Systemic Therapy Update

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EDITOR'S CHOICE

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

The **Neuro-Oncology Tumour Group** has introduced **Bevacizumab** therapy (UCNBEV) for patients with relapsed malignant gliomas after prior treatment with adjuvant temozolomide in standard dose schedule (CNAJTZRT) *and* metronomic dosing (UCNTEMOZMD). In patients with relapse after temozolomide and radiation, Bevacizumab was associated with an objective response rate (ORR) of 28.2% and 6- month progression free survival (PFS) rate of 42.6%. These results showed significant improvement compared to the historical ORR of less than 10% and the 6-month PFS of less than 20%.

The **Lymphoma/Myeloma Group** has reduced the **Pamidronate dose** from 90 mg to 30 mg monthly when used for the prevention of *skeletal-related events* (MYPAM protocol). In a double-blind, randomized controlled study involving 504 patients with multiple myeloma and bony involvement, both doses were shown to be equally effective in delaying the time to first skeletal event, as well as improving physical function, pain and fatigue (*Gimsing et al. Lancet Oncol 2010*). **Note:** the dose remains at 90 mg for the acute treatment of *hypercalcemia* (see SCHYPCAL protocol for more details).

The **Gastrointestinal (GI) Tumour Group** has revised the eligibility criteria for using **long-acting Octreotide** (SANDOSTATIN LAR®) in the symptomatic management of neuroendocrine tumours (NETs) of the GI tract (UGIOCTLAR). Until now, only monthly doses higher than 30 mg required approval via the BCCA Compassionate Access Program (CAP). Starting in 1 May, CAP approval is required for all doses of long-acting octreotide (***new and refill*** prescriptions).

The currently funded indication of this protocol is for patients with metastatic or unresectable NETs of fore, mid and hind gut origin who have functional (secretory) tumours and related symptoms. For patients who are being treated outside of a BCCA centre and whose progress notes are not available in CAIS (Cancer Agency Information System), CAP requests should be accompanied with notes documenting symptoms related to their NET. Recent data suggest that long-acting octreotide may also delay disease progression in patients with asymptomatic NETs (Rinke et al. *J Clin Oncol 2009*). This indication is currently under review by the Tumour Group.

CARBOplatin Dosing Based on Serum Creatinine has been revised to cap the estimated glomerular filtration rate (GFR) or creatinine clearance (CrCl) at 125 mL/min when it is being used to calculate CARBOplatin dose. This would affect the estimated GFR reported by clinical laboratories using the MDRD equation and CrCl calculated with predicted formulas like the Cockcroft-Gault equation. The capping does not apply when measured GFR is used (e.g., nuclear renogram).

The change is a result of the standardized Isotope Dilution Mass Spectrometry (IDMS) method introduced over the past few years to measure serum creatinine levels in clinical laboratories in BC. The IDMS method tends to underestimate serum creatinine levels when they are relatively low (e.g., ~60 micromol/L). This could therefore lead to an overestimation of GFR or CrCl in some patients with normal renal function and higher than desired CARBOplatin dose.

More information can be found at www.fda.gov/AboutFDA/CentersOffices/CDER/ucm228974.

Use of Pyridoxine for Capecitabine-Related Hand-Foot Syndrome has been removed from all protocols. This is based on the emerging evidence that pyridoxine is ineffective in improving or preventing hand-foot syndrome. Similar changes have already been made to the protocol-specific patient handouts and the Cancer Drug Manual. For more details on the background of this change, see the January issue of the Systemic Therapy Update (www.bccancer.bc.ca/HPI/ChemotherapyProtocols/stupdate).

BENEFIT DRUG LIST

The following program has been added on the benefit list effective 1 April 2011:

- **Bevacizumab** (case-by-case) as second-line therapy for patients with relapsed malignant gliomas (**UCNBEV**)

CANCER MANAGEMENT GUIDELINES

The Breast Tumour Group and Oncology Nutrition has recently updated the **Patient Guidelines for the Prevention of Osteoporosis in Women** on the BCCA website. Changes were based on the 2010 Canadian osteoporosis guidelines (Papaioannou *et al.* Can Med Assoc J 2010) and the revised Dietary Reference Intakes (DRIs) in 2010 (www.hc-sc.gc.ca/fn-an/nutrition/reference/index-eng.php). The recommended daily calcium intake is now 1200 mg for all women and the maximum daily calcium intake should not exceed 2000 mg. Previously, the recommended daily intake for calcium was 1500 mg for postmenopausal women and 1000 mg for premenopausal women, with a maximum daily intake of 2500 mg. The recommended daily vitamin D intake remains unchanged at 1000 units. However, the upper limit of daily intake has been increased from 2000 units to 4000 units.

Updated information is available in the following locations of the BCCA website:

Health Professionals:
- www.bccancer.bc.ca/HPI/CancerManagementGuidelines/Breast/Followup/PatientGuidelinesforthePreventionofOsteoporosis+in+Women

Patient & Public Information:
- www.bccancer.bc.ca/PPI/copingwithcancer/specificresources/Nutrition
- www.bccancer.bc.ca/PPI/copingwithcancer/specificresources/breastresources
- www.bccancer.bc.ca/PPI/TypesofCancer/Breast/Menopause

Please note that the calcium and vitamin D intake recommendations for men with prostate cancer will be undergoing a similar review. Revisions to the associated Patient Handout will be announced in Systemic Therapy Update once finalized.

DRUG UPDATE

The **Goserelin (ZOLADEX®) Community Care Program**, funded by AstraZeneca, is being phased out.
- **S**tarting 14 March, no new breast cancer patients will be enrolled.
- Patients already in the program may continue to have injections given by the Shoppers Drug Mart (SDM) nurse in their homes until early to mid May. Thereafter, they will have to continue their injections through their family doctor, a publicly funded nursing unit, or their cancer clinic.
- Oncologists will receive a list from the Community Care Program of their patients who are affected by this change, so they can ensure continuity of therapy

For more information, call SDM Specialty Health Network at 1-866-733-7511.

PharmaCare Coverage of Dalteparin for Venous Thromboembolism (VTE) Effective 17 March 2010, the PharmaCare Special Authority Program has expanded the coverage of dalteparin (FRAGMIN®), a low molecular weight heparin (LMWH), to include a new treatment indication – 6-month coverage for the treatment of VTE associated with cancer in patients who have either failed or are unable to tolerate warfarin therapy.

Note that Special Authority approval cannot be provided retroactively. For more details, see www.health.gov.bc.ca/pharmacare/sa/criteria/restricted/dalteparin.html.

LMWH is recommended by the ASCO Guidelines 2007 as the preferred agent for the treatment of established VTE in cancer patients. In two randomised controlled studies, the incidence of recurrent VTE was significantly lower in patients treated with LMWH (7-9%) compared to warfarin (16-17%) after 6 months of therapy.

CANCER DRUG MANUAL

Gemcitabine Monograph has been revised. Information about vascular changes has been added to the Side Effects table and a new paragraph has been added after the table. Fixed dose rate infusion (FDR) information has been added as a paragraph after the Side Effects table, and the Parenteral Administration and Dosing Sections have been updated to include this regimen as a BCCA approved method of administration (see SAAVGEMD Sarcoma protocol). The Supply and Storage and Solution Preparation and Compatibility sections have been revised to reflect current template standards.

Erlotinib Monograph and **Patient Handout** have been revised to include new information about the management of interactions with stomach pH lowering drugs (specifically ranitidine). Patients are now advised to take erlotinib either 2 hours before or 10 hours after a dose of ranitidine. Cautions regarding other stomach pH lowering drugs remain unchanged in the documents.

Letrozole Monograph and **Patient Handout** have been revised to delete the grapefruit interaction. The interaction was originally included based on the **Compendium of Pharmaceuticals and Specialties** (**CPS**) which listed letrozole as a substrate of cytochrome P450 3A4 (CYP 3A4) substrate and grapefruit juice as an inhibitor of CYP 3A4. The current CPS now has a separate section on grapefruit juice interactions which no longer include letrozole as a clinical concern.

Thalidomide Monograph has been revised to include the newly available 100 and 200 mg capsules in the Supply and Storage section.

The Cancer Drug Manual Team would like to welcome **Fran Topp** to the Editorial Board as a nurse representative. Fran is a staff nurse with the BCCA – Vancouver Centre Ambulatory Care Chemotherapy Unit.

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
UCNBEV	☑	☑	☑	Palliative Therapy for Recurrent Malignant Gliomas Using Bevacizumab
ULUAVPMTN	☐	☐	☑	Maintenance therapy of advanced non-small cell lung cancer (NSCLC) with pemetrexed

CODE	Protocol	PPPO	Patient Handout	Protocol Title
ULUAVPP	☐	☐	☑	Treatment of advanced non-small cell lung cancer with CISplatin and pemetrexed
ULUAVPP *(CARBOplatin Option)*	☐	☐	☑	Treatment of advanced non-small cell lung cancer with CARBOplatin and pemetrexed

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

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
LUMMPP	☐	☐	☑	*Interim bloodwork added*	Treatment of malignant mesothelioma with CISplatin and pemetrexed
LUMMPP *(CARBOplatin Option)*	☐	☐	☑	*Interim bloodwork added*	Treatment of malignant mesothelioma with CARBOplatin and pemetrexed
MYPAM	☑	☑	☐	*Dose reduced*	Treatment of multiple myeloma with pamidronate

REVISED PROTOCOLS RELATED TO CARBOPLATIN DOSING AND ESTIMATED GLOMERULAR FILTRATION RATE

CODE	Protocol Title
UBRAJDCT	Adjuvant therapy for breast cancer using DOCEtaxel, CARBOplatin and trastuzumab
BRAVTPC	Palliative therapy for metastatic breast cancer using trastuzumab, PACLItaxel and CARBOplatin as first-line treatment for advanced breast cancer
GOCXCAD	Treatment of advanced/recurrent non-small cell cancer of the cervix with CARBOplatin and DOCEtaxel in ambulatory care settings
GOCXCAT	Primary treatment of advanced/recurrent non-small cell cancer of the cervix with CARBOplatin and PACLItaxel in ambulatory care settings
GOENDCAD	Treatment of primarily advanced or recurrent endometrial cancer using CARBOplatin and DOCEtaxel
GOENDCAT	Treatment of primary advanced or recurrent endometrial cancer using CARBOplatin and PACLItaxel
GOOVCADM	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	Second line treatment using DOCEtaxel and CARBOplatin for epithelial ovarian cancer relapsing after primary treatment

CODE	Protocol Title
GOOVCADX	Primary treatment of visible residual (extreme risk) invasive epithelial ovarian cancer using CARBOplatin and DOCEtaxel
GOOVCAG	Treatment of advanced ovarian cancer in patients who have progressed or recurred following first-line platinum-based treatment using CARBOplatin and gemcitabine
GOOVCARB	First or second line therapy for invasive epithelial ovarian cancer using single-agent CARBOplatin
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
GOOVIPPC	Primary treatment of stage III less than or equal to 1 cm visible residual invasive epithelial ovarian cancer or stage I grade 3 or stage II Grade 3 papillary serious ovarian cancer using intravenous and intraperitoneal PACLItaxel and intraperitoneal CARBOplatin
GOSMCCRT	Treatment of small cell or neuroendocrine carcinoma of gynecologic system origin using PACLItaxel, CISplatin, etoposide and CARBOplatin with radiation
GUAVPG	Palliative therapy for urothelial carcinoma using CISplatin and gemcitabine
GUBCV	Therapy for transitional cell cancers using CARBOplatin-vinBLAStine
GUSCARB	Adjuvant therapy for stage I high risk seminoma using CARBOplatin
GUSCPERT	Therapy of genitourinary small cell tumours with a platin and etoposide with radiation.
UHNNAVPC	Treatment of recurrent or metastatic nasopharyngeal carcinoma with CARBOplatin and PACLItaxel
LUAJPC	Adjuvant CARBOplatin and PACLItaxel following resection of stage I, II And IIIA non-small cell lung cancer
LUAVPC	First-line treatment of advanced non-small cell lung cancer (NSCLC) with CARBOplatin and PACLItaxel
LULAPERT	Treatment of locally advanced non-small cell lung cancer using CISplatin and etoposide with radiation therapy
LUOTPE	Treatment of thymoma with CISplatin and etoposide
LUOTPERT	Treatment of thymoma using CISplatin and etoposide with radiation therapy
LUSCPE	Therapy of extensive stage small cell lung cancer (SCLC) with CISplatin and etoposide
LUSCPERT	Therapy of limited stage small cell lung cancer using CISplatin and etoposide with radiation
PUCAT	Primary treatment of cancer of unknown primary origin using CARBOplatin and PACLItaxel

REVISED PROTOCOLS RELATED TO DELETION OF PYRIDOXINE FOR CAPECITABINE-RELATED HAND-FOOT SYNDROME

CODE	Protocol Title
BRAVCAP	Therapy for metastatic breast cancer using capecitabine
BRAVDCAP	Palliative Therapy for metastatic breast cancer using DOCEtaxel and capecitabine
GIAJCAP	Adjuvant therapy of colon cancer using capecitabine
GIAVCAP	Palliative therapy of advanced colorectal cancer using capecitabine
UGIAVTZCAP	Palliative therapy of metastatic neuroendocrine cancer using temozolomide and capecitabine
GICART	Curative combined modality therapy for carcinoma of the anal canal using mitomycin, capecitabine and radiation therapy
GICPART	Curative combined modality therapy for carcinoma of the anal canal using CISplatin, capecitabine and radiation therapy
UGIGAVCCT	Palliative treatment of metastatic or inoperable, locally advanced gastric or gastroesophageal junction adenocarcinoma using CISplatin, capecitabine and trastuzumab
GIGAVECC	Palliative therapy for metastatic or locally advanced gastric or esophagogastric cancer using epirubicin, CISplatin and capecitabine
GIGECC	Perioperative treatment of resectable adenocarcinoma of the stomach, gastroesophageal junction or lower 1/3 esophagus using epirubicin, CISplatin and capecitabine
GIRCAP	Adjuvant therapy for stage II and III rectal cancer previously treated with preoperative radiation therapy using capecitabine
GIRCRT	Combined modality adjuvant therapy for high risk rectal carcinoma using capecitabine and radiation therapy
GIRINFRT	Combined modality adjuvant therapy for high risk rectal carcinoma using capecitabine, infusional fluorouracil and radiation therapy
UHNNAVCAP	Treatment of recurrent or metastatic nasopharyngeal cancer with capecitabine

WEBSITE RESOURCES AND CONTACT INFORMATION

WEBSITE RESOURCES	www.bccancer.bc.ca
REIMBURSEMENT AND FORMS: BENEFIT DRUG LIST, CLASS II, BC CANCER AGENCY 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

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