Systemic Therapy Update

BC Cancer Agency
CARE + RESEARCH
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For Health Professionals Who Care For Cancer Patients

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EDITOR'S CHOICE

NEW PROGRAMS

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

Gastrointestinal:

Panitumumab in Combination with Chemotherapy for Metastatic Colorectal Cancer (UGIFFOXPAN) – The BCCA Gastrointestinal Tumour Group is launching this new first-line treatment option for patients with RAS wild-type metastatic colorectal cancer who are not suitable for bevacizumab therapy. In a phase III trial, panitumumab in combination with fluorouracil/leucovorin and oxaliplatin (FOLFOX) was associated with improved overall survival (25.8 vs. 20.2 mos) and progression free survival (10.1 vs. 7.9 mos).[1] In a phase II trial, panitumumab with FOLFOX was comparable with bevacizumab with FOLFOX in overall survival (41.3 vs. 28.9 mos, p=0.058).[2] Please note that for patients treated using panitumumab with FOLFOX, BCCA will not fund second-line bevacizumab therapy or third-line panitumumab therapy.

References:

1. Douillard JY, et al. Randomized, phase III trial of panitumumab with infusional fluorouracil, leucovorin, and oxaliplatin (FOLFOX4) versus FOLFOX4 alone as first-line treatment in patients with previously untreated metastatic colorectal cancer: the PRIME study. J Clin Oncol 2010;28(31):4697-705.
2. Schwartzberg LS, et al. PEAK: a randomized, multicenter phase II study of panitumumab plus modified fluorouracil, leucovorin, and oxaliplatin (mFOLFOX6) or bevacizumab plus mFOLFOX6 in patients with previously untreated, unresectable, wild-type KRAS exon 2 metastatic colorectal cancer. J Clin Oncol 2014;32(21):2240-7.

EDITOR'S CHOICE

Oxaliplatin, Fluorouracil and Leucovorin (FOLFOX) with Radiation Therapy for Locally Advanced Esophageal Cancer (GIEFFOXRT) – The BCCA Gastrointestinal Tumour Group is introducing this regimen as a better tolerated treatment than the current standard of cisplatin and fluorouracil (GIEFUPRT). In a phase III trial, chemoradiotherapy with FOLFOX compared to with cisplatin and fluorouracil was associated with similar overall survival (20.2 vs. 17.5 mos) but less treatment-related deaths (1% vs. 5%).

Reference:
Conroy et al. Definitive chemoradiotherapy with FOLFOX versus fluorouracil and cisplatin in patients with oesophageal cancer (PRODIGE5/ACCORD17): final results of a randomised, phase 2/3 trial. Lancet Oncol 2014;15:305-14.

Blinatumomab for Relapsed or Refractory Acute Lymphoblastic Leukemia (ALL) (ULKBLINA) – The Leukemia/BMT Group is introducing blinatumomab as a treatment for adult patients with Philadelphia chromosome negative (Ph-), relapsed or refractory pre-B-cell ALL after at least two prior lines of therapy. In a phase III trial, blinatumomab compared to chemotherapy was associated with improved overall survival (7.7 vs. 4.0 mos, HR 0.71). Toxicities include infusion reactions, cytokine release syndrome, neurological side effects (e.g., encephalopathy). The treatment delivery of blinatumomab is complex, with continuous intravenous infusion given slowly titrated to reduce the risk of cytokine release syndrome. Patients are treated initially as inpatients and then later on as outpatients. Currently funding is restricted to treatments prescribed by the Leukemia/BMT physicians and delivered at the Vancouver General Hospital.

Reference:
Kantarjian H, et al. Blinatumomab versus Chemotherapy for advanced acute lymphoblastic leukemia. N Engl J Med 2017;376:836-47.

DRUG UPDATE

SUBCUTANEOUS RITUXIMAB INJECTION

Effective November 1, patients who have tolerated their first dose of rituximab as intravenous (IV) infusion can have their subsequent doses administered by subcutaneous (SC) injection for lymphoma treatment protocols using rituximab IV 375 mg/m^2 dosing (see complete list at the end of this newsletter).

Administration of subcutaneous rituximab

Rituximab IV infusion is part of the standard treatment of many non-Hodgkin lymphomas. However, its infusion-related reactions are common and close monitoring is needed during the infusion. Rituximab SC injection has been shown to be equally efficacious without the infusion-related reactions. Local SC injection site reactions are mostly mild to moderate (e.g., mild pain, swelling, erythema).

Compared to the IV infusion, SC injection of rituximab has several advantages, including:

1. Shorter administration time: SC injection is given over 5 minutes.
2. Fixed dose of 1400 mg: this reduces the potential for dosing errors and the preparation time.
3. Improved convenience: for patients, pharmacy preparation, and nursing administration and monitoring.

Rituximab SC injection can be used in patients who have tolerated their first dose given by IV infusion with no grade 3 or 4 infusion-related events. The volume of the 1400 mg dose is 11.7 mL, which is larger than most SC injections. To facilitate the absorption of this volume and reduce discomfort, rituximab SC injection is formulated with hyaluronidase which expands the injection space by degrading the interstitial hyaluronan fibres. This increased permeability of subcutaneous tissue may last for 24-48 hours. Therefore, subsequent

Drug Update

SC injections of other medications should be administered at a different site than the SC rituximab injection. More details regarding the administration of SC rituximab can be found in the revised treatment protocols.

Medication safety strategies in product selection

Rituximab IV and SC drug vials look and sound alike. Both are clear, colourless solution in ready-to-use glass vials stored in the refrigerator. They have the same generic drug name (rituximab) and similar brand names (Rituxan® vs. Rituxan® SC). Strategies to reduce the risk of potential mix-up include:

1. Physical separation: store the two products in distinct bins and never have both products in the same IV preparation hood at the same time
2. Product differentiation: distinguish the two products for order entry and on drug label, create visible alerts for product selection at storage site
3. Raise awareness: educate all staff involved in handling both products in medication management process

Benefit Drug List

New Programs

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

Protocol Title	Protocol Code	Benefit Status
Combined modality therapy for locally advanced esophageal cancer using **oxaliplatin**, **fluorouracil**, **leucovorin**, and radiation therapy	**GIEFFOXRT**	**Class I**
Palliative combination chemotherapy for metastatic colorectal cancer using **oxaliplatin**, **fluorouracil**, **leucovorin**, and **panitumumab**	**UGIFFOXPAN**	**Restricted**
Treatment of Philadelphia chromosome negative refractory or relapsed pre-B-cell acute lymphoblastic leukemia with **blinatumomab**	**ULKBLIN**	**Restricted**

Revised Programs

Subcutaneous rituximab injectable (RITUXAN® SC) has been added to the BCCA Benefit Drug List effective 1 November 2017. For the protocols involved, see the list under Revised Protocols, PPPOs and Patient Handouts.

Cancer Drug Manual

New Monographs and Patient Handouts

The following drug is currently not funded by BCCA. The monograph and handout are being made available for reference only:

The **Ceritinib Interim Monograph** and **Patient Handout** have been developed with expert review provided

CANCER DRUG MANUAL

by Dr. Christopher Lee (oncologist) and Alysha Bharmal (pharmacist) of the BCCA Lung Tumour Group. Ceritinib is a second-generation, orally active, highly selective inhibitor of anaplastic lymphoma kinase (ALK). Ceritinib is supplied as 150 mg capsules. Usual dose is 750 mg once daily on an empty stomach. Grapefruit and grapefruit juice should be avoided while on therapy. Transaminase increases and gastrointestinal toxicities (nausea, vomiting, diarrhea, and abdominal pain) are the most frequent adverse events that lead to dose reduction or interruption. Fatigue is a common patient concern. Serious toxicities such as bradycardia, QT interval prolongation, pneumonitis, and pancreatitis may also occur.

REVISED MONOGRAPHS AND PATIENT HANDOUTS

Ibritumomab Interim Monograph

- Updated: *Mechanism of Action, Special Precautions, Side Effect table* and *paragraphs, Supply and Storage, Solution Preparation and Compatibility, Parenteral Administration table, and Dosage Guidelines*

Rituximab Monograph and Handout

- Updated: *Special Precautions, Side Effect table* and *paragraphs, Supply and Storage, Solution Preparation and Compatibility, Parenteral Administration table, and Dosage Guidelines, Patient Information*

PROVINCIAL SYSTEMIC THERAPY PROGRAM

REVISED POLICIES

Physician Coverage for Medical Emergencies During Delivery of Selected Chemotherapy Drugs: (Policy III-60)

- Policy title revised
- Observation time for blinatumomab and subcutaneous rituximab added

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
CNELTZRT	☐	☐	☑	Treatment of elderly newly diagnosed gliomas with concurrent temozolomide and radiation therapy, followed by adjuvant temozolomide
GIEFFOXRT	☑	☑	☑	Combined modality therapy for locally advanced esophageal cancer using oxaliplatin, fluorouracil, leucovorin, and radiation therapy

NEW PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)				
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Protocol Title**
UGIFFOXPAN	☑	☑	☑	Palliative combination chemotherapy for metastatic colorectal cancer using oxaliplatin, fluorouracil, leucovorin, and panitumumab
ULKBLIN	☑	☐	☐	Treatment of Philadelphia chromosome negative refractory or relapsed pre-B-cell acute lymphoblastic leukemia with blinatumomab

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)					
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Changes**	**Protocol Title**
CNAJTZRT	☐	☐	☑	*Side effects clarified*	Treatment of newly diagnosed malignant gliomas with concurrent temozolomide and radiation therapy, followed by adjuvant temozolomide
GIPAJGCAP	☑	☐	☐	*Eligibility clarified)*	Adjuvant chemotherapy for resected pancreatic adenocarcinoma using capecitabine and gemcitabine
UGUPABI	☑	☐	☐	*Eligibility clarified*	Therapy for metastatic castration resistant prostate cancer using abiraterone and prednisone
GUVIP2	☑	☐	☐	*Premedications clarified*	Consolidation and salvage therapy for nonseminoma using etoposide, cisplatin, ifosfamide, mesna
SAAVTC	☑	☑	☐	*Hydration clarified*	Treatment of recurrent and refractory neuroblastoma, Ewing's Sarcoma, osteogenic sarcoma or rhabdomyosarcoma with topotecan and cyclophosphamide

RITUXIMAB PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)				
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Protocol Title**
ULYBENDR	☑	☑	☐	Treatment of non-Hodgkin lymphoma with bendamustine and rituximab
LYCHLRR	☑	☑	☐	Treatment of indolent B-cell lymphoma and chronic lymphocytic leukemia with chlorambucil and rituximab
LYCHOPR	☑	☑	☑	Treatment of lymphoma with doxorubicin, cyclophosphamide, vincristine, prednisone and rituximab
LYCHOPRMTX	☑	☑	☐	Central nervous system prophylaxis with high dose methotrexate, CHOP and rituximab in diffuse large B-cell lymphoma
LYCODOXMR	☑	☑	☐	Treatment of Burkitt lymphoma and leukemia with cyclophosphamide, vincristine, doxorubicin, methotrexate, leucovorin and rituximab
LYCVPR	☑	☑	☑	Treatment of advanced indolent lymphoma using cyclophosphamide, vincristine, prednisone and rituximab

RITUXIMAB PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)				
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Protocol Title**
LYFCR	☑	☑	☐	Treatment of chronic lymphocytic leukemia or prolymphocytic leukemia with fludarabine, cyclophosphamide and rituximab
LYFLUDR	☑	☑	☐	Treatment of chronic lymphocytic leukemia or prolymphocytic leukemia and relapsed indolent lymphoma with fludarabine and rituximab
LYGDPR	☑	☑	☑	Treatment of lymphoma with gemcitabine, dexamethasone and cisplatin with rituximab
LYHDMRP	☑	☑	☐	Treatment of primary intracerebral lymphoma with high dose methotrexate and rituximab
LYIVACR	☑	☑	☐	Treatment of Burkitt lymphoma and leukemia with ifosfamide, mesna, etoposide, cytarabine and rituximab
ULYRICE	☑	☑	☐	Treatment of relapsed or refractory advanced stage aggressive B-cell non-Hodgkin's lymphoma with ifosfamide, carboplatin, etoposide and rituximab
LYRITUX	☑	☑	☐	Treatment of lymphoma with single agent rituximab
LYRMTN	☑	☑	☐	Maintenance rituximab for indolent lymphoma

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, 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		
BCCA-Sindi Ahluwalia Hawkins Centre for the Southern Interior	250-712-3900 Toll Free 888-563-7773		
BCCA-Vancouver Centre	604-877-6000 Toll Free 800-663-3333		
BCCA-Vancouver Island Centre	250-519-5500 Toll Free 800-670-3322		

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