Systemic Therapy Update

March 2018 Volume 21, No. 3

BC Cancer Agency CARE + RESEARCH

An agency of the Provincial Health Services Authority

For Health Professionals Who Care For Cancer Patients

Inside This Issue:

- Editor's Choice <u>New Programs</u>: Nivolumab for Squamous Cell Cancer of the Head and Neck, Ibrutinib for Mantle-Cell Lymphoma, Dose-Adjusted Chemotherapy for Aggressive Lymphoma, Treatments for Extranodal Natural Killer and T-Cell Lymphoma
- Benefit Drug List <u>New</u>: UHNAVNIV, ULYMIBRU, LYASPMEDEX, LYEPOCHR, LYSMILE, LYVIPDRT <u>Revised</u>: GOOVAI
- Communities Oncology Network OSCAR Submission Deadline
- Cancer Drug Manual <u>Revised</u>: Imatinib, Lanreotide, Temozolomide, Trastuzumab, Vemurafenib
- Provincial Systemic Therapy Program <u>Revised Policies</u>: Drug Reaction Management – Physician Coverage During Delivery of Selected Systemic Therapy Drugs (III-60)
- List of New and Revised Protocols, Provincial Pre-Printed Orders and Patient Handouts: <u>New</u>: UHNAVNIV, ULYMIBRU, LYASPMEDEX, LYEPOCHR, LYSMILE, LYVIPDRT <u>Revised</u>: UBRAJACTW, UBRAJPAM, UBRAJTW, BRAJZOL, BRAVTW, BRLATWAC, GIAJCAPOX, GIAJFL, GIAVCETIR, GIAVFL, GIAVPANI, GICAPOX, GIFFIRB, UGIFFOXPAN, GIFIRINOX, GIFOLFIRI, GIGFOLFIRI, GIPGEMABR, GIRAJCOX, GOCXAJCAT, GOENDCAD, GOENDCAT, GOOVAI, GOOVCADM, GOOVCADR, GOOVCADX, GOOVCARB, GOOVCATM, GOOVCATR, GOOVCATX, GOOVDCAT, GOOVPLDC, GUBEP, HNLAPRT, LYRMTN, OCIFN, OCMITO, SCESA, USMAVDT, USMAVTRA, SMMCCPE
- Website Resources and Contact Information

EDITOR'S CHOICE

New Programs

Effective 1 March 2018, the BC Cancer Provincial Systemic Therapy Program has approved the following programs.

Head and Neck:

Nivolumab for Advanced, Platinum-Refractory Squamous Cell Cancer of the Head and Neck (SCCHN) (UHNAVNIV) – The BC Cancer Head and Neck Tumour Group is introducing nivolumab as the new immunotherapy for patients with unresectable, recurrent or metastatic SCCHN. Compared to standard single-agent systemic therapy (methotrexate, docetaxel or cetuximab), nivolumab is associated with increased overall survival (7.5 vs. 5.1 mos). Toxicities are similar to those seen when nivolumab is used for other indications.

Reference:

Ferris RL, et al. Nivolumab for recurrent squamous-cell carcinoma of the head and neck. N Engl J Med 2016;375(19):1856-67.

Lymphoma:

EDITOR'S CHOICE

Ibrutinib for Relapsed or Refractory Mantle Cell Lymphoma (ULYMIBRU) – The BC Cancer Lymphoma Group is introducing ibrutinib as a new treatment for patients with relapsed after or refractory to standard treatments. Currently, treatment options include reuse of alkylators, gemcitabine and other palliative single agents, which are all associated with response rates lower than 30% and rarely durable response. In a phase III trial, ibrutinib was associated with increased progression free survival (14.6 vs. 6.2 mos) and response rate (72% vs. 40%), and a trend towards increased overall survival (median not reached vs. 21.3 mos), compared to temsirolimus. Although not an option in BC, temsirolimus has been shown to be comparable with other historical treatments for this population. Toxicities of ibrutinib are similar to those seen when it is used for other indications. Note that ibrutinib is given at 560 mg daily, which is a higher dose than that used in chronic lymphocytic leukemia.

Reference:

Dreyling M, et al. Ibrutinib versus temsirolimus in patients with relapsed or refractory mantle-cell lymphoma: an international, randomised, openlabel, phase 3 study. Lancet 2016;387(10020):770-8.

Dose-Adjusted Etoposide, Doxorubicin, Vincristine, Cyclophosphamide, Prednisone and Rituximab (EPOCH-R) for Aggressive Lymphoma (LYEPOCHR) – The BC Cancer Lymphoma Group is introducing EPOCH-R and intrathecal methotrexate as an inpatient protocol for patients with aggressive B-cell lymphoma with dual translocation of MYC and BCL2 (double-hit) lymphoma. These patients usually have poor prognosis when treated with the conventional LYCHOPR treatment and have been shown to have improved outcomes with more intensive regimens. Note that LYEPOCHR is a complex inpatient program that requires adequate support for the delivery of a <u>96-hour continuous infusion</u> regimen which has been designed to improve cytotoxic efficacy by optimizing the delivery schedule of chemotherapy agents for highly proliferative lymphomas.¹⁻³

Reference:

- 1. Dunleavy K, et al. Low-intensity therapy in adults with Burkitt's lymphoma. N Engl J Med 2013;369(20):1915-25.
- 2. Dunleavy K, et al. Dose-adjusted EPOCH-rituximab therapy in primary mediastinal B-cell lymphoma. N Engl J Med 2013;369(20):1408-16.
- 3. Petrich AM, et al. Impact of induction regimen and stem cell transplantation on outcomes in double-hit lymphoma: a multicenter retrospective analysis. Blood 2014;124(15):2354-61.

Treatments of Extranodal Natural Killer (NK) and T-Cell Lymphoma (LYSMILE, LYVIPDRT, LYASPMEDEX) -

The BC Cancer Lymphoma Group is introducing three regimens for the treatment of this patient population. Nasal-type, extranodal NK/T-cell lymphoma is a rare but aggressive disease with poor prognosis. Initial treatment of the localized disease is concurrent radiation and weekly cisplatin followed by etoposide, ifosfamide, cisplatin and dexamethasone (LYVIPDRT).¹ Patients with disseminated, relapsed or refractory disease should be treated with LYSMILE, which involves dexamethasone, methotrexate, ifosfamide, asparaginase and etoposide.²⁻⁴ For patients who are not candidates for this intensive regimen, LYASPMEDEX is an alternative that involves asparaginase, methotrexate and dexamethasone.⁵ Both LYSMILE and LYASPMEDEX are complex inpatient programs that need to be delivered with adequate support.

Reference:

- 1. Kim SJ, et al. Phase II trial of concurrent radiation and weekly cisplatin followed by VIPD chemotherapy in newly diagnosed, stage IE to IIE, nasal, extranodal NK/T-cell lymphoma. J Clin Oncol 2009;27:6027-6032.
- 2. Yamaguchi M, et al. Phase II study of SMILE chemotherapy for newly diagnosed stage IV, relapsed, or refractory extranodal natural killer (NK)/Tcell lymphoma, nasal type: the NK-Cell Tumor Study Group Study. J Clin Oncol 2011;29:4410-6.
- 3. Kwong YL, et al. SMILE for natural killer/T-cell lymphoma: analysis of safety and efficacy from the Asia Lymphoma Study Group. Blood 2012;120(15):2973-80.
- 4. Yamaguchi M, et al. Phase I study of dexamethasone, methotrexate, ifosfamide, L-asparaginase, and etoposide (SMILE) chemotherapy for advanced-stage, relapsed or refractory extranodal natural killer (NK)/T-cell lymphoma and leukemia. Cancer Sci 2008; 99:1016–20.
- 5. Jaccard A, et al. Efficacy of L-asparaginase with methotrexate and dexamethasone (AspaMetDex regimen) in patients with refractory or relapsing extranodal NK/T-cell lymphoma, a phase 2 study. Blood 2011;117(6):1834-9.

CANCER DRUG MANUAL

REVISED MONOGRAPHS AND PATIENT HANDOUTS

Imatinib Handout

- Other names: removed US brand name and synonym
- Administration: removed direction to take with a large glass of water because this instruction is unrelated to the mechanism of action or toxicity of the drug; therefore, it does not meet the criteria for inclusion

Lanreotide Monograph

- Uses: updated Health Canada approved indications
- Cautions: updated Pregnancy section
- Supply and Storage: updated supplier and product information
- Parenteral Administration table: added site of injection for cases where self-administration is necessary
- Dosing: updated BC Cancer standard regimens and protocols

Temozolomide Monograph

- Pharmacokinetics: updated routes of elimination
- Supply and Storage: removed injectable formulation as it is no longer available in Canada
- Dosing: revised dosing in concurrent radiation

Trastuzumab emtansine Monograph

Dosing: updated hepatic dosing

Vemurafenib Monograph

- *Side Effects:* added Dupuytren's contracture and plantar fascial fibromatosis to table and paragraphs
- Interactions: added rifampin interaction

Provincial Systemic Therapy Program

REVISED POLICY OF DRUG REACTION MANAGEMENT – PHYSICIAN COVERAGE (III-60)

The policy on Drug Reaction Management – Physician Coverage During Delivery of Selected Systemic Therapy Drugs has been revised, effective 1 March 2018. The key changes are to clarify the purpose and scope of the policy to include management of reactions to drugs when administered as parenteral injectables.

BENEFIT DRUG LIST

New Programs

Effective 1 March 2018, these treatment programs have been added to the BC Cancer <u>Benefit Drug List</u>:

Protocol Title	Protocol Code	Benefit Status
Palliative therapy for unresectable, platinum-refractory, recurrent or metastatic squamous cell cancer of the head and neck using nivolumab	UHNAVNIV	Restricted
Treatment of relapsed/refractory mantle-cell lymphoma using ibrutinib	ULYMIBRU	Restricted
Treatment of refractory or relapsing extranodal natural killer or T-cell lymphoma using asparaginase, methotrexate and dexamethasone	LYASPMEDEX	Class I
Treatment of lymphoma with dose-adjusted etoposide, doxorubicin, vincristine, cyclophosphamide, prednisone and rituximab with intrathecal methotrexate	LYEPOCHR	Class I
Treatment of natural killer or T-cell lymphoma using dexamethasone , methotrexate, ifosfamide, asparaginase and etoposide	LYSMILE	Class I
Treatment of newly diagnosed nasal, extranodal natural killer (NK) or T-cell lymphoma, stage IE to IIE using concurrent radiation and weekly cisplatin followed by etoposide, ifosfamide, cisplatin and dexamethasone	LYVIPDRT	Class I

REVISED PROGRAMS

Anastrozole has been added to GOOVAI effective 1 March 2018 on the BC Cancer Benefit Drug List.

COMMUNITIES ONCOLOGY NETWORK

REMINDER: OSCAR SUBMISSION DEADLINE - 5 APRIL 2018

The 2017-18 fiscal year will end on Saturday, 31 March 2018. To meet the deadlines for external reporting to the Ministry of Health, all claims for drug reimbursement for the fiscal year must be invoiced by 11:59 pm on Thursday, 5 April 2018 via OSCAR (Online System for Cancer drugs Adjudication and Reimbursement).

Any claims invoiced after this date will not be eligible for reimbursement. For more information, please contact <u>oscar@bccancer.bc.ca</u>.

LIST OF NEW AND 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	РРРО	Patient Handout	Protocol Title	
UHNAVNIV	V	V	V	Palliative therapy for unresectable, platinum-refractory, recurrent or metastatic squamous cell cancer of the head and neck using nivolumab	
ULYMIBRU	V	V		Treatment of relapsed/refractory mantle-cell lymphoma using ibrutinib	
LYASPMEDEX	V			Treatment of refractory or relapsing extranodal natural killer or T-cell lymphoma using asparaginase, methotrexate and dexamethasone	
LYEPOCHR	V		V	Treatment of lymphoma with dose-adjusted etoposide, doxorubicin, vincristine, cyclophosphamide, prednisone and rituximab with intrathecal methotrexate	
LYSMILE	\checkmark			Treatment of natural killer or T-cell lymphoma using dexamethasone, methotrexate, ifosfamide, asparaginase and etoposide	
LYVIPDRT	V	V		Treatment of newly diagnosed nasal, extranodal natural killer (NK) or T-cell lymphoma, stage IE to IIE using concurrent radiation and weekly cisplatin followed by etoposide, ifosfamide, cisplatin and dexamethasone	

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)					
CODE	Protocol	РРРО	Patient Handout	Changes	Protocol Title
UBRAJACTW	V	V		Pre-meds clarified	Adjuvant therapy for early breast cancer using doxorubicin and cyclophosphamide followed by weekly paclitaxel
UBRAJPAM	\checkmark			Eligibility updated	Adjuvant treatment of postmenopausal women using pamidronate
UBRAJTTW	V	\checkmark		Eligibility and premedications clarified	Adjuvant therapy for breast cancer using weekly paclitaxel and trastuzumab (HERCEPTIN)
BRAJZOL	\checkmark			Eligibility updated	Adjuvant treatment of post-menopausal women using zoledronic acid
BRAVTW	\checkmark	\checkmark		Institution name and tests updated	Palliative therapy for metastatic breast cancer using weekly paclitaxel (3 weeks out of 4 weeks schedule)
BRLATWAC	V	V		Institution name and tests updated	Neoadjuvant therapy for locally advanced breast cancer using weekly paclitaxel followed by doxorubicin and cyclophosphamide

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)					
CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
GIAJCAPOX	V	\checkmark		Institution name and tests updated	Adjuvant combination chemotherapy for Stage III and stage IIB colon cancer using oxaliplatin and capecitabine
GIAJFL	V	\checkmark		IV administration clarified, institution name and tests updated	Adjuvant therapy of colon cancer using fluorouracil injection and infusion and leucovorin infusion
GIAVCETIR	V	\checkmark		Institution name, Tests, magnesium infusion updated	Third line treatment of metastatic colorectal cancer using cetuximab in combination with irinotecan
GIAVFL	V	\checkmark		IV administration clarified, institution name and tests updated	Palliative combination chemotherapy for metastatic colorectal cancer using fluorouracil injection and infusion and leucovorin infusion
GIAVPANI	V	\checkmark		Institution name, Tests, magnesium infusion updated	Palliative third line treatment of metastatic colorectal cancer using panitumumab
GICAPOX	V	\checkmark		Institution name and tests updated	Palliative combination chemotherapy for metastatic colorectal cancer using oxaliplatin, and capecitabine
GIFFIRB	V	V		Institution name and tests updated	Palliative combination chemotherapy for metastatic colorectal cancer using irinotecan, fluorouracil, leucovorin, and bevacizumab
UGIFFOXPAN	V	\checkmark		Institution name and tests updated	Palliative combination chemotherapy for metastatic colorectal cancer using oxaliplatin, fluorouracil, leucovorin, and panitumumab
GIFIRINOX	V	\checkmark		Institution name and tests updated	Palliative combination chemotherapy for advanced pancreatic adenocarcinoma using irinotecan, oxaliplatin, fluorouracil and leucovorin
GIFOLFIRI	\checkmark	\checkmark		Institution name and tests updated	Palliative combination chemotherapy for metastatic colorectal cancer using irinotecan, fluorouracil and leucovorin
GIGFOLFIRI	V	\checkmark		Institution name and tests updated	Second line palliative combination chemotherapy for metastatic gastric or esophageal adenocarcinoma using irinotecan, fluorouracil and leucovorin
GIPGEMABR	V	\checkmark		Institution name and tests updated	First line treatment of locally advanced and metastatic pancreatic cancer with paclitaxel-nab (ABRAXANE) and gemcitabine
GIRAJCOX	V	\checkmark		Institution name and tests updated	Adjuvant combination chemotherapy for stage III rectal cancer using oxaliplatin and capecitabine
GOCXAJCAT	Ŋ			Institution name and tests updated	Primary adjuvant treatment of adenocarcinoma/adenosquamous cancer of the cervix with carboplatin and paclitaxel preceding or following irradiation with or without cisplatin
GOENDCAD	V	\checkmark		Institution name and tests updated	Primary advanced or recurrent endometrial cancer using carboplatin and docetaxel
GOENDCAT	V	\checkmark		Institution name and tests updated	Primary advanced or recurrent endometrial cancer using carboplatin and paclitaxel

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)					
CODE	Protocol	РРРО	Patient Handout	Changes	Protocol Title
GOOVAI	V	\checkmark		Eligibility updated	Therapy for advanced ovarian cancer using an aromatase inhibitor
GOOVCADM	V			Institution name and tests updated	Primary treatment of invasive epithelial ovarian, fallopian tube and primary peritoneal cancer, with no visible residual tumour (moderate-high risk) using carboplatin and docetaxel
GOOVCADR	V	V		Institution name and tests updated	Second line treatment using docetaxel and carboplatin for epithelial ovarian cancer relapsing after primary treatment
GOOVCADX		\checkmark		Institution name and tests updated	Primary treatment of visible residual (extreme risk) invasive epithelial ovarian cancer using carboplatin and docetaxel
GOOVCARB	\checkmark	\checkmark		Institution name and tests updated	First or second line therapy for invasive epithelial ovarian cancer using single- agent carboplatin
GOOVCATM	Ø	V		Institution name and tests updated	Primary treatment of no visible residual (moderate-high risk) invasive epithelial ovarian, fallopian tube and primary peritoneal cancer using carboplatin and paclitaxel
GOOVCATR	V			Institution name and tests updated	Second line treatment of invasive epithelial ovarian, fallopian tube or peritoneal cancer relapsing after primary treatment using paclitaxel and carboplatin
GOOVCATX	V	\checkmark		Institution name and tests updated	Primary treatment of visible residual (extreme risk) invasive epithelial ovarian, fallopian tube or peritoneal cancer using carboplatin and paclitaxel
GOOVDDCAT	V			Test, booking and labs clarified, institution name updated	Primary treatment of advanced epithelial ovarian, primary peritoneal, or fallopian tube carcinoma using carboplatin and weekly paclitaxel
GOOVPLDC	V			Institution name and tests updated	Treatment of epithelial ovarian cancer relapsing after primary treatment using doxorubicin pegylated liposomal (CAELYX) and carboplatin
GUBEP	\checkmark	\checkmark		Treatment schedule clarified	Curative therapy for germ cell cancer using with bleomycin, etoposide, cisplatin for germ cell cancers
HNLAPRT		\checkmark		Test clarified	Combined chemotherapy cisplatin and radiation treatment for locally advanced squamous cell carcinoma of the head and neck
LYRMTN	V			Rituximab administration clarified	Maintenance rituximab for indolent lymphoma
OCIFN	V			Contact information updated	Topical therapy for ocular malignancies using interferon-alfa-2b eye drops
осміто	V			Contact information updated	Topical therapy for ocular malignancies using mitomycin eye drops

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)					
CODE	Protocol	РРРО	Patient Handout	Changes	Protocol Title
SCESA	\checkmark			Precautions updated	Guidelines for the use of erythropoiesis- stimulating agents in patients with cancer
USMAVDT			V	Storage information updated	Treatment of BRAF V600 mutation- positive unresectable or metastatic melanoma using dabrafenib and trametinib
USMAVTRA			V	Storage information updated	Treatment of BRAF V600 mutation- positive unresectable or metastatic melanoma using trametinib
SMMCCPE		V		Administration tubing clarified	Treatment of recurrent or metastatic Merkel cell carcinoma with cisplatin and etoposide

CONTACT INFORMATION	PHONE	FAX	EMAIL
Systemic Therapy Update Editor	604-877-6000 x 672247		bulletin@bccancer.bc.ca
Provincial Systemic Therapy Program	604-877-6000 x 672247		mlin@bccancer.bc.ca
To update contact information of any CON sites, p	lease contact:		bulletin@bccancer.bc.ca
Oncology Drug Information	604-877-6275		druginfo@bccancer.bc.ca
Education Resource Nurse	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
Nursing Professional Practice			ella.may1@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 Centre	604-851-4710 Toll Free 877-547-3777		
BC Cancer-Centre for the North	250-645-7300 Toll Free 888-775-7300		
BC Cancer-Fraser Valley Centre	604-930-2098 Toll Free 800-523-2885		
BC Cancer-Sindi Ahluwalia Hawkins Centre for the Southern Interior	250-712-3900 Toll Free 888-563-7773		
BC Cancer-Vancouver Centre	604-877-6000 Toll Free 800-663-3333		
BC Cancer-Vancouver Island Centre	250-519-5500 Toll Free 800-670-3322		

EDITORIAL REVIEW BOARD

Mario de Lemos, PharmD, MSc (Oncol) (Acting Editor) James Conklin, BSc(Pharm), ACPR Mark Goodwin, MLIS Jagbir Kaur, RN, MN Caroline Lohrisch, MD Judi Piper-Wallace, BSN Alison Pow, BSc(Pharm)