Systemic Therapy Update

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

Inside This Issue:

EDITOR'S CHOICE

NEW PROGRAMS

Breast:

Pertuzumab with Trastuzumab and Docetaxel for First-Line Treatment of Advanced HER2-Positive Breast Cancer (UBRAVPTRAD) – The Breast Tumour Group has approved dual anti-HER2 treatment with pertuzumab and trastuzumab in combination with docetaxel for the first-line treatment of metastatic HER2-positive breast cancer. This regimen is given every three weeks, with pertuzumab and trastuzumab continuing until disease progression or toxicity after docetaxel completion. A randomized phase III trial (CLEOPATRA) showed a significant improvement in median progression free survival with pertuzumab, trastuzumab and docetaxel compared to trastuzumab and docetaxel alone (18.5 vs. 12.4 months, HR 0.62, 95% CI 0.51-0.75). *[Baselga et al. NEJM 2012;366:109-119]* While survival data are not mature, a recent update demonstrated a median overall survival of 36.7 months in the trastuzumab-docetaxel arm, and as yet not reached for the pertuzumab-trastuzumab-docetaxel arm *[Swain et al. Lancel Oncol 2-13;14(6):461-471]*. Treatment was well tolerated overall and pertuzumab did not increase the risk of left ventricular systolic dysfunction. The pertuzumab arm had higher rates of diarrhea, rash, mucosal inflammation, dry skin and febrile neutropenia.

Please note that pertuzumab and trastuzumab are supplied from the manufacturer as PERJETA®-HERCEPTIN® Combo Pack, where the two medications are packaged in the same box (see figure 1). It is recommend that upon receiving the PERJETA®-HERCEPTIN® Combo Pack, immediately open the box and store pertuzumab and trastuzumab separately to prevent selection errors.

EDITOR'S CHOICE

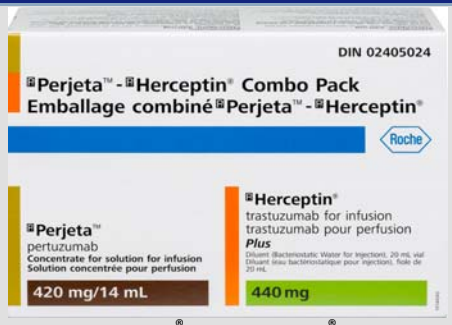

Figure 1. PERJETA® -HERCEPTIN® Combo Pack
(Photo courtesy of Hoffman-La Roche Limited)

Leukemia:

Ruxolitinib for Symptomatic Myelofibrosis (ULKMFRUX) – The Leukemia/BMT Group has introduced the use of ruxolitinib for the treatment of symptomatic myelofibrosis. Myelofibrosis is an uncommon myeloproliferative neoplasm. It can present as primary myelofibrosis or evolve from pre-existing essential thrombocythemia or polycythemia vera (post-essential thrombocythemia myelofibrosis or post-polycythemia vera myelofibrosis). Clinical features include splenomegaly, anemia, fatigue, weight loss, night sweats, pruritis and bone pain. About 30% of patients with myelofibrosis progress to acute myeloid leukemia. The current standard therapy for most patients is supportive care.

Ruxolitinib is an oral agent that belongs to a new class of tyrosine kinase inhibitors called Janus kinase (JAK) inhibitor. All patients with myelofibrosis have increased JAK activity and about half of patients carry the activating JAK2 V617F gene mutation. Two phase III trials involving a total of 528 patients compared ruxolitinib to placebo (COMFORT-I) *[Verstovsek et al. NEJM 2012;366:799-807]* and to best supportive care (COMFORT-II) *[Harrison et al. NEJM 2012;366:787-798]*. Ruxolitinib was associated with significant reduction in splenomegaly (COMFORT I – 41.8% vs. 0.7%; COMFORT II – 31.9% vs. 0%) and improved quality of life (COMFORT I). There was no difference in response rates between JAK2 V617F positive and negative patients. For information about the dosing and toxicity profile of ruxolitinib, please see the Cancer Drug Manual section below.

HIGHLIGHTS OF CHANGES IN PROTOCOLS, PRE-PRINTED ORDERS AND PATIENT HANDOUTS

Eligibility Criteria for Chronic Myeloid Leukemia Protocols Revised to Reflect Updated Guidelines:

The Leukemia/BMT Group has updated the treatment guidelines for Chronic Myeloid Leukemia (CML) in the chronic phase. While imatinib remains the front-line treatment, the milestones for cytogenetic and molecular responses have been modified in keeping with the new European LeukemiaNet (ELN) recommendations *[Baccarani et al. Blood 2013;122(6):872-884]*. As per the new guidelines, treatment failure with imatinib is defined as less than a 1-log reduction in BCR-ABL transcripts by 3 to 6 months of imatinib therapy, or less than a 2-log reduction by 12 months. In such cases, patients may be candidates for alternative treatments (i.e. second generation tyrosine kinase inhibitors, stem cell transplant, etc). Affected BCCA chemotherapy protocols include ULKCMLD and ULKCMLN.

DRUG UPDATE

UPDATE: SHORTAGE OF PEGYLATED LIPOSOMAL DOXORUBICIN (CAELYX®)

Pegylated liposomal doxorubicin (CAELYX®) is once again on drug shortage alert. It is unclear when the supply issue will resolve. No new patients should be initiated on pegylated liposomal doxorubicin at this time. Prescribers and pharmacies are collaborating to develop a process to allocate the existing stock for patients already on treatment.

The affected BCCA chemotherapy protocols include GOOVLDOX, GOOVPLDC and KSLDO. The Gynecology Tumour Group and physicians managing Kaposi's sarcoma patients have provided a number of recommended treatment alternatives which are listed in no particular order of preference in the table below.

Tumour Group	Affected Protocols	Recommended Alternatives
GYNE	GOOVLDOX	a) Treatment break if appropriate b) Delay treatment if appropriate c) If treatment initiation or continuation (depending on the prior treatment history and response to prior therapy) is indicated, consider substituting pegylated liposomal doxorubicin with: ▪ Single-agent gemcitabine (GOOVGEM), or ▪ Single-agent oral etoposide (GOOVETO), or ▪ Single-agent vinorelbine (GOOVVIN), or ▪ Single-agent paclitaxel (GOOVTAX3), or ▪ Single-agent topotecan (GOOVTOP), or ▪ Single-agent docetaxel (GOOVDOC), or ▪ Single-agent doxorubicin 40 mg/m^2 IV push (as per GOOVLDOX) – In cases where liposomal doxorubicin is felt to be the only viable treatment option, single-agent doxorubicin may be considered as a possible substitution although it has not been directly compared to liposomal doxorubicin in a clinical trial setting. It is important to note the unique adverse effect profile between the two drugs, particularly with liposomal doxorubicin having less alopecia and cardiotoxicity/contraindication in coronary artery disease.
	GOOVPLDC	a) Treatment break if appropriate b) Delay treatment if appropriate c) If treatment initiation or continuation is indicated, switch to: ▪ GOOVCATR or GOOVCADR or GOOVCAG, or ▪ Single-agent carboplatin (as per GOOVPLDC) until pegylated liposomal doxorubicin supply is re-established
Kaposi's Sarcoma	KSLDO	a) Substitute with liposomal daunorubicin 40 mg/m^2 IV. Repeat every 14 days.* b) Substitute with weekly doxorubicin (KSAD)

*Liposomal daunorubicin is obtained through the Health Canada Special Access Programme (SAP). Submission and approval through the BCCA Compassionate Access Program (CAP) is also required.

Drug Update

Trastuzumab: Look-Alike/Sound-Alike Medication Alert

Health Canada has issued an alert regarding the potential risk for mix-up between trastuzumab (HERCEPTIN®) and trastuzumab emtansine (KADCYLA®) (also known as T-DM1). Medication errors due to name confusion have occurred during the clinical trial phase in the US. Health Canada recommends using both generic and brand names when prescribing trastuzumab emtansine (KADCYLA®). Effective 01 December 2013, all BCCA medication related databases will include the generic and brand names for both trastuzumab (HERCEPTIN®) and trastuzumab emtansine (KADCYLA®) to clearly distinguish the two drugs. Trastuzumab-containing chemotherapy protocols and pre-printed orders will also be updated to include the brand name (HERCEPTIN®) on a gradual basis over the next few months. Please note that trastuzumab emtansine (KADCYLA®) is currently not a BCCA benefit drug.

Continuing Professional Development

XIV International Symposium on Oncology Pharmacy Practice (ISOPP 2014)

Date: April 2-5, 2014
Location: Montreal, Quebec
Early Bird Registration Deadline: January 20, 2014
Website: www.isoppxiv.org

This international symposium is hosted every two years by the International Society of Oncology Pharmacy Practitioners (ISOPP). In 2014, it will be held in beautiful Montreal in conjunction with the National Oncology Pharmacy Symposium (NOPS). The theme for this symposium is "Building Partnerships in Care". Registration will soon be open. Please visit the conference website for details about the program and speakers.

Cancer Drug Manual

New Monographs and Patient Handouts

Romidepsin Interim Monograph, Chemotherapy Preparation and **Stability Chart (CPSC)** have been developed. Romidepsin is a selective histone deacetylase inhibitor and causes tumour growth inhibition, cell cycle arrest and apoptosis. It has been used in peripheral and cutaneous T-cell lymphoma at a dose of 14 mg/m^2 IV, given on days 1, 8 and 15 of a 4-week cycle. Romidepsin is not a benefit drug of the BCCA.

Ruxolitinib Monograph and **Patient Handout** have been developed with expert review provided by Dr. Lynda Foltz (Hematologist, St. Paul's Hospital). Ruxolitinib is an oral kinase inhibitor used in the treatment of primary and secondary myelofibrosis. It is given at a starting dose of 5 mg to 25 mg orally twice daily depending on platelet count, with subsequent doses adjusted according to response and toxicities. Treatment interruptions are associated with rapid return of symptoms of myelofibrosis, including splenomegaly and systemic symptoms. Therefore, dosing should be tapered according to protocol recommendations if therapy needs to be stopped for toxicity or disease progression. Ruxolitinib is otherwise generally well tolerated. Common side effects include myelosuppression, fever, headache and hypercholesterolemia.

CANCER DRUG MANUAL

REVISED MONOGRAPHS AND PATIENT HANDOUTS

Tamoxifen Monograph:

- *List of Antidepressants and Tamoxifen Interactions* – Sertraline has been changed from a weak to a moderate inhibitor of CYP2D6 based on a review of new evidence. Therefore, like other moderate CYP2D6 inhibitors, the safest course of action is to avoid co-administration with tamoxifen. However, this should be balanced against each patient's particular needs and circumstances. Users are reminded that this list is not all-inclusive and is not intended as the sole source of information in the evaluation of tamoxifen-antidepressant interactions.

BENEFIT DRUG LIST

NEW PROGRAMS

The following programs have been added to the Benefit Drug List effective 01 November 2013:

Protocol Title	Protocol Code	Benefit Status
Palliative Therapy for Metastatic Breast Cancer Using Pertuzumab, Trastuzumab (HERCEPTIN®), and DOCEtaxel as First-Line Treatment for Advanced Breast Cancer	UBRAVPTRAD	Restricted
Treatment of Symptomatic Myelofibrosis with Ruxolitinib	ULKMFRUX	Restricted

DELETED PROGRAMS

The following program has been removed from the Benefit Drug List effective 01 November 2013:

Protocol Title	Protocol Code
Palliative Therapy for Metastatic Colorectal Adenocarcinoma Using Fluorouracil Infusional Chemotherapy	GIFUINF

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 treatments requiring "Compassionate Access Program" (previously Undesignated Indications Request) approval are prefixed with the letter "**U**".

NEW PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED):

CODE	Protocol	PPPO	Patient Handout	Protocol Title

NEW PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED):				
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Protocol Title**
UBRAVPTRAD	☑	☑	☐	Palliative Therapy for Metastatic Breast Cancer using Pertuzumab, Trastuzumab (HERCEPTIN®), and DOCEtaxel as First-Line Treatment for Advanced Breast Cancer
ULKMFRUX	☑	☑	☐	Treatment of Symptomatic Myelofibrosis with Ruxolitinib

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED):					
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Changes**	**Protocol Title**
GIAJFL	☑	☐	☐	*Hematologic dose modifications clarified*	Adjuvant Therapy of Colon Cancer Using Fluorouracil Injection and Infusion and Folinic Acid (Leucovorin) Infusion
GIAVFL	☑	☐	☐	*Hematologic dose modifications clarified*	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Fluorouracil Injection and Infusion and Leucovorin Infusion
GICART	☐	☐	☑	*Mitomycin dosing schedule clarified*	Curative Therapy for Cancer of the Anal Canal Using Combined Mitomycin, Capecitabine and Radiation Therapy
UGIGAVCCT	☑	☐	☐	*Eligibility clarified*	Palliative Treatment of Metastatic or Inoperable, Locally Advanced Gastric or Gastroesophageal Junction Adenocarcinoma Using CISplatin, Capecitabine and Trastuzumab
GUAVPG	☑	☐	☐	*Eligibility clarified*	Palliative Therapy for Urothelial Carcinoma Using CISplatin and Gemcitabine
ULKCMLD	☑	☐	☐	*Eligibility and Tests updated*	Treatment of Chronic Myeloid Leukemia and Ph+ Acute Lymphoblastic Leukemia Using Dasatinib
LKCMLI	☑	☐	☐	*Dosing updated*	Treatment of Chronic Myeloid Leukemia and Ph+ Acute Lymphoblastic Leukemia Using Imatinib
ULKCMLN	☑	☐	☐	*Eligibility, Tests and Precautions updated*	Treatment of Chronic Myeloid Leukemia Using Nilotinib
ULYBENDR	☑	☐	☐	*Reference added*	Treatment of Non-Hodgkin Lymphoma with Bendamustine and riTUXimab
PUCAT	☑	☐	☐	*Treatment cycle updated*	Primary Treatment of Cancer of Unknown Primary Origin Using CARBOplatin and PACLitaxel

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED):					
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Changes**	**Protocol Title**
SAVAC	☑	☐	☐	*Treatment section clarified, TALLman lettering*	Adjuvant Therapy for Newly Diagnosed Ewing's Sarcoma/Peripheral Neuroectodermal Tumour (PNET) or Rhabdomyosarcoma Using vinCRIStine, DOXOrubicin and Cyclophosphamide

DELETED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED):				
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Protocol Title**
GIFUINF	☑	☑	☑	Palliative Therapy for Metastatic Colorectal Adenocarcinoma Using Fluorouracil Infusional Chemotherapy

Website Resources and Contact Information

Website Resources	www.bccancer.bc.ca
Systemic Therapy Update	www.bccancer.bc.ca/HPI/ChemotherapyProtocols/stupdate
Reimbursement & Forms: Benefit Drug List, Class II, Compassionate Access Program	www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Forms
Cancer Drug Manual	www.bccancer.bc.ca/cdm
Cancer Management Guidelines	www.bccancer.bc.ca/CaMgmtGuidelines
Cancer Chemotherapy Protocols, Pre-printed Orders, Protocol Patient Handouts	www.bccancer.bc.ca/ChemoProtocols
Systemic Therapy Program Policies	www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Policies
CON Pharmacy Educators	http://www.bccancer.bc.ca/HPI/Pharmacy/ContactUs.htm

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Library/Cancer Information	604.675.8003 Toll Free 888.675.8001 x 8003		requests@bccancer.bc.ca
Pharmacy Professional Practice	250. 519.5574		jkippen@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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