Free 888-775-7300		
BCCA-Fraser Valley Centre	604-930-2098 Toll Free 800-523-2885		
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