Systemic Therapy Update

BC Cancer Agency
CARE + RESEARCH
An agency of the Provincial Health Services Authority

October 2017
Volume 20, No. 10

For Health Professionals Who Care For Cancer Patients

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EDITOR'S CHOICE

NEW PROGRAMS

Effective 1 October 2017, the BCCA Provincial Systemic Therapy Program has approved the following programs.

Gastrointestinal:

Capecitabine as Second Line Treatment for Advanced Pancreatic Cancer (GIPAVCAP) – The BCCA Gastrointestinal Tumour Group is introducing capecitabine as a second-line treatment option for patients with metastatic or unresectable pancreatic cancer. Currently, there are no preferred treatments for this population. Capecitabine has evidence of activity in pancreatic cancer.[1] In a phase III study, second-line treatment with capecitabine after gemcitabine was shown to be non-inferior to using gemcitabine after capecitabine.[2] In another prospective, single-center study, second-line capecitabine after first-line treatment with gemcitabine was associated with disease stabilization in 39% of patients.[3] Finally, the US NCCN guidelines also recommend that fluoropyrimidine-based chemotherapy regimens are acceptable second-line treatments for patients with advanced disease who have received prior gemcitabine-based therapies.[4]

References:

1. Cartwright TH, et al. Phase II study of oral capecitabine in patients with advanced or metastatic pancreatic cancer. J Clin Oncol 2002;20(1):160-4.
2. Heinemann V, et al. Gemcitabine plus erlotinib followed by capecitabine versus capecitabine plus erlotinib followed by gemcitabine in advanced pancreatic cancer. Gut 2013;62(5):751-9.
3. Boeck S, et al. Oral capecitabine in gemcitabine-pretreated patients with advanced pancreatic cancer Oncology. 2007;73(3-4):221-7.
4. Tempero MA, et al. Pancreatic adenocarcinoma, version 2.2014: featured updates to the NCCN guidelines J Natl Compr Canc Netw. 2014;12(8):1083-93.

EDITOR'S CHOICE

Gynecology

Bevacizumab for Platinum-Resistant Ovarian Cancer (UGOOVBEVLD, UGOOVBEVP) – The BCCA Gynecologic Oncology Group has introduced the use of bevacizumab in combination with standard single agent chemotherapy for patients with advanced platinum-resistant ovarian cancer. Protocols and PPPOs have been developed for addition of bevacizumab to paclitaxel and pegylated liposomal doxorubicin (CAELYX). In a phase III trial, the addition of bevacizumab to chemotherapy has been shown to improve progression free survival (6.7 vs. 3.4 mos) and a trend towards better overall survival (16.6 vs. 13.3 mos). The toxicity profile of bevacizumab was comparable to that seen with its use in other tumour sites.[1]

References:

1. Pujade-Lauraine E, et al. Bevacizumab combined with chemotherapy for platinum-resistant recurrent ovarian cancer: the AURELIA open-label randomized phase III trial. J Clin Oncol 2014;32(13):1302-8.

Head and Neck

Lenvatinib for Radioiodine-Refractory Differentiated Thyroid Cancer (UHNOTLEN) – The BCCA Head and Neck Tumour Group has introduced lenvatinib as a new treatment option for patients with locally recurrent or metastatic, radioiodine-refractory differentiated thyroid cancer. In a phase III trial, response rate was 65% (4 CR, 165 PR) vs. 1.5% in the placebo arm.[1] Median progression free survival was 18.3 vs. 3.6 mos. Median overall survival was not reached. Treatment related adverse effects of any grade occurred in more than 40% of patients in the lenvatinib arm, with the most common side effects being hypertension, diarrhea, fatigue/asthenia, decreased appetite, decreased weight, and nausea. Overall, 14.2% of patients dropped out of the lenvatinib arm due to adverse effects compared to 2.3% of patients in the placebo arm.

References:

1. Schlumberger M, Tahara M, Wirth LJ, et al. Lenvatinib versus placebo in radioiodine-refractory thyroid cancer. N Engl J Med 2015;372:621-30.

Skin and Melanoma

Imiquimod as Topical Immunotherapy for In-Transit Melanoma Metastases, Cutaneous Lymphoma, Basal Cell Carcinoma (SMIMI) – the BCCA Skin and Melanoma Tumour Group has introduced imiquimod for several skin-related tumours. The efficacy of imiquimod is supported by a number of small case series reports.[1-9] Therefore, it should be used as a last resort when radiation or systemic chemotherapy is not suitable. Note that imiquimod is only reimbursable when prescribed by BC Cancer Agency dermatologic oncology physicians.

References:

1. Bong AB, et al. Imiquimod, a topical immune response modifier, in the treatment of cutaneous metastases of malignant melanoma. Dermatology. 2002;205(2):135–8.
2. Steinmann A, et al. Topical imiquimod treatment of a cutaneous melanoma metastasis. J Am Acad Dermatol 2000;43(3):0555–6.
3. Wolf IH, et al. Topical imiquimod in the treatment of metastatic melanoma to skin. 2003;139(3):273–6.
4. Suchin K J-HJ. Treatment of stage IA cutaneous t-cell lymphoma with topical application of the immune response modifier imiquimod. 2002;138(9):1137–9.
5. Didona B, et al. Primary cutaneous CD30+ T-cell lymphoma responsive to topical imiquimod (Aldara®). Br J Dermatol 2004;150(6):1198–201.
6. Stavrakoglou A, et al. Successful treatment of primary cutaneous follicle centre lymphoma with topical 5% imiquimod. Br J Dermatol 2007;157(3):620–2.
7. Garcia-Martin E, et al. Comparison of imiquimod 5% cream versus radiotherapy as treatment for eyelid basal cell carcinoma. Br J Ophthalmol. 2011;95(10):1393–6.
8. Schulze H, et al. Imiquimod 5% cream for the treatment of superficial basal cell carcinoma: results from a randomized vehicle-controlled phase III study in Europe. Br J Dermatol 2005;152(5):939–47.
9. Lacarrubba F, et al. Successful treatment and management of large superficial basal cell carcinomas with topical imiquimod 5% cream: A case series and review. J Dermatol Treat 2011;22(6):353–8.

Drug Update

First Nations Health Authority Transitions to PharmaCare

On October 1, 2017, First Nations Health Authority (FNHA) clients will join BC PharmaCare. For FNHA clients who received benefits through Health Canada's Non-Insured Health Benefits (NIHB) program, they will be eligible for coverage of prescribed medications and pharmacy services with PharmaCare. PharmaCare Plan W (Wellness) is the PharmaCare plan designed for First Nations in BC.

FNHA clients will follow the same protocols as other BC residents for cancer care. For FNHA clients with a cancer diagnosis who are not currently enrolled with the BC Cancer Agency, they should visit their doctor as soon as possible. While clients are going through this enrollment process, a six-month transition period is in place to ensure continuity of care. Moving forward, FNHA clients should have their cancer medication prescriptions filled at a BC Cancer Agency regional centre pharmacy or a BC hospital pharmacy, provided that they are BC Cancer Agency patients being prescribed cancer medications on the BC Cancer Agency drug benefit list for the treatment of cancer, and fit the eligibility criteria.

Information about the PharmaCare transition is available on the website www.FNHA.ca/pharmacare. For further details, contact FNHA Health Benefits Support at 1.855.550.5454 or HealthBenefits@fnha.ca.

Revised Drug Registration Form

A revised electronic form is now available at www.bccancer.bc.ca/health-professionals/clinical-resources/systemic-therapy. This is the form that needs to be completed to obtain a BCCA registration number in order to receive funding/reimbursement for all eligible cancer drugs on the BCCA Drug Benefit List.

Benefit Drug List

New Programs

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

Protocol Title	Protocol Code	Benefit Status
Second line treatment of metastatic or unresectable pancreatic adenocarcinoma using **capecitabine**	**GIPAVCAP**	Class I
Treatment of platinum resistant epithelial ovarian cancer with **bevacizumab** and **paclitaxel**	**UGOOVBEVP**	Restricted
Treatment of platinum resistant epithelial ovarian cancer with **bevacizumab** and **pegylated liposomal doxorubicin (CAELYX)**	**UGOOVBEVLD**	Restricted
Therapy for locally recurrent or metastatic, RAI-refractory differentiated thyroid cancer using **lenvatinib**	**UHNOTLEN**	Restricted
Topical immunotherapy for in-transit melanoma metastases, cutaneous lymphoma, basal cell carcinoma using **imiquimod**	**SMIMI**	Class I

CANCER DRUG MANUAL

NEW MONOGRAPHS AND PATIENT HANDOUTS

Lenvatinib Monograph and **Patient Handout** have been developed with expert review provided by Dr. Cheryl Ho (medical oncologist) and Karen Mason (pharmacist) from the BCCA Head and Neck Tumour Group. Lenvatinib is an oral, multi-kinase inhibitor of vascular endothelial-derived growth factor receptors, fibroblast growth factor receptors, platelet derived growth factor receptor-α, KIT, and RET. Lenvatinib inhibits tyrosine kinases known to play a role in pathogenic angiogenesis, tumour growth, and cancer progression. Lenvatinib is used in the treatment of thyroid cancer. Usual starting dose is 24 mg daily taken continuously, with or without food. Starting doses are reduced for renal or hepatic impairment. Common adverse events include hypertension, proteinuria, diarrhea, nausea/vomiting, QT prolongation, and nosebleeds. Blood pressure should be controlled prior to starting treatment and monitored closely throughout treatment. Diarrhea and vomiting may lead to electrolyte disturbances and should be managed early with standard anti-diarrheal therapy, anti-emetics, and oral hydration to prevent renal impairment.

Imiquimod Monograph and **Patient Handout** have been developed with expert review provided by Dr. Vincent Ho, BCCA Dermatologic Oncology Department Head, and Robert Tillmanns (pharmacist) from the BCCA Skin and Melanoma Tumour Group. Imiquimod 5% topical cream is an immune response modifier that stimulates innate and cell-mediated immunity to induce anti-tumour effects. It is used to treat basal cell carcinoma, cutaneous lymphoma and in-transit melanoma metastases. Imiquimod application frequency and duration of treatment is individualized depending on indication for use, patient tolerance, and response to therapy. The most frequent adverse effects are mild to moderate local inflammatory reactions at the application site. Rarely, systemic flu-like symptoms (e.g., fever, malaise, nausea, rigors) may accompany or precede local inflammatory reactions. In the event of a severe skin reaction, patients may require a rest period until the skin is healed enough to continue on treatment.

The following monographs and patient handouts for drugs currently not funded by BCCA are being made available for reference:

Blinatumomab Monograph and **Patient Handout** have been developed with expert review provided by Dr. Yasser Abou Mourad and Katie Lacaria (pharmacist) of the Leukemia/BMT Program of British Columbia. Blinatumomab is a bispecific T cell engaging (BiTE) antibody construct used to treat Philadelphia chromosome-negative relapsed or refractory B precursor acute lymphoblastic leukemia. Blinatumomab is given by continuous infusion for four weeks, followed by a 2 week treatment-free interval, for a total of five cycles. Side effects include infusion reactions, cytokine release syndrome, tumour lysis syndrome, serious infections, and neurologic events. To prevent and treat infusion reactions, patients are hospitalized for the first nine days of cycle 1 and the first two days of cycle 2. Premedication with dexamethasone is used to decrease the risk of CRS and TLS.

Carfilzomib Monograph and **Patient Handout** have been developed with expert review provided by Dr. Kevin Song (medical oncologist) and Linda Hamata (pharmacist) of the BC Cancer Agency Lymphoma Tumour Group. Carfilzomib is an irreversible inhibitor of the 20S core of the 26S proteasome. Proteasome inhibition causes accumulation of polyubiquinated proteins, which induces cell cycle arrest and apoptosis. Carfilzomib is used in the treatment of multiple myeloma. Dosing is protocol dependent. To prevent infusion reactions, carfilzomib is given at a reduced dose for the first two infusions, in addition to dexamethasone premedication prior to each infusion. Common side effects are anemia, thrombocytopenia,

hypertension, dyspnea, and diarrhea. Less common, but more severe side effects include cases of acute renal failure and cardiac failure. Adequate oral and intravenous hydration prior to treatment is necessary to prevent renal toxicity.

Olaparib Monograph and **Patient Handout** have been developed with expert review provided by Dr. Anna Tinker (medical oncologist) and James Conklin (pharmacist) from the BCCA Gynecologic Oncology Tumour Group. Olaparib is a poly (ADP-ribose) polymerase (PARP) inhibitor that has demonstrated activity in platinum-sensitive, BRCA-mutated high grade serous epithelial ovarian, fallopian tube, and primary peritoneal cancers. Usual dose is 400 mg (8 x 50 mg capsules) twice daily, with or without food. Grapefruit and grapefruit juice should be avoided during treatment. Dose modifications may be necessary when given with potent CYP3A inhibitors and with impaired renal function. The most common side effects are nausea, fatigue, and anemia. There are rare incidences (<1%) of patients developing pneumonitis and MDS/AML.

Palbociclib Monograph and **Patient Handout** have been developed with expert review provided by Dr. Sophie Sun (medical oncologist) and Khushminder Rai (pharmacist) of the BCCA Breast Tumour Group. Palbociclib is an oral, reversible, small-molecule inhibitor of cyclin-dependant kinases 4 and 6. It is used in the treatment of breast cancer. Usual daily dose is 125 mg orally for 21 consecutive days in a 28 day cycle. Palbociclib is taken with food. Grapefruit and grapefruit juice should be avoided. The most common treatment-emergent adverse effect is neutropenia; however the incidence of neutropenic fever is low. Neutropenia caused by palbociclib is self-limited and characterized by recovery after a dose interruption or delay. Other adverse reactions include infections, pulmonary embolism, anemia, fatigue, and mild GI disturbances.

REVISED MONOGRAPHS AND PATIENT HANDOUTS

Idelalisib Patient Handout

- *Side Effect table:* revised instructions regarding loperamide dosing

EDITORIAL BOARD MEMBERSHIP

The **Cancer Drug Manual Team** would like to welcome **Jennifer Cowie** to the Cancer Drug Manual Editorial Board. Jennifer is the Pharmacy Professional Practice Leader for BC Cancer Agency Abbotsford Centre. Welcome Jennifer!

The **Cancer Drug Manual Team** would also like to bid farewell to **Dennis Jang** and **Fran Topp** (both from BCCA Vancouver Centre) as they step down from the Cancer Drug Manual Editorial Review Board to pursue other opportunities. Thank you for your many contributions to the Cancer Drug Manual during your service on the Board.

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
GIPAVCAP	☑	☑	☑	Second line treatment of metastatic or unresectable pancreatic adenocarcinoma using capecitabine
UGOOVBEVLD	☑	☑	☐	Treatment of platinum resistant epithelial ovarian cancer with bevacizumab and pegylated liposomal doxorubicin (CAELYX)
UGOOVBEVP	☑	☑	☐	Treatment of platinum resistant epithelial ovarian cancer with bevacizumab and paclitaxel
UHNOTLEN	☑	☑	☑	Therapy for locally recurrent or metastatic, RAI-refractory differentiated thyroid cancer using lenvatinib
SMIMI	☑	☑	☐	Topical immunotherapy for in-transit melanoma metastases, cutaneous lymphoma, basal cell carcinoma using imiquimod

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

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
CNAJTZRT	☑	☐	☐	*Treatment duration clarified*	Concomitant (dual modality) and adjuvant temozolomide for newly diagnosed malignant gliomas with radiation
CNELTZRT	☑	☐	☐	*Treatment duration clarified*	Treatment of elderly newly diagnosed glioma patient with concurrent and adjuvant temozolomide and radiation therapy
GOOVLDOX	☑	☑	☑	*Title, drug name, administration clarified*	Treatment of epithelial ovarian cancer relapsing after primary treatment using pegylated liposomal doxorubicin (CAELYX)
GOOVPLDC	☑	☑	☑	*Title, exclusion, drug name, administration clarified*	Treatment of epithelial ovarian cancer relapsing after primary treatment using pegylated liposomal doxorubicin (CAELYX) and carboplatin
HNLACETRT	☑	☑	☐	*Bloodwork clarified*	Combined cetuximab and radiation treatment for locally advanced squamous cell carcinoma of the head and neck
HNNAVPC	☑	☑	☐	*Paclitaxel dose modified*	Treatment of recurrent or metastatic nasopharyngeal carcinoma with carboplatin and paclitaxel
KSLDO	☑	☑	☐	*Drug name clarified*	Therapy of Kaposi's sarcoma using pegylated liposomal doxorubicin (CAELYX)

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)					
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Changes**	**Protocol Title**
LUAVAFAT	☐	☐	☑	*Dispensed quantity clarified*	First-line treatment of epidermal growth factor receptor mutation-positive advanced non-small cell lung cancer with afatinib
LUOTPERT	☐	☐	☑	*Diluent clarified*	Treatment of thymoma using cisplatin and etoposide with radiation therapy
ULYROMI	☐	☑	☐	*Lab tests clarified*	Treatment of relapsed or refractory peripheral T-cell lymphoma with romidepsin
UMYLDF	☐	☑	☐	*RevAid requirement updated*	Treatment of previously untreated multiple myeloma and not eligible for stem cell transplant using lenalidomide with low-dose dexamethasone
UMYLDREL	☑	☑	☑	*Dosing clarified, RevAid requirement and Precautions updated*	Therapy of relapsed multiple myeloma using lenalidomide with dexamethasone
UMYLENMTN	☐	☑	☐	*RevAid requirement updated*	Maintenance therapy of multiple myeloma using lenalidomide
UMYPOMDEX	☐	☑	☐	*RevAid requirement updated*	Therapy of multiple myeloma using pomalidomide with dexamethasone
UMYTHALID	☐	☑	☐	*RevAid requirement updated*	Therapy of multiple myeloma using thalidomide

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
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BCCA-Fraser Valley Centre	604-930-2098 Toll Free 800-523-2885		
BCCA-Sindi Ahluwalia Hawkins Centre for the Southern Interior	250-712-3900 Toll Free 888-563-7773		
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