Systemic Therapy Update

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Inside This Issue:

EDITOR'S CHOICE

2011-2012 NEW DRUG PROGRAMS

The **Provincial Systemic Therapy Program** has approved funding for three new treatment programs based on reviews and recommendations by the Priorities and Evaluation Committee.

Breast:

- **Trastuzumab with Capecitabine as Second-Line Treatment of HER-2 Positive Metastatic Breast Cancer after Prior Treatment with Trastuzumab (UBRAVTCAP) –** In the German Breast Group 26/Breast International Group 03-05 Study, combination therapy with trastuzumab and capecitabine significantly prolonged TTP (8.2 mo) compared to capecitabine alone (5.6 mo). The overall toxicity profile was similar in both treatment groups. (von Minckwitz *et al. JCO* 2009;27:1999-2006) Eligible patients may receive second-line treatment with either trastuzumab/capecitabine combination therapy

OR

- **Lapatinib with Capecitabine as Second-Line Treatment of HER-2 Positive Metastatic Breast Cancer after Prior Treatment with Trastuzumab (UBRAVLCAP)** – A phase III trial showed a 4-month improvement in time-to-progression (TTP) with lapatinib/capecitabine combination therapy compared to capecitabine alone (8.4 mo vs. 4.4 mo, respectively). No overall survival benefit was observed, but this is likely confounded by the high rate of cross-over. There was no significant increase in serious toxic events or symptomatic cardiac toxicity. (Geyer *et al. NEJM* 2006;355:2733-2743). Note that patients who are currently on the TYKERB® Patient Assistance Program (closed on June 3, 2010) will need to apply to the BCCA Compassionate Access Program (CAP) for approval to have lapatinib covered by BCCA.

Lung:

- **Erlotinib as Maintenance Therapy in Advanced Non-Small Cell Lung Cancer (NSCLC) for Patients with Stable Disease after First-Line Chemotherapy (ULUAVMTNE)** – In a phase III trial involving 899 patients, erlotinib was associated with a significant overall survival (OS) benefit of 1 month (12 mo vs. 11 mo [$p<0.05$]). The OS benefit was more pronounced in a pre-planned subgroup analysis of 487 patients with stable disease (i.e. failure to achieve a complete or partial response) after chemotherapy (11.9 mo vs. 9.6 mo [HR 0.72, 95% CI 0.59-0.89]). (Cappuzzo *et al. Lancet Oncol* 2010;11:521-529) Patients are eligible for treatment if they have stable disease (defined as best response after 4 cycles of first-line platinum-based doublet therapy), and must commence maintenance therapy 21 to 42 days after the fourth cycle of the first-line doublet chemotherapy.

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

Funding of Gefitinib in First-Line Treatment of EGFR Mutation-Positive Advanced NSCLC:

The **Provincial Systemic Therapy Program** is funding first-line **Gefitinib** therapy for epidermal growth factor receptor (EGFR) mutation-positive advanced non-small cell lung cancer (NSCLC) effective 01 June 2011.

- Patients who had previously accessed gefitinib through Astra Zeneca's IRESSA® Alliance Program on or before 15 March 2011 will continue to receive gefitinib through the program.
- Patients who had registered with the IRESSA® Alliance Program between 16 March 2011 and 31 May 2011 will now be eligible for gefitinib to be funded by the BCCA through the Compassionate Access Program (CAP).
- Effective 01 June 2011, patients with newly diagnosed NSCLC may also receive EGFR testing through funding by the BCCA.
- Physicians should obtain a current requisition that is available on the BCCA website at: http://www.bccancer.bc.ca/HPI/CancerManagementGuidelines/PathologyRequestForms.htm and select EGFR request form

  This process is similar to the previous, but the link will now lead directly to the Cancer Genetics Laboratory EGFR requisition rather than the AstraZeneca EGFR Canada website.

Instructions for completing the requisition are available with the requisition, which should be faxed to the host laboratory housing the tissue block(s) required for testing.

- Patients who test positive for EGFR mutation will receive gefitinib as a benefit of the BCCA via the CAP approval process. For more details, see ULUAVGEFF: http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Lung/default.htm.

Bortezomib – Subcutaneous Administration for Treatment of Multiple Myeloma:

The **Bortezomib-Containing Multiple Myeloma Protocols (UMYBORPRE, UMYBORREL, UMYMBOR)** have been modified to include the option to administer bortezomib by subcutaneous (SC) injection. Since bortezomib is a hazardous drug, SC administration should only be given by chemotherapy certified nurses at centres equipped to prepare and handle hazardous (cytotoxic) drugs. A Phase III trial demonstrated comparable efficacy, toxicity, and pharmacokinetic-pharmacodynamic properties between the IV and SC injections of bortezomib. Subcutaneous injections were administered to the thighs or abdomen, and injection sites were rotated within a treatment cycle. The SC administration route was associated with a lower incidence of peripheral neuropathy (38% vs. 53%). Injection site reactions occurred in 6% of patients in the SC group. (Moreau *et al. Lancet Oncol* 2011;12:431-440)

Currently, bortezomib IV is diluted to yield a 1 mg/mL solution. The BCCA has approved bortezomib SC to be prepared using the same dilution. The Phase III trial above used a more concentrated dilution to prepare the SC injections in order to allow for single-syringe dosing. Continuing with BCCA's current bortezomib dilution to a 1 mg/mL solution will result in some SC doses requiring two syringes. However, this may lead to a lower risk for significant dosing errors than if two different dilutions were used (i.e. one for bortezomib IV and one for bortezomib SC). The 1 mg/mL dilution was used in an initial Phase I trial; no pharmacokinetic differences were observed between the two dilutions. (Moreau *et al. Haematologica* 2008;93:1908-1911)

CANCER DRUG MANUAL

REVISED MONOGRAPHS

Bevacizumab Monograph and **Patient Handout** have been revised. Important monograph updates include: addition of dosing information for the treatment of glioblastoma, revision of information about administration before and after surgery, revised Side Effects table, additional side effect paragraphs, and revised Interactions table. The Supply and Storage section and Solution Preparation and Compatibility section have also been updated to reflect current template standards.

Cytarabine Monograph has been revised to update the Supply and Storage section with currently available brands. The Solution Preparation and Compatibility section has also been updated to reflect current template standards, and the hyperlink to BC Cancer Agency Policy III-50 has been restored.

Methotrexate Monograph has been revised. The Parenteral Administration table has been updated to include a statement on the lack of further information regarding direct IV administration rate.

Oxaliplatin Monograph has been revised to update the Supply and Storage section with the currently available brand. The Side Effects table and Solution Preparation and Compatibility section have also been revised to reflect current template standards.

Pemetrexed Monograph has been revised. The Supply and Storage section and the Solution Preparation and Compatibility section have been revised to reflect current template standards.

BENEFIT DRUG LIST

The following programs have been added on the benefit list effective 01 July 2011:

- **Erlotinib** (case-by-case) as maintenance therapy in advanced non-small cell lung cancer for patients with stable disease after first-line chemotherapy (ULUAVMTNE)
- **Lapatinib and Capecitabine** (case-by-case) as second-line treatment of HER-2 positive metastatic breast cancer after prior treatment with trastuzumab (UBRAVLCAP)
- **Trastuzumab and Capecitabine** (case-by-case) as second-line treatment of HER-2 positive metastatic breast cancer after prior treatment with trastuzumab (UBRAVTCAP)
- **Pegylated Liposomal DOXOrubicin** (class I) **and CARBOplatin** (class II) for epithelial ovarian cancer relapsing after primary treatment (GOOVPLDC)

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
UBRAVLCAP	☑	☑	☐	Lapatinib with Capecitabine as Second-Line Treatment of HER-2 Positive Metastatic Breast Cancer After Prior Treatment with Trastuzumab
UBRAVTCAP	☑	☑	☐	Trastuzumb with Capecitabine as Second-Line Treatment of HER-2 Positive Metastatic Breast Cancer After Prior Treatment with Trastuzumab

GOENDCAT	☐	☐	☑	Treatment of Primary Advanced or Recurrent Endometrial Cancer using CARBOplatin and PACLitaxel
GOOVCATM	☐	☐	☑	Primary Treatment of Invasive Epithelial Ovarian, Fallopian Tube and Primary Peritoneal Cancer, with No Visible Residual Tumour (Moderate-High Risk) Using CARBOplatin and PACLitaxel
GOOVCATR	☐	☐	☑	Second Line Treatment Using PACLitaxel and CARBOplatin for Epithelial Ovarian Cancer Relapsing After Primary Treatment
GOOVCATX	☐	☐	☑	Primary Treatment of Visible Residual (Extreme Risk) Invasive Epithelial Ovarian Cancer in Ambulatory Care Settings Using PACLitaxel and CARBOplatin
LUAVERL	☐	☐	☑	Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC) with Erlotinib
ULUAVMTNE	☑	☑	☑	Maintenance Therapy of Advanced Non-Small Cell Lung Cancer (NSCLC) with Erlotinib After First-Line Chemotherapy
LUSCPOE	☐	☐	☑	Palliative Therapy of Extensive Stage Small Cell Lung Cancer (SCLC) with Oral Etoposide
ULUOTPAC	☐	☐	☑	Treatment of Thymoma with Platinum, Doxorubicin and Cyclophosphamide
SMCCNU	☐	☐	☑	Palliative Therapy for Metastatic Melanoma Using Lomustine (CCNU)

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

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
CNCCNU	☑	☐	☐	*Eligibility revised*	Lomustine (CCNU) for Treatment of Recurrent Malignant Brain Tumours
GOOVCIS	☑	☐	☐	*Revised Tests Section*	Therapy for Invasive Epithelial Ovarian Cancer using CISplatin
GOOVPLDC	☑	☑	☑	*Eligibility revised*	Second Line Treatment Using Pegylated Liposomal DOXOrubicin (PLD) and CARBOplatin for Epithelial Ovarian Cancer Relapsing after Primary Treatment
HNLAPRT	☑	☐	☐	*Revised Eligibility and Exclusion Criteria*	Combined Chemotherapy CISplatin and Radiation Treatment for Locally Advanced Squamous Cell Carcinoma of the Head and Neck

LYCODOXMR	☑	☑	☐	*Added Laboratory and Premedication Sections; clarified riTUXimab dose to be calculated based on actual BSA; Updated Chemotherapy Section with chart for calculating correct BSA for cyclophosphamide, DOXOrubicin, methotrexate and vinCRIStine; clarified administration of riTUXimab*	Treatment of Burkitt's Lymphoma and Leukemia (ALL-L3) with Cyclophosphamide, VinCRIStine, DOXOrubicin, Methotrexate, Leucovorin (CODOX-M) and RiTUXimab
LYIVACR	☑	☑	☐	*Added Laboratory and Premedication Sections; clarified riTUXimab dose to be calculated based on actual BSA; Updated Chemotherapy Section with chart for calculating correct BSA for cyclophosphamide, DOXOrubicin, methotrexate and vinCRIStine; clarified administration of riTUXimab*	Treatment of Burkitt's Lymphoma and Leukemia (ALL-L3) with Ifosfamide, Mesna, Etoposide, Cytarabine (IVAC) and RiTUXimab
UMYMPBOR	☑	☑	☐	*Added subcutaneous route of administration; added peripheral neuropathy to Precautions; added valacyclovir prophylaxis under Treatment*	Treatment of Multiple Myeloma using Melphalan, Prednisone and Weekly Bortezomib With the Option of Substituting Cyclophosphamide for Melphalan
UMYBORPRE	☑	☑	☐	*Added subcutaneous route of administration; added valacyclovir prophylaxis under Treatment*	Treatment of High Risk Multiple Myeloma Using Bortezomib, Dexamethasone With or Without Cyclophosphamide as Induction Pre-Stem Cell Transplant
UMYBORREL	☑	☑	☐	*Added subcutaneous route of administration; Added valacyclovir prophylaxis under Treatment*	Treatment of Relapsed Multiple Myeloma using Bortezomib, Dexamethasone With or Without Cyclophosphamide
UMYTHALID	☑	☑	☐	*Revised thalidomide access; included thyroid testing and clarified Tests section*	Therapy of Multiple Myeloma Using Thalidomide
SMAJIFN	☑	☑	☑	*Clarified blood tests, added multi-dose pen stability; SC dose added to PPPO*	Adjuvant Therapy of High Risk Malignant Melanoma with High Dose Interferon (HDIFN) Alfa-2b
SMCCNU	☑	☑	☐	*Lab tests and dose modifications clarified*	Palliative Therapy for Metastatic Melanoma Using Lomustine (CCNU)

Website Resources and Contact Information

Website Resources	www.bccancer.bc.ca
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
Systemic Therapy Update	www.bccancer.bc.ca/HPI/ChemotherapyProtocols/stupdate
CON Pharmacy Educators	www.bccancer.bc.ca/RS/CommunitiesOncologyNetwork/Educators/Pharmacists

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Nursing Professional Practice	604.877.6000 x 2623		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
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BCCA-Centre for the Southern Interior	250.712.3900 Toll Free 888.563.7773		
BCCA-Fraser Valley Centre	604.930.2098 Toll Free 800.523.2885		
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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